TOUR1A

Bimekizumab Efficacy and Safety in Biologic DMARD-Naïve Patients With Psoriatic Arthritis Was Consistent With or Without Methotrexate: 52-Week Results from The Phase 3 Active-Reference Study Be Optimal

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Objectives: To report bimekizumab (BKZ) efficacy and safety to Week 52 from the phase 3 study BE OPTIMAL in biologic disease-modifying anti-rheumatic drug (bDMARD)-naïve patients with psoriatic arthritis (PsA), with (+) or without (–) ongoing concomitant methotrexate (MTX).

Methods: BE OPTIMAL (NCT03895203) comprised a 16-week double-blind placebo (PBO)-controlled period and a 36-week active treatment-blind period. Patients were randomised 3:2:1 to subcutaneous BKZ 160 mg every 4 weeks (Q4W):PBO: reference arm (adalimumab [ADA] 40 mg Q2W). From Week 16, PBO patients received BKZ 160 mg Q4W. Patients could not adjust their background medication during the 16-week PBO-controlled period. Efficacy and safety were evaluated by concomitant MTX use at baseline. Missing data were imputed using non-responder (discrete) or multiple (continuous) imputation.

Results: 761/852 (89.3%) patients completed Week 52 (+ MTX: 454/497 [91.3%], – MTX: 307/355 [86.5%]). Baseline characteristics were generally similar + MTX vs – MTX: mean age 48.1 vs 49.4 years, BMI 29.1 vs 29.4 kg/m2, 5.7 vs 6.2 years since diagnosis, 47.3% vs 46.2% male, 49.5% vs 50.4% with psoriasis affecting ≥3% body surface area. To Week 52, the proportion of BKZ-randomised patients who achieved American College of Rheumatology (ACR)50, complete skin clearance (Psoriasis Area and Severity Index [PASI]100), and minimal disease activity (MDA) were similar regardless of baseline MTX use. Fewer patients receiving ADA – MTX achieved ACR50 or MDA at Week 52 compared to ADA + MTX. [Figure] Other Week 52 efficacy responses on BKZ were generally of a similar magnitude + MTX vs – MTX. To Week 52, patients with ≥1 treatment-emergent adverse event + MTX vs – MTX: PBO/BKZ, 124/158 (78.5%) vs 89/113 (78.8%); BKZ, 214/252 (84.9%) vs 150/179 (83.8%); ADA, 63/82 (76.8%) vs 50/58 (86.2%).

Conclusion: BKZ treatment demonstrated consistent sustained clinical efficacy across disease manifestations to Week 52 in bDMARD-naïve patients with PsA, irrespective of concomitant MTX. BKZ was well tolerated in patients with PsA with or without MTX.

TOUR1B

Multi-Omics Analyses Identify Metabolic Pathways that Differentiate Psoriatic Arthritis from Psoriasis

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Objectives: There is a lack of clinically useful diagnostic biomarkers or a full understanding of molecular mechanisms that can help distinguish Psoriatic Arthritis (PsA) from psoriasis without arthritis (PsC). Here, we aimed to conduct integrated multiomics analyses using data from previously identified panels of SNPs and proteins, RNA and miRNA sequencing, and serum metabolomics obtained from carefully phenotyped individuals with psoriatic disease to identify pathways that differentiate PsA from PsC.

Methods: Serum, RNA, and DNA from 102 PsA and 100 PsC patients were retrieved from a biobank of patients with psoriatic disease. Serum samples were used for miRNA sequencing, ELISA of 15 proteins, and liquid chromatography-high resolution mass spectrometry (LC-HRMS) for metabolites. DNA was used for genotyping 42 SNPs of 19 'PsA weighted' genes, and peripheral blood RNA was used for RNA sequencing. Resulting molecular data were analysed with clinical data to identify the best set of biomarkers able to discriminate between PsA and PsC. Random Forest machine learning algorithm was used to identify the best combination of diagnostic biomarkers. We then used mirDIP 4.1 data portal with a threshold of "very high" to identify biomarker mRNAs targeted by biomarker miRNA. pathDIP 4 data portal was used to perform pathway enrichment analysis for such mRNAs, while clusterProfiler 4.8.0 was used to perform Gene Ontology enrichment analysis. Analyses and visualization were performed in R 4.3.0.

Results: A total of 200 biomarkers, comprising 97 metabolites, 77 miRNAs, and 26 mRNAs were identified as the best performers to discriminate between PsA and PsC (AUROC of 0.979, p-value < 0.001). [Figure 1A] Among the 77 miRNAs, 9 targets 6 of the 26 mRNAs present among the 200 biomarkers. [Figure 1B] Pathway and Gene Ontology enrichment analyses performed using the 6 genes identified several terms linked to phospho- and glycerophospholipid metabolism. [Figure 1C-E] Interestingly, of the 97 metabolites, 40 were mapped to known metabolites. Of these, 12 (30%) were either glycero- or phospholipids. Further validation is

undergoing to confirm the diagnostic value of the 200 biomarkers and the role of the phospholipid pathways in differentiating PsC and PsA.
Conclusion: This study highlights that integrating multiple types of molecular data with AI algorithms, networks and pathways better characterizes differences between PsA and PsC. Our preliminary analysis shows that metabolic pathways may have a central role in differentiating PsA from PsC, a signal identified at the genetic level and confirmed through metabolomics analysis.

TOUR1C

Sex-Related Differences in Participation and Trial Outcomes in Axial Spondyloarthritis Randomized Clinical Trials: A Systematic Literature Review and Meta-Analysis

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Objectives: Sex-related differences in clinical manifestations and disease outcomes are prevalent in axial spondyloarthritis (axSpA); however, limited data exists on these differences in axSpA randomized controlled trials (RCTs). Using a systematic literature review and meta-analysis, we aimed to assess sex-related differences in participation, patient characteristics, treatment efficacy, and safety endpoints of advanced therapies in axSpA patients enrolled in RCTs.
Methods: We searched MEDLINE, EMBASE, and Central databases from January 2000 to June 2023. Studies were included if they assessed the efficacy of advanced therapies among axSpA adults in an RCT setting. Two reviewers extracted the rates of the following endpoints by sex at the primary endpoint of each trial: Assessment in Spondylarthritis International Society criteria (ASAS40/20) and the Ankylosing Spondylitis Disease Activity Score low disease activity/inactive disease (ASDAS-LDA/ID; ASDAS < 2.1). We used a random-effects model to calculate pooled effects for responses in males vs. females for the different classes of advanced therapies (Odds ratio (OR) and 95% Confidence interval (CI)).
Results: The literature search yielded 89 RCTs including 17,974 patients with a male-to-female ratio of approximately 2:1 (67.9% male). Only 12 trials (13.5%, 3,512 participants) reported sex-disaggregated baseline characteristics, 24 trials (26.9%, 6,159 participants) reported sex-disaggregated efficacy endpoints, and 2 trials (2.2%, 816 participants) reported sex-disaggregated safety endpoints. There were significant differences in the pooled estimates of efficacy endpoints between males and females. Overall, axSpA males on advanced therapies were more likely to achieve an ASAS40 response compared to females (OR 1.79, 95% CI 1.30 to 2.47). This was significant for both IL-17 inhibitors (IL-17i) and TNFi (IL-17i: OR 1.65, 95% CI 1.15 to 2.37; TNFi OR 2.41, 95% CI 1.19 to 4.88). [Figure 1a] Male patients were also more likely to achieve an ASDAS-ID or LDA response (OR 1.79, 95% CI 1.19 to 2.69). A similar effect size was found for achieving ASDAS-LDA/ID in males vs. females on IL-17i (OR 1.81 95% CI 1.06 to 3.07) and TNFi (OR 1.75, 95% 0.92 to 3.35). [Figure 1b]
Conclusion: Female axSpA patients participating in RCTs are less likely to achieve efficacy outcomes than their male counterparts. Similar sex differences were found for IL-17i and TNFi. Further investigation is imperative, as it may help the development of sex-specific treatment approaches and novel drug targets. Future clinical trials should diligently report sex-disaggregated data to better understand the differential drug efficacy between males and females.

Best Abstract by a Medical Student

TOUR1D

How Do Early Disease Activity and Early Clinical Response Associate With Long-Term Outcomes With Ixekizumab in Radiographic Axial Spondyloarthritis?

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Objectives: To explore the association between treatment response at Week (W)12 and W24, and attainment of the Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1 treat-to-target (T2T) recommendation at W52 in patients with radiographic axial spondyloarthritis (r-axSpA) treated with ixekizumab (IXE).

Methods: This post hoc analysis included patients randomly assigned to IXE 80 mg every 4 weeks (N= 81) from COAST-V, a Phase 3 trial that investigated the efficacy of IXE in bDMARD-naïve patients with r-axSpA. The proportion of patients who achieved the ASDAS < 2.1 at W52 was evaluated among those in inactive disease (ID), low disease activity (LDA), high disease activity (HDA) or very high disease activity (VHDA) at W12 or W24. The proportion of patients who achieved ASDAS < 2.1 at W52 was also measured among those who attained meaningful clinical response at W12 or W24, as defined by a clinically important (CII, ΔASDAS ≥1.1) or a major improvement (MI, ΔASDAS ≥2.0) in ASDAS, improvement of ≥50% in Bath Ankylosing Spondylitis Disease Activity Index score (BASDAI50), or achievement of BASDAI < 4.

Results: Of the 81 patients, 34 (42%) were in ID (n= 8) or LDA (n= 26) at W12 and most of these patients met the ASDAS < 2.1 t at W52 (ID= 100%, LDA= 85%. [Figure 1A] 47 patients achieved ASDAS CII at W12 and of those, 33 (70%) were in ID or LDA at W52. [Figure 1B] Similarly, most patients who met the ASDAS MI, BASDAI50 or BASDAI < 4 at W12 met ASDAS < 2.1 at W52 (81–94%. [Figure 1B] 37 patients (46%) were in ID (n= 13) or LDA (n = 24) at W24 and of those, 29 (78%) achieved ASDAS < 2.1 at W12, and most also met ASDAS < 2.1 at W52 (ID= 100%, LDA= 79% [Figure 1A]; 52 patients achieved ASDAS CII at W24 and among them, 37 (71%) were in ID or LDA at W52. [Figure 1B] Most patients who met the ASDAS MI, BASDAI50 or BASDAI < 4 at W24 met ASDAS < 2.1 at W52 (80–89%). [Figure 1B] 39 patients were in HDA or VHDA (ASDAS ≥ 2.1) at both W12 and W24 and 9 (23%) of these patients (11% of the 81 included patients) met the ASDAS < 2.1 target at W52.

Conclusion: These data regarding IXE-treated patients with r-axSpA reinforce the current ASAS-EULAR and T2T recommendations, in that those who achieved ASDAS CII or ASDAS < 2.1 at W12 and/or W24 were highly likely to attain the treatment target of ID or LDA at W52.

TOUR2A

Real World Patterns of Advanced Therapy Tapering in Early Rheumatoid Arthritis: Data from The Canadian Early Arthritis Cohort

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Objectives: To describe real-world patterns of advanced therapy tapering in a large pan-Canadian cohort of patients with early rheumatoid arthritis (RA) who would be eligible to taper and identify predictors of which patients are reducing their therapy in routine care.
Methods: Data from patients enrolled in the Canadian early ArThritis CoHort (CATCH) in January 2007-August 2022 were analyzed. CATCH is a prospective, observational cohort of patients with early inflammatory arthritis. The analysis cohort included patients with a diagnosis of RA who were prescribed advanced therapy (i.e., tumour necrosis factor (TNF) inhibitors, Janus kinase (JAK) inhibitors, non-TNF inhibitor advanced therapy) and in sustained remission (sREM) or had low disease activity (LDA) for at least 6 months. Patients were considered to taper advanced therapy if they reduced the dose of therapy by at least 25% through dose reduction or dose spacing for at least 3 months. Survival analysis using the Kaplan-Meier method was used to estimate the median time to taper advanced therapy and Cox regression analysis was used to identify predictors of tapering advanced therapy.
Results: Data were analyzed from 306 RA patients treated with advanced therapy who reached sREM or LDA for at least 6 months. These patients were predominantly white (87%), female (73%), and had seropositive RA (82%) with a mean age of 50 years. At the time of sREM or LDA patients were treated with TNF inhibitors [n= 218 (71%)], JAK inhibitors [n= 52 (17%)], and non-TNF biologic therapy [n= 36 (12%)]. Treatment tapering occurred in 72 (24%) patients and was more frequent for treatment with non-TNF-inhibitors [n= 15/36 (42%)] compared to TNF inhibitors [n= 51/218 (23%)] or JAK inhibitors [n= 6/52 (12%)]. The median time to taper advanced therapy after achieving sREM or LDA was 14 months (IQR: 5, 35 months). [Figure 1] In adjusted Cox regression analyses, treatment with non-TNF inhibitor was associated with a higher likelihood of tapering (HR: 2.73, 95% CI:1.35, 5.55) and having higher patient reported fatigue was associated with a decreased likelihood of tapering (HR 0.89: 95% CI 0.80 – 0.99).
Conclusion: In this real-world study of early RA patients, tapering was attempted in approximately 1 in 4 patients who would be considered eligible based on current recommendations, with a median time of 14 months. Tapering was associated with the type of advanced therapy and was less common in patients with worse fatigue, suggesting real-world decisions to taper are influenced by factors beyond typical measures of RA disease activity.
TOUR2B
The Prevalence of Frailty Among Individuals With Rheumatoid Arthritis: A Population-Based Cohort Study
Alexandra Legge (Dalhousie University, Halifax); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)
Objectives: Studies have demonstrated a link between frailty and chronic inflammation, raising the question of whether chronic inflammatory diseases like rheumatoid arthritis (RA) may be associated with increased rates of frailty. Our objective was to evaluate the prevalence of frailty among individuals living with RA when compared to the general population without RA.
Methods: We conducted a population-based cohort study using administrative health data for the

province of British Columbia from 1990-2018. A previously validated case definition based on physician billing data was used to assemble an incident cohort of all RA cases with onset from 1996-2008. To capture the health state of individuals living with RA, the baseline date was defined as 5 years after the index date for RA diagnosis. A random sample of 50% of incident RA cases was included in this analysis, none of which were used for the derivation of our frailty measure. Each RA individual was matched 2:1 by sex, birth year, and index year with randomly selected individuals from the general population without inflammatory arthritis. Frailty was measured using a frailty index (FI) comprised of 40 health deficits. The presence of each deficit was assessed using administrative health data for the 3 years prior to the baseline date. Each item was scored from 0 (absent) to 1 (present) and individual scores were summed and divided by the total number of deficits to produce a baseline FI score. Frailty was defined as a baseline FI score > 0.21. We compared the prevalence of frailty among RA patients and non-RA controls using conditional logistic regression, while the number of health deficits present was compared using negative binomial regression. Multivariable models were stratified by age, sex, and calendar year, and adjusted for rurality, socioeconomic status, and baseline Charlson comorbidity index scores.

Results: Baseline characteristics for RA patients (n= 13367) and non-RA controls (n= 26734) are shown in Table 1. Baseline FI scores were higher among RA patients compared to non-RA controls and a greater proportion of RA patients were considered frail at baseline. In multivariable analysis, the number of health deficits present (Rate Ratio 1.47; 95%CI 1.44-1.50) and the odds of frailty (Odds Ratio 2.30; 95%CI 2.03-2.60) were significantly higher among RA patients compared to non-RA controls.

Conclusion: Frailty is significantly more common among individuals living with RA when compared to age- and sex-matched individuals without inflammatory arthritis. Future work will aim to identify strategies to prevent and treat frailty in RA.

TOUR2C

Assessing the Timeliness of Referrals in Rheumatology from a Centralized Referral System in Québec

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Objectives: Since 2018 in Québec, general practitioners (GP) are required to send patient requests for first rheumatology consultations to the regional centralized referral system (called CRDS), which allocates appointments according to the GP-specified reasons for consultation and level of priority using a standardized form. Our objectives were: to describe the delays for CRDS allocated rheumatology appointments compared with target waiting times in the CRDS, and to compare delays and characteristics of referrals between the pre- and peri-pandemic periods.

Methods: We collected data in one regional CRDS (490K inhabitants), over four periods of 4 months (November to February 2018 to 2022). We analyzed the characteristics of the demand for rheumatology referrals including priority levels and status of referrals as of September 2023. We calculated CRDS system delays, defined as the difference between the date of referral receipt and the date of first appointment allocation and compared these delays with the CRDS target

waiting times for each priority level. Median delays and survival curves were compared between the pre- and peri-pandemic periods.
Results: There were respectively 283, 476, 468 and 385 processed rheumatology referrals for the four periods of observation. Overall, there were 91 priority B referrals (target waiting time < 10 days), 254 priority C (<28 days), 730 priority D (<90 days) and 270 priority E (< 365 days). The CRDS target waiting times were met for 74% of priority B, 63% of priority C, 24% of priority D and 40% of priority E. Median delays and Kaplan-Meier survival curves did not significantly differ between the pre- and peri-pandemic periods for high-priority referrals (B and C). However, priority D referrals (e.g.: suspicion of chronic polyarthritis, inflammatory spondylarthropathy, connective tissue disease) had significantly higher delays in the 2020-21 pandemic period versus the 2019-20 pre-pandemic period (respective medians: 532 and 124 days, $p < 0.001$).
Conclusion: These preliminary results, coming from one region of Québec with nearly 100% of the demand by GPs for rheumatology care managed by the CRDS, suggest that prioritization of the referrals in the CRDS helped mitigate the effect of the pandemic for high-priority referrals. Impact of the pandemic on the increased delays was however significant for priority D referrals. Next steps will document consequences of rheumatology first appointment delays on health care services utilization and will explore associations of patient and system factors with these delays.
Supported by a CIORA grant.

TOUR2D

Persistent Cigarette Smoking is Associated With Rheumatoid Arthritis Onset and Neutrophil Activation in a Prospective Study of At-Risk First-Degree Relatives

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Objectives: Cigarette smoking is a major environmental risk factor for the development of Rheumatoid Arthritis (RA). Studies have shown that smoking is associated with the development of autoantibodies, such as anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF). However, it remains unclear precisely how, and at which stage of pre-clinical RA, smoking influences the development of inflammatory arthritis. We sought to better understand the relationship between cigarette smoking and RA onset in a large, prospective cohort of First-Degree Relatives (FDR) of RA patients. Complimentary translational studies sought to understand the immunologic mechanism by which cigarette smoke influences pre-clinical RA pathogenesis.
Methods: We follow an established cohort of FDR of RA patients longitudinally for incident RA. At study inception, and each subsequent visit, a smoking survey was conducted, which included questions regarding past and current smoking, and smoking intensity. Neutrophils from healthy donors were stimulated with cigarette smoke extract (CSE) and analyzed by flow cytometry, enzymatic profiling, immunofluorescence, protein citrullination and extracellular DNA release (SYTOX green).
Results: At the study baseline visit for each participant (n= 569), cigarette smoking patterns were modestly associated with autoantibody status. For example, in RF+ (n= 84) or ACPA+ individuals (n= 53) pack-year smoking history was higher compared to RF- (10.8 vs 7.9, $p = 0.08$) and ACPA-(9.6 vs 8.2, $p= 0.69$) individuals respectively. No differences in baseline visit smoking status (past/current) or intensity were observed in FDR Progressors (n= 19). However, longitudinal smoking patterns were strongly associated with RA development, [Figure 1A] p =

0.009), with higher rates of persistent smoking in Progressors (90.0% vs 60.2%). In a logistic regression model, both persistent smoking (OR 8.0, 1.7 - 37.7) and ACPA positivity (15.9, 5.7 - 44.5) were independently associated with the development of RA. Neutrophils cultured in-vitro with CSE (20%) skewed neutrophils away from degranulation and toward neutrophil extracellular trap (NET) formation, leading to the release of neutrophil proteases such as Proteinase-3, extracellular DNA, and citrullinated proteins. [Figure 1B, C, D]
Conclusion: We show for the first time that persistent cigarette smoking, rather than incident smoking, was associated with RA onset in FDR. Neutrophils treated with CSE release NETs, but do not degranulate. These data suggest a mechanism by which smoking may stimulate neutrophils to undergo NET formation and release citrullinated antigens which may be relevant for RA progression in FDR.

TOUR3A

Mortality After Autologous Hematopoietic Stem Cell Transplant for Autoimmune Disease: Do Scleroderma Patients Fare Worse?

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Objectives: Autologous hematopoietic stem cell transplantation (HSCT) benefits some patients with severe autoimmune disease (AD) but is associated with toxicity and treatment-related mortality. Among rheumatic diseases, autologous HSCT is most often considered in scleroderma, a disease associated with high mortality. Our objectives were to describe individuals undergoing autologous HSCT for AD, including scleroderma, and to evaluate mortality.
Methods: Using chart review, we collected and analyzed HSCT data from two Canadian tertiary care centre programs. We included consecutive adults (18+) undergoing autologous (self-donor) peripheral blood HSCT for AD (1999-2022). Patient characteristics were summarized using median/interquartile range (IQR) or frequency/percentage. We evaluated person-time from index date (HSCT) to death, loss to follow-up, or end of study. Overall survival was calculated for 2 and 5 years after transplant. To compare mortality in scleroderma versus other AD, we calculated adjusted hazard ratios (aHR) with 95% confidence intervals (CI), adjusting for age at transplant, sex, time from AD diagnosis to HSCT and calendar year.
Results: We studied 228 individuals undergoing HSCT, most commonly for multiple sclerosis (42%) and scleroderma (26%). Over half of the sample (54%) were women. Median age at HSCT was 40 (IQR 33-49) and median time between AD diagnosis and HSCT was 4.7 years (IQR 2.4-9.1) years. Over a median follow-up of 3.9 (IQR 1.7-6.5) years, 28 of 228 patients died (23 deaths/1,000 PY). Less than a third (27%) of deaths were due to AD progression/relapse (5.7 deaths/1,000 PY). 35% were due to HSCT complications (defined as occurring within the first 100 days, including respiratory complications, n= 3, multi-organ failure, n= 2 and infections, n= 2), and 38% were due to late events that occurred beyond the 100 days post-HSCT (sudden death, infection, organ failure, and cancer). Survival post-HSCT was 94% at 2 years and 89% at 5 years (Table 1). There was a trend for worse survival in scleroderma, which disappeared after

controlling for sex, age, time since diagnosis, and calendar year (adjusted HR 1.02, 95%CI 0.34-3.09, compared to other AD). In scleroderma, half of the deaths were due to disease relapse.
Conclusion: In this sample of mostly young adults undergoing HSCT for AD, 5-year survival was 89%. A trend to worse outcomes in scleroderma may be due to differences in demographics (i.e., age distribution), time trends, and/or other factors. Half of deaths in scleroderma patients post-HSCT were due to disease relapse.

TOUR3B

Fine Particulate Matter Components and Interstitial Lung Disease in Systemic Autoimmune Rheumatic Diseases

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Objectives: Different fine particulate matter (PM2.5) chemical components may have different influences on health. Moreover, these influences may be modified by other air pollutant co-exposures. We investigated associations between exposure to PM2.5 component mixtures and interstitial lung disease (ILD) onset in systemic autoimmune rheumatic diseases (SARD) by considering potential effect modification by ozone exposure.
Methods: Using United States MarketScan data from 2011-2019, we identified 240,193 people with new-onset SARD (without ILD) based on ≥2 ICD SARDs billing codes within 2 years or ≥1 hospitalization codes. Individuals were followed until ILD onset (using ICD codes), loss of insurance coverage, or end of study. Exposures of PM2.5 chemical components (i.e., ammonium, black carbon, mineral dust, sulfate, nitrate, organic matter, and sea salt), estimated by satellite retrievals, refined by geographically weighted regression, and delimited for developed areas, were assigned to subjects based on their residential metropolitan division or core-based statistical area codes. We used the extended quantile g-computation to assess potential associations of SARD-ILD with the PM2.5 component mixture adjusting for age, sex, and prior chronic obstructive pulmonary disease (as a proxy for smoking and a potential confounder) and to examine effect modification of those associations by ozone exposure.
Results: Risk of SARD-ILD onset increased 41% (95% confidence interval 36-47%) with every decile increase in all PM2.5 components at the median ozone level. Across different ozone levels, similar positive associations were observed, and ammonium always contributes most to SARD-ILD onset (Table 1). Ozone was positively associated with SARD-ILD, respectively, and there was evidence of interaction such that at low PM2.5 levels, ozone was highly significantly associated with SARD-ILD.
Conclusion: Exposure to PM2.5 components, especially ammonium, increases the SARD-ILD risk. Ozone was also associated with SARD-ILD risk. The findings point to the need for sophisticated methods to study correlated environmental exposures.

TOUR3C

Does Chronic Fatigue Syndrome Reflect a More Severe Chronic Hypoxic State in Patients With Limited Cutaneous Systemic Sclerosis (lcSSc)? A Cross-Sectional Study

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Objectives: Symptoms resembling myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and fibromyalgia (FM) frequently plague rheumatic disease patients. We have recently shown that patients with SSc commonly exhibit symptoms compatible with ME/CFS early in their disease. Recently, a chronic hypoxic state has been proposed to underlie some of the symptoms in patients with certain forms of ME/CFS, although this has not been previously explored in SSc.
Methods: We determined the frequency and severity of ME/CFS, pain (via the fibromyalgia symptom severity score and the widespread pain index), and disability (via the HAQ-DI and SF-36) in patients with lcSSc early in disease duration (median, 2 years). We also determined if indicators of hypoxia: namely elevated red cell distribution width (RDW) levels and diffusion lung capacity (DLCO SB), and if other disease-associated parameters associated with vascular remodeling and/or visceral complications (e.g. nailfold video capillaroscopy changes) were more prevalent in lcSSc patients with ME/CFS compared to those without ME/CFS.
Results: We show that patients with lcSSc who also have SSc-CFS (N = 22 patients) have significantly increased pain and disability compared to those without ME/CFS (N = 20 patients). We show for the first time that SSc-CFS patients have elevated markers of hypoxia – namely: elevated RDW (14.15 vs 13.25; p= 0.02), and a statistical trend towards reduced diffusing lung capacity (15.2 vs 19.28; p= 0.06), and reduced oximetry measurements (97 vs 98, p= 0.06), compared to lcSSc patients without fatigue. Intriguingly, SSc-CFS patients also had a higher frequency of telangiectasia, and a statistical trend was evident for reduced capillary density in the SSc-CFS group (6.3 vs 7.75; respectively, p= 0.07). No differences were noted in capillary microhemorrhages, enlarged/giant capillaries or iron indices. Finally, elevated RDW levels also inversely correlated with diffusion lung capacity (-0.49) (p= 0.001).
Conclusion: lcSSc patients with ME/CFS have elevated RDW, associated with markers of hypoxia. We propose that ME/CFS in patients with SSc may reflect a more severe hypoxic state that may be associated with early visceral complications. Future mechanistic studies and prospective multicentered studies assessing the severity of fatigue and post-exertional malaise may provide added insights into this.

TOUR3D

Renal Complications Following Autologous Stem Cell Transplantation for Systemic Sclerosis

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Objectives: Rapidly progressive diffuse systemic sclerosis (SSc) is a devastating autoimmune disease with high morbidity and mortality. Autologous hematopoietic stem cell transplantation (AHSCT) is recognized as an effective treatment option with randomized controlled trials demonstrating improvement in skin fibrosis, pulmonary function, and survival. [1] Although the risk of renal complications following AHSCT for hemato-oncologic conditions has been well established, [2] the risk in SSc remains unclear. Furthermore, this subset of patients with rapidly

progressive, severe SSc is particularly vulnerable to developing scleroderma renal crisis (SRC), a life-threatening complication of SSc characterized by malignant hypertension and AKI. [3]
Methods: We conducted a retrospective review of all patients with SSc treated with AHSCT between 2001 and 2023 at The Ottawa Hospital. Data was sought for baseline patient characteristics and the development of AKI and SRC as defined by the KDIGO 2012 definition or the International Scleroderma Renal Crisis Survey Criteria respectively, during the first 120 days following AHSCT.
Results: 34 patients underwent AHSCT, the mean age was 49.6 years (21-65), 53% were female, 10 received cyclophosphamide (CTX), equine anti-thymocyte globulin (ATG), total body irradiation (TBI) conditioning and 26 received CTX, rabbit ATG conditioning (table 1). The mean modified Rodnan skin score was 25 (2-43) before AHSCT. The median follow-up time was 29.9 months (0-72). 50% (n= 17) experienced renal complications following AHSCT with 29% (n= 10) experiencing AKI alone, 20% (n= 7) with SRC alone and 3% (n= 1) having SRC without AKI. AKI occurred at a mean of 18 days (-3 to 92) following AHSCT and SRC with a mean of 44 days (-1 to 109). 4 of the 7 patients with SRC required admission to the ICU and 2 required permanent hemodialysis. Of those with AKI only, 8 were diagnosed with pre-renal AKIs and 2 had cardiorenal AKIs. Transient hemodialysis was required in 2 AKI patients. Five patients with SRC were receiving steroids at the time of diagnosis. There was no statistically significant difference in overall survival associated with the development of renal complications post-AHSCT.
Conclusion: Although renal complications were common following AHSCT, affecting half of our cohort, there was no significant impact on survival observed with renal injury. Nonetheless, given the frequency and often the severity of renal morbidity, close monitoring both before and after transplant is warranted as early intervention could be effective. Ideally, with much-needed prospective studies, high-risk patients may be identified prior to AHSCT and provided with pre-emptive supportive interventions to mitigate renal morbidity. References: [1.] Sullivan KM. New England Journal of Medicine. 2018;378:35-47. [2.] Lopes JA. Bone Marrow Transplant. 2016;51:755-62. [3.] Chrabaszcz M. Kidney and Blood Pressure Research. 2020;45:532–548.

TOUR4A

Actionable Adverse Events in a Real-Practice Cohort of Children With Juvenile Idiopathic Arthritis. Results from The Capri Registry

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Objectives: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic disease of childhood. Adverse events (AE) during treatment may negatively influence disease control and quality of life and may result in permanent harm. Using an inception cohort of children with JIA, the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry, we describe the frequency, seriousness, and consequences of physician-reported actionable AE.

Methods: The CAPRI JIA registry prospectively collects information on children recruited within 3 months of JIA diagnosis at 20 participating sites across Canada. Core data are collected at every clinic visit including any actionable AE since the previous visit reported by clinicians. An actionable AE was defined as any untoward medical occurrence that requires additional medical visits, investigations, treatment, or a change in arthritis medications, irrespective of its cause. A serious AE was defined as an event that results in death, is life-threatening, requires hospitalization, or results in a significant disability or a congenital anomaly (or requires medical intervention to prevent these).
Results: Actionable AE were reported in 376 out of 967 patients (38.9%) at 713 of 7221 visits (9.9%). Of these, 46 events were serious affecting 32 patients (3.3%). During a total observation period of 2045.8 patient-years, the AE and serious AE rates were 34.9 and 2.2 per 100 patient-years, respectively. Most patients had reported AE at only one visit, but 166 (44.1%) were reported to have AE at multiple visits. The most frequently reported AE were gastrointestinal, primarily nausea/vomiting (n= 296, 41.5%) and abdominal pain (n= 58, 8.1%) (Table 1). The most frequent serious AE were infection with hospitalization (n= 16), followed by gastrointestinal bleed (n= 4) and eye surgery (n= 4). There were no reported deaths or demyelinating disease. However, there was one case of acute lymphoblastic leukemia in a 9-year-old. The most commonly reported medication in visits with an AE were non-steroidal anti-inflammatory drugs and methotrexate which were often given in combination. The most common actions taken by the clinician reporting an AE were additional treatment (n= 263, 27.2%), followed by stopping a medication (n= 203, 21%).
Conclusion: Actionable AE was reported in 38.9% of our JIA patients, but serious AE were rare. Most AE were gastrointestinal in nature and managed with additional treatment. Increasing awareness of these actionable AE is likely important to improve the health outcomes of patients with JIA.

TOUR4B

Understanding Variability in Depression Screening Scores in Young Adults With Rheumatic Diseases: A Retrospective Chart Review

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Objectives: Pediatric patients with chronic rheumatic diseases require ongoing care into adulthood. McMaster University Medical Center has established a multidisciplinary Young Adult Clinic (YAC) for patients aged 18-22 to support newly transitioned patients to independently manage their chronic health condition(s). Recognizing that this population is at risk for mental health disorders, in October 2021 we began routine screening of patients for depression prior to each clinical visit. Our study's objective is to understand the temporal variability in symptoms of major depressive disorder (MDD) among patients with rheumatic diseases in the YAC.
Methods: We conducted a chart review of patients aged 18-22 years followed in the YAC since October 1, 2021. Patients completed the validated Patient Health Questionnaire-9 (PHQ9) prior to each clinic visit. Patients with ≥2 PHQ9 scores (0-27, higher scores indicate more severe depressive symptoms) were included. Age, diagnosis and PHQ9 scores at each visit were extracted from charts. PHQ9 scores were converted into predetermined categories: none-minimal depression symptoms (0-4), mild (5-9), moderate (10-14), moderately severe (15-19) and severe (20-27). Changes in score categories over time were described.

Results: Sixty-six patients, mean (SD) age 19.6 (1.3) years were included. The mean (SD) number of appointments per patient where a PHQ9 score was recorded was 3.6 (1.5). Mean (SD) follow-up was 13.3 (5.9) months, mean (SD) time between appointments was 5.2 (2.7) months. Thirty-six (54%) patients had no change in PHQ9 categories, and 35 (97%) of them remained in either none-minimal or mild categories. Eighteen (27%) patients changed by one category; seven (39%) moved between mild and moderate, while three (17%) moved between moderate and moderately severe. Of ten (15%) whose scores changed by 2 categories, seven (70%) moved between none-minimal and moderate, and three (30%) moved between mild and moderately severe. The PHQ9 scores for patients with at least one category change are shown. [Figure 1]
Conclusion: In young adults with rheumatic disease followed in the YAC at McMaster, many patients recorded consistent PHQ9 scores over time, but many varied greatly over time. Often these changes correspond to situational life changes, making treatment decisions based on a single time point challenging. Longitudinally monitoring PHQ9 scores may help providers differentiate a temporary increase from a trend that could require intervention. Additionally, a low score at any single time point does not preclude the need for regular monitoring.

TOUR4C

Relationship Between Brain Injury Markers and Executive Function in Children With Systemic Lupus Erythematosus and Healthy Controls

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Objectives: Patients with childhood-onset systemic lupus erythematosus (cSLE) commonly experience impaired executive function (EF), and attribution to neuropsychiatric lupus (NPSLE) is challenging. Serum markers of brain injury may be useful potential biomarkers for EF in NPSLE. We investigated the relationship between serum brain injury markers and EF in cSLE.
Methods: We utilized prospectively collected cross-sectional data from children with SLE ages 12-17 years recruited from the SickKids Lupus Clinic from January 2020–December 2022, and age, sex-matched healthy controls. Serum brain injury marker levels for glial fibrillary acidic

protein (GFAP), serum neurofilament light chain (sNFL), and Tau were quantified using the Simoa Human Neurology 4–Plex B assay (Quanterix, Billerca, MA, USA). EF was assessed using the Delis Kaplan Executive Function System (DKEFS) Color Word Interference test (inhibition and inhibition/switch trials scaled score normative mean= 10, standard deviation= 3; lower scores indicate more difficulties). Descriptive data included disease duration, activity (SLEDAI-2K), damage (SLICC damage index, SDI> 0) and clinical manifestations. We compared brain injury marker levels between the cSLE and control groups using the Wilcoxon rank-sum test and examined associations between the markers and EF scores (Inhibition and Switching) using Spearman correlations.

Results: Participants included 31 children with cSLE (mean age= 15.6 years ± SD 1.5, 87% female) and 30 healthy controls (mean age= 15.5 years ± 1.6, 83% female). For cSLE, the median disease duration was 27.7 months (IQR 29.8), median disease activity was 2 (IQR 2), 13% had disease damage, and one had a NPSLE diagnosis. There were no statistically significant differences between median levels of brain injury markers in the cSLE group versus controls for GFAP (77.6, IQR 69.3 vs 69.1, IQR 37), sNFL (4.9, IQR 2.7 vs 5.4, IQR 4) or Tau (2.6, IQR 2.2 vs 2.5, IQR 1.5). Scores for EF measures in the cSLE group versus controls were similar on the inhibition (median 9, IQR 4 vs 12, IQR 3) and inhibition/switch trials (10, IQR 4 vs 11, IQR 4). There was no correlation between brain injury markers and EF scores across the whole cohort. In the cSLE group, worse performance on DKEFS Inhibition correlated with higher sNFL (r= -0.29, p= 0.11) and GFAP (r= -0.28, p= 0.13), though not statistically significant.

Conclusion: Our study results indicate similar levels of brain injury markers and EF in group-wise comparisons of cSLE and controls, and a possible relationship between EF and the markers in the cSLE group. Further analysis will investigate the relationship between these markers and other clinical features.

TOUR4D

Introduction of a Transition Policy to Improve The Transition of Youth With Juvenile Idiopathic Arthritis from Pediatric to Adult Healthcare

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Objectives: Youth with juvenile idiopathic arthritis (JIA) are at high risk for healthcare interruption while transitioning from pediatric to adult healthcare providers (HCPs) - frequently

resulting in poor outcomes as young adults. Transition may be improved by teaching youth self-management skills, which improves their ability to navigate the adult healthcare system. There is currently no standardized method at our centre to ensure that HCPs are preparing patients for transition. Therefore, our aim was to distribute a transition policy and discuss transition with at least 50% of adolescents with JIA being seen in the pediatric general rheumatology clinics by May 2023.
Methods: A multidisciplinary stakeholder workgroup was formed to create a transition policy, identify barriers to discussing transition in clinic, and to develop change ideas to target the problem. The outcome measure was the rate of flowsheet transition documentation in the EMR. Process measures included the rate of transition policy distribution. The balancing measure was HCPs' reasons for not completing a transition discussion. A transition policy distribution workflow was modified over multiple plans, do, study, act (PDSA) cycles and educational resources were created to support this initiative.
Results: Baseline chart review over one week revealed that 0/10 adolescents with JIA had documented transition discussions. A transition policy and its distribution workflow were created in an iterative fashion over three PDSA cycles from March-May 2023. Resources developed to help facilitate the workflow included examination room reminders, QR codes, and EMR SmartPhrases. HCPs received an education session to review the proposed workflow. In the initial PDSA, 4/16 (25%) patients received the transition policy and 3/16 (19%) had documented transition discussions. HCPs and patients had positive feedback regarding transition discussions, but HCPs found documentation tedious. During the second PDSA, HCPs received reminder emails about incomplete transition documentation for eligible patients, and the documentation process was simplified. 12/21 (57%) patients received the transition policy and 12/21 (57%) had transition discussion documentation. For the third PDSA, one patient created an infographic of the transition policy. At the end of the project, the rate of transition policy distribution fell to 43% and transition documentation was sustained at 57%.
Conclusion: Although the clinic has started to distribute the transition policy and discuss the transition with its adolescents with JIA, additional PDSA cycles are needed to achieve a reliable workflow with fidelity. Once the goal is reached sustainably, the clinic plans to implement additional initiatives that will help patients prepare for the transition to adult healthcare.
References: [1.] Spiegel L, Tucker L, Duffy KW et al. Ped Rheu 2021; 19:83 [2.] Wood DL, Sawicki GS, Miller MD et al. Acad Pediatr 2014;14(4):415-22.

TOUR5A

Intracranial Giant Cell Arteritis: A Comprehensive Systematic Review

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Objectives: The occurrence of intracranial vasculitis in cases of giant cell arteritis (GCA) has been increasingly recognized. While traditionally associated with stroke, its clinical significance is incompletely understood. We identified all reported cases of intracranial GCA to describe presentations, investigations, treatments, and outcomes reported to date.
Methods: Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, we conducted a systematic review using MEDLINE, Embase, and PubMed to identify studies that reported cases of intracranial manifestations of GCA.1 The study was

registered on a systematic review database (PROSPERO 42023412373). We defined intracranial involvement as any vessel cranial to the dura mater that was confirmed by either histopathology or imaging. Abstract screening, full-text screening, and data abstraction were performed in duplicate with any disagreements adjudicated by a third investigator. Data was described using summary statistics.

Results: A total of 1554 papers underwent title and abstract screening, 424 underwent full-text screening and 114 papers were included. We found 374 patients with intracranial GCA. The median age was 73.0 (interquartile range (IQR) 65.9-80.0) and 143 (38.2%) patients were female (Table 1). GCA diagnosis was made through a combination of clinical assessment, inflammatory markers, imaging, and/or biopsy. One hundred eighty-seven (50.0%) patients presented with stroke, 128 (34.2%) presented with vision loss, and 69 (18.5%) presented with constitutional symptoms. The most common vessels involved were 159 (42.5%) internal carotid, 147 (39.3%) vertebrobasilar, and 49 (13.1%) ophthalmic arteries. Across patients with strokes, 113 (60.4%) had cerebral strokes, 44 (23.5%) had brainstem strokes, and 35 (18.7%) had cerebellar strokes. Of the 193 cases which reported treatment, the most common treatment was glucocorticoids, administered to 182 (94.3%) of patients. A further, 45 (23.3%) patients were treated with cyclophosphamide, 33 (17.1%) with methotrexate and 30 (15.5%) with tocilizumab. Median follow-up was 12 (IQR 3-36) months during which 34 (9.0%) intracranial GCA patients experienced a relapse of their intracranial or non-intracranial disease, 17 (4.6%) had a recurrent stroke, and 52 (14.0%) died.

Conclusion: This data suggests that intracranial vasculitis in GCA is not a rare occurrence. Most intracranial GCA is a disease that extends from extracranial vessels, however about 15% has exclusively intracranial disease. Half of intracranial GCA presents with stroke, and 14% of patients with intracranial GCA die. These findings suggest that individuals with GCA who present with stroke should be evaluated for intracranial GCA. Optimal therapy for intracranial GCA is unclear, but these patients may benefit from more intensive therapy. References: [1.] Page M, McKenzie J, Bossuyt P, Boutron I, Hoffman T, Mulrow C et al. BMJ 2021;372:n71.

TOUR5B

Autoantibody Positivity and Antigen Specificity Have Predictive Utility in Pediatric-Onset Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis

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Objectives: In adults with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), ANCA specificity towards proteinase-3 (PR3) and myeloperoxidase (MPO) have been identified as predictive biomarkers for severe disease, renal-involvement, and relapse. [1] As such, they are now used to select and inform treatment decisions in the adult clinical setting. [2] The objective of this project is to evaluate whether ANCA seropositivity and antigen specificity also have predictive utility in the assessment of pediatric-onset AAV.

Methods: Eligible participants included children and youth (< 18 yrs of age) with a diagnosis of one of the following subtypes of AAV: GPA (granulomatosis with polyangiitis), MPA

(microscopic polyangiitis), ANCA positive pauci-immune glomerulonephritis or unclassified vasculitis. Participants were stratified according to the absence (n = 44) or presence of ANCA for MPO (n = 127) and PR3 (n = 233). Retrospective clinical data from the ARChiVe/PedVas registry was used in regression models, adjusted for age and sex as baseline variables, to compare overall and renal-specific disease activity at diagnosis and outcomes at 1-year post-diagnosis between individuals grouped by ANCA type. Disease activity was assessed according to the pediatric vasculitis activity score (pVAS).
Results: In this cohort (n = 404), the median age at diagnosis was 14.0 years (IQR: 11.0 – 16.0) and 69.3% (n = 280) of individuals were female. Overall disease activity at diagnosis was significantly higher in children with ANCA-positive versus ANCA-negative vasculitis. [Figure 1] At diagnosis, children with MPO-ANCA exhibited similar levels of overall disease activity to those with PR3-ANCA but had 2.29 times higher odds of renal involvement (P = 0.010), while children with PR3-ANCA had 5.26 times higher odds of ear, nose, and throat involvement (P < 0.0001). MPO-ANCA seropositive children also exhibited a 6.07 times higher likelihood of severe renal dysfunction (Kidney Disease Improving Global Outcome (KDIGO) stage 4-5) at diagnosis yet demonstrated improved renal function by 6 months in comparison to PR3-ANCA seropositive children (P < 0.001). There were neither significant differences in the likelihood of achieving remission (50%), experiencing improvement (86%), or, unfortunately, acquiring damage (61%) at 1-year post-diagnosis, nor in the likelihood of having a relapse within 1- and 2-years of diagnosis, in children stratified by ANCA positivity or specificity.
Conclusion: ANCA positivity and specificity exhibited predictive utility with regard to overall and organ-specific disease activity and trajectory in pediatric AAV. These findings identify ANCA as biomarkers that, with prospective validation, could personalize treatment decisions for children with AAV. References: [1.] Tedesco M, Gallieni M, Pellegata F, et al. J Nephrol 2019;32(6):871-882. [2.] Lionaki S, Blyth ER, Hogan SL, et al. Arthritis Rheum 2012;64(10):3452-3462.

TOUR5C

Severe Infection Rate in Giant Cell Arteritis Patients Treated With Corticosteroids: A Systematic Review With Meta-Analysis

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Objectives: Giant cell arteritis (GCA) is the most common idiopathic vasculitis in people over 50 years old. [1] Despite the side effects associated with corticosteroid therapy, it remains the main therapeutic option. [2] This study aims to conduct a systematic review with meta-analysis of GCA patients treated with corticosteroids, to characterize the incidence of severe infections and other serious side effects leading to hospitalization or mortality. Understanding the outcomes associated with corticosteroid therapy will enable the identification of the optimal prevention strategies to mitigate these adverse effects.
Methods: A systematic review was conducted to compare and interpret data from relevant literature sources published until March 22, 2022. A rapid literature review in August 2023 found no significant changes from the initial results. An exhaustive search in three databases and the Grey Literature yielded 7073 initial articles. After eliminating duplicates, 6786 articles underwent evaluation based on their titles and abstracts. Subsequently, 835 studies were assessed for inclusion and exclusion criteria, ultimately selecting 140 for full reading. Thus, 35 studies

were finally included while case reports, systematic reviews, and studies with less than 30 patients were excluded. A meta-analysis was performed using data from 10 studies to assess the rate of severe infections and infection-related mortality.
Results: Our systematic review included 24,664 patients with an average age of 72.6 [71.5 - 73.7], of which 71% [0.69 - 0.72] were women. Among patients receiving corticosteroid therapy, the incidence of serious infections and/or requiring hospitalization was 17% [0.13; 0.23 95% CI]. The observed heterogeneity (71%) was attributed to the lack of standardization of treatments and types of infection assessed. [3] The infection-related mortality rate was 4% [0.03; 0.04 95% CI]. Pneumocystis Jiroveci infections were mentioned in 2 out of 35 articles (rate between 1.85 and 6.45%). Tuberculosis and other mycobacteria infections were mentioned in 4 studies (rate between 0 to 3.36%). Common side effects included fractures (0 to 30% of patients), hypertension (1.67% to 29.79%), diabetes (2% to 38.39%) and glaucoma/cataract (0.1% and 28.5%).
Conclusion: The existing literature highlights a significant rate of serious infections in our study population. However, the lack of consistency in infection characterization across studies hinders the establishment of strong statistical conclusions with direct change in clinical practice. Notably, the highly concerning Pneumocystis Jiroveci infections were mentioned in only 2 articles with prophylaxis of infections and side effects rarely discussed. Thus, further studies are warranted to assess the relevance of prophylaxis and the potential vaccination benefits.
References: [1.] Li, K., Semenov, D., Turk, M. et al. A meta-analysis of the epidemiology of giant cell arteritis across time and space. Arthritis Res Ther 2021;23: 82. PMID: 33706808. PMCID: PMC7948334. [2.] Maz M, Chung SA, Abril A, et al. American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. Arthritis Rheumatol. 2021 Aug;73(8):1349-1365. PMID: 34235884. [3.] Meta-Analysis: Severe infection rates and infection-related hospitalization across 10 studies
TOUR5D
New Canadian Fast-Track Ultrasound Clinic by Rheumatologists for Diagnosis of Giant Cell Arteritis: Are Temporal Artery Biopsies a Story from The Past?
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Objectives: Giant Cell Arteritis (GCA) can present diagnostic challenges and early diagnosis is crucial due to potential ischemic complications. Recent guidelines suggest that a suspected diagnosis should be confirmed with temporal artery biopsy (TAB) or imaging, including ultrasound (US). In our Canadian setting, point-of-care TA US was near unavailable, and biopsy remains the standard of care. We hypothesize that launching a Fast-Track US Clinic by a rheumatologist may spare the need for a biopsy. This study aimed to assess the diagnostic performance of the US in this newly launched Fast-Track clinic.
Methods: This was a single-center retrospective cross-sectional analysis spanning from January 2020 to July 2022. Each subject had a US of the temporal and axillary arteries according to a standardized protocol for suspicion of either new-onset or relapse of GCA. Sonographers were rheumatologists and acquired training on vascular US techniques 6 months before launching the clinic. For each patient presenting with suspected new-onset GCA, the pre-test probability was calculated using the Southend GCA probability score (GCAPS). The sensitivity (Sn), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated using the rheumatologist clinical diagnosis as the gold standard for GCA diagnosis.

Results: A total of 97 patients were included in the study with 2 patients having 2 visits. Of those, 23 had a diagnosis of GCA and 76 had another diagnosis. Patients with and without GCA were, respectively, 81.8% vs 72.7% females, had a mean age of 76.6 vs 74.8 years and mean CRP of 80.7 vs 37.7 mg/L. TA US demonstrated a Sn of 82.6% (95% confidence interval (CI), 67.1%-98.1%), Sp of 90.9% (95% CI, 84.5%-97.3%), PPV of 73.1% (95% CI, 56.1%-90.1%) and negative predictive value (NPV) of 95.6% (95% CI, 91.3%-100%). (see Table). 14 US were performed for suspicion of relapse and among subjects with suspicion of new-onset 27, 34 and 24 US were performed for high, intermediate, and low pretest probability of GCA, respectively. The high-risk subgroup demonstrated higher PPV with a lower NPV, while similar Sn/Sp were observed between all three subgroups.
Conclusion: Our results highlight the benefits of the US as a key diagnostic tool for GCA, particularly when combined with clinical evaluations. An excellent discriminative ability for diagnosis of GCA was shown in this newly launched clinic suggesting that the role of TAB may need to be redefined. These findings will guide broader adoption of US programs for GCA across the country. References: [1.] Maz M. Arthritis Rheumatol 2021;73:1349-65. Sebastian A. RMD Open 2020;6. Dejaco C. Ann Rheum Dis 2018;77:636-43. Best Abstract on Quality Care Initiatives in Rheumatology Award

TOUR6A

Interferon-α as a Biomarker to Predicts Renal Outcomes Flares in Lupus Nephritis

Laura Patricia Whittall Garcia (University Health Network, Toronto); Dafna Gladman (Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, University Health Network, University of Toronto, Toronto); Murray Urowitz (Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto); Zahi Touma (Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto); Joan Wither (Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto)

Objectives: We have recently shown that IFN-I gene expression predicts the risk of SLE flares and a more severe disease course in SLE patients. Furthermore, recently it has been suggested that patients with lupus nephritis (LN) with higher IFN-I gene expression in their renal tubular cells are less likely to respond to conventional therapy. This study aimed to determine if the amount of IFN-α in serum at the time of an LN flare predicts response to therapy, subsequent LN flares, and decline in kidney function.
Methods: All patients included in the study had 1) active LN (24H urine protein > 500mg/day with a subsequent modification in therapy by the treating physician), and 2) baseline estimated glomerular filtration rate (eGFR) ≥ 60ml/min (prior to the flare). Outcomes: 1) Complete Response (CR), defined as proteinuria < 500 mg/day and a serum creatinine within 15% of the baseline at 1 and 2 years after the flare, 2) number of LN flares during follow-up (defined by an increase in proteinuria of at least 1000 mg/d if the baseline was < 500 mg/d or doubling of proteinuria if baseline was ≥500 mg/d and a change in therapy by the treating physician, and 3) decline in eGFR to ≤59ml/min, and < 15ml/min during follow-up. Serum IFN-α was measured by Simoa®
Results: A total of 95 patients with active LN were included in the study. The median (IQR) age of the patients was 29 (23-41) years, 79 (83.7%) were women, and the disease duration was 6.0 (0.2-10.0) years. Forty (42.1%) were Caucasian, 21 (22.1%) were Afro-Caribbean, and 22 (23.1%) were Asian. The baseline eGFR was 112 (98.7-127) ml/min, and the median (IQR) follow-up was 132 (96-156) months. 76.8% had a kidney biopsy at the time of the LN flare, 54.7% had a proliferative or mixed class, and 17.8% class V. The serum baseline levels of IFN-α

predicted CR at 2 years from the LN flare. Furthermore, patients with higher baseline levels of IFN-α had a greater risk of having 2 or more subsequent renal flares (Table 1). Using ROC analysis, two IFN-α cut-offs were identified, 0.6 and 1.3 for predicting ≥2 LN flares and progression to eGFR ≤15, respectively., these cutoffs continued to predict renal outcomes on Cox regression analysis (Table 1).
Conclusion: IFN-α serum levels predicted failure to respond to treatment at year 2 after the renal flare, the development of ≥2 LN flares, and decline in kidney function during follow-up.

TOUR6B

Urinary Biomarker to Predict Renal Outcomes in Lupus Nephritis

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Objectives: It has been shown that per-protocol repeat kidney biopsies (KB) performed after 24 months from the last lupus nephritis (LN) flare can predict renal flares and long-term renal dysfunction. Unfortunately, KBs are invasive, and proteinuria has known drawbacks, including a disconnect with the histopathological findings. Five urinary biomarkers (UB), including PF4, sVCAM-1, Adiponectin, MCP-1, and CD163, have been shown to discriminate between LN and non-active LN patients and reflect clinical improvement. The aim of this study was to determine if the levels of these 5 UB measured 24 months after the LN flare predict subsequent LN flares and decline in kidney function.
Methods: Patients who had an LN flare and stored urine samples 24 months after their LN flare were included in the study. UBs were measured by ELISA. The following outcomes were ascertained: 1) Time to a subsequent LN flare during follow-up (defined by an increase in proteinuria of at least 1000 mg/d if the baseline was < 500 mg/d or doubling of proteinuria if the baseline was ≥ 500 mg/d, prompting a change in therapy, and 2) decline in eGFR to ≤59ml/min or < 15ml/min during follow-up.
Results: Seventy LN patients were included in the study. The median (IQR) age was 25 (21-42) years, 56 (80.0%) were women, and the median disease duration was 7.3 (2.1-10.8) years. 28 (25.7%) were Caucasian, 11 (19.6%) were Black, and 18 (25.7%) were Asian. The median (IQR) time between the LN flare and the urine sample was 25.3 (23.0-27.4) months. 75.7% had a kidney biopsy at the time of the LN flare, 51.4% had a proliferative or mixed class, 22.8% class V, and 1 class II. The median steroid dose at the time of the LN flare and 24 months after was 40 (25-50) and 8 (5-12) mg, respectively. 24 months after the LN flare the median eGFR was 109 (93-120) mm/m2, serum albumin 43 (37-46) g/L and 24H urinary protein was 390 (220-1000) mg. On multivariable regression analysis, after adjusting for ethnicity, serum creatinine, and 24H urinary protein 24 months after the flare, the urinary levels of MCP-1 and CD163 predicted a subsequent LN flare. Furthermore, Adiponectin, MCP-1, and CD163 predicted a decline in eGFR to ≤59ml/min and < 15ml/min during follow-up (Table 1).
Conclusion: UB measured 24 months after the LN flare predicted a subsequent LN flare and decline in kidney function during follow-up and may be useful in detecting residual renal inflammation.

TOUR6C

Therapeutic Drug Monitoring of Azathioprine and Tacrolimus in Systemic Lupus Erythematosus Pregnancies: Preliminary Results from The Legacy Cohort

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Objectives: Pregnant systemic lupus erythematosus (SLE) women still face an unacceptably high risk of maternal and fetal morbidity, particularly when their disease is active. Though guidelines strongly recommend azathioprine (AZA) and tacrolimus (TAC) in specific SLE pregnancy scenarios, evidence to guide drug monitoring in this context is non-existent. Our aim is to evaluate the characteristics of SLE pregnancies according to the levels of AZA metabolites (erythrocyte-free 6-thioguanine, 6-TG) and TAC trough levels at the first pregnancy (baseline) visit.

Methods: LEGACY is a prospective cohort enrolling unselected SLE pregnancies ≤16 6/7 gestational weeks at 7 Systemic Lupus International Collaborating Clinics. We record demographics, disease activity, and drugs. In addition, whole blood samples are collected at baseline to determine AZA metabolites (e.g., 6-TG) and trough TAC levels if applicable. The present study included Montreal LEGACY participants prescribed either AZA or TAC ≥3 months prior to their first pregnancy visit. We characterized AZA metabolite and TAC levels as continuous and categorical variables (i.e., non-adherent, sub-therapeutic, therapeutic, and supra-therapeutic, using established cut-offs in non-pregnant populations). We defined patients as non-adherent if they had undetectable or barely detectable levels despite appropriate dosing.

Results: Of 70 LEGACY pregnancies enrolled in Montreal, 23 (33%) and 6 (9%) were prescribed AZA and TAC, respectively. Among those prescribed AZA, only 9% had therapeutic levels, while 91% were sub-therapeutic or non-adherent (Table 1). Compared to those with therapeutic levels, pregnancies with sub-therapeutic or non-adherent AZA levels were more likely to occur in women of non-Caucasian ethnicity/race, on steroids, with longer SLE duration, and with prior lupus nephritis (Table 1). Among those prescribed TAC, 50% (3/6) had therapeutic levels, while 33% (2/6) and 17% (1/6) were sub-therapeutic and supra-therapeutic, respectively. No patients on TAC were identified as non-adherent. Less than half (43%) of pregnancies non-adherent to AZA were in Lupus Low Disease Activity State (LLDAS) at baseline. Of the pregnancies with sub-therapeutic TAC levels, 50% (1/2) were not in LLDAS, while all (4/4) pregnancies with therapeutic or supra-therapeutic TAC levels were in LLDAS at baseline.

Conclusion: We observed that most SLE pregnancies prescribed AZA had sub-therapeutic levels, with nearly a third identified as non-adherent. Pregnancies with lower AZA and TAC levels may be less likely to achieve LLDAS. Despite low numbers, our preliminary results suggest the value of personalized drug monitoring as a novel approach to precision medicine in pregnant SLE women, that might improve efficacy, safety, and adherence in a high-risk

population. Supported by a CIORA grant.

TOUR6D

Deucravacitinib, an Oral, Allosteric, Tyrosine Kinase 2 (Tyk2) Inhibitor, in Patients With Active Systemic Lupus Erythematosus: Patient-Reported Outcomes in a Phase 2 Trial

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Objectives: Deucravacitinib is a first-in-class, oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor approved in the US, EU, and other countries for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy. In PAISLEY, a 48-week, phase 2, randomized controlled trial that assessed deucravacitinib in patients with active systemic lupus erythematosus (SLE), a greater proportion of patients receiving deucravacitinib treatment achieved SLE Responder Index-4 (SRI[4]) responses at Weeks 32 and 48 vs placebo. Patient-reported outcomes (PROs) were collected as exploratory endpoints.

Methods: All patients met Systemic Lupus International Collaborating Clinics classification criteria, were seropositive for antinuclear antibody, anti-double-stranded DNA, or anti-Smith antibody, and had Systemic Lupus Erythematosus Activity Index 2000 total score ≥ 6 points and clinical score ≥4 points. Patients (N= 363) were randomized 1:1:1:1 to placebo (n= 90) or deucravacitinib 3 mg twice daily (BID; n= 91), 6 mg BID (n= 93), or 12 mg once daily (QD; n= 89). Patients assessed pain levels on a numeric rating scale (NRS) and completed the Patient-Reported Outcome Measurement Information System (PROMIS) Fatigue 7a Short Form and 36-Item Short Form Health Survey (SF-36). Missing data were inputted using control-based pattern imputation. Results were descriptive.

Results: Baseline characteristics were comparable across groups. At Week 48, greater mean changes from baseline in pain and fatigue were reported with deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD vs placebo, including achievement of the minimal clinically important differences (MCID) of −1 and −4 for both pain and fatigue with all doses of deucravacitinib vs for pain only with placebo. Patients treated with deucravacitinib reported greater achievement of changes associated with MCID for pain (−1), fatigue (−4), and SF-36 MCS and PCS (−2.5) vs placebo (Table). Mean scores (SD) at Week 48 numerically improved with deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD vs placebo, respectively: Pain NRS: 3.6 (2.7), 3.7 (2.6), 3.6 (2.8), and 4.7 (2.7); PROMIS Fatigue: 52.4 (10.2), 52.6 (10.0), 51.9 (10.6), and 54.4 (10.9); SF-36 PCS: 44.7 (10.0), 44.6 (9.3), 45.1 (11.0), and 41.5 (10.5); and SF-36 MCS: 46.7 (12.6), 46.3 (13.1), 47.3 (12.6), and 45.2 (12.9).

Conclusion: Patients with SLE who received deucravacitinib reported improvements over patients who received placebo on pain and fatigue, and in health-related quality of life at Week 48.

TOUR7A

Artificial Intelligence Models for Computer-Assisted Joint Detection and Sharp-Van Der Heijde Score Prediction in Hand Radiographs from Patients With Rheumatoid Arthritis

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Objectives: To develop and validate a deep learning system for automated detection and prediction of Sharp van der Heijde (SVH) scores in hand radiographs of patients with Rheumatoid arthritis (RA).

Methods: We used a convolutional neural network (CNN) based algorithm (You Only Look Once (YOLO)v5l6) trained on an object detection model (COCO-Common Objects in Context) to detect joints in 240 training and 89 test pediatric hand radiographs from the Radiologic Society of North America database. Radiographs were annotated by boxing and labeling the joints of interest: proximal interphalangeal, metacarpophalangeal, wrist, distal radius, distal ulna. The joint detection model was validated with 54 clinician-annotated radiographs from 4 adult RA patients followed for 9-13 years (10-12 images per patient) (joint detection gold standard). We applied a supervised vision transformer model (VTM) to predict each joint's SVH erosion and JSN score. VT models convert the image into data sequences which are then used to predict the SVH scores. The VTM was validated using 2249 hand radiographs with clinician assigned SVH scores from 381 RA patients from the Canadian Early Arthritis Cohort (SVH score gold standard). As the joint detection model was trained to detect the whole wrist and we had clinician assigned SVH scores for individual wrist joints, we trained a separate multi-task model to predict wrist joint scores from whole wrist images. The performance of the VTM model to predict joint scores was compared to other CNN-based models (EfficientNetV2 and MobileNetV3). Model accuracy for joint detection is reported as the F1-score (reflecting model precision and model recall) and mean absolute precision (mAP) for a range of Intersection-over-Union (IoU) measures reflecting the overlap between clinician and model-assigned bounding boxes of detected joints. Accuracy for SVH score prediction is reported as root mean squared error (RMSE) and balanced accuracy.

Results: The joint detection model accurately identified target joints (pediatric data FI-score = 0.991, map0.1 = 0.993 with an IoU threshold of 0.1 ; adult data F1-score = 0.812, map0.1 = 0.871 (n= 54). The VTM predicted JSN and erosion SVH scores with high accuracy (RMSE JSN 0.91, erosion 0.93). The multi-task models predicted SVH erosion and JSN scores of wrist joints with moderately high accuracy (0.6-0.91). EfficientNetV3 performed better for wrist joints (VTM vs EfficientNetV3 average difference 0.10). [Figure]

Conclusion: Automated deep learning systems accurately identify and predict joint damage in hand radiographs from patients with rheumatoid arthritis and may aid in monitoring joint damage.

TOUR7B

Applying Similarity Network Fusion to Identify Patient Clusters for People With Systemic Inflammatory Disease

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Objectives: Systemic inflammatory diseases (SIDs) are characterized by non-infectious multisystem inflammation. Genetic panels only diagnose 25% of suspected SID patients, due to the clinical and genetic heterogeneity of SIDs. We hypothesize that the integration of clinical and laboratory data will improve the evaluation and diagnosis of SIDs by creating more biologically-driven patient phenotypes. Our study aims to employ similarity network fusion (SNF), a method for multifactorial data integration, to identify patient clusters with shared clinical and laboratory features within a heterogeneous SID cohort.

Methods: We included genetically undiagnosed SID patients with available clinical, laboratory, and whole-exome sequencing data. Included patients were clinically heterogenous and had undifferentiated SID. Relevant variables were divided into clinical and laboratory data structures, weighted by missingness and the number of variables in each data structure, then input into SNF. Fisher's exact test (Bonferroni adjusted $p < 0.0004$) identified variables with different distributions between clusters. We validated our model with 2 simulations (1000 simulated SNF iterations each). Simulation 1: each iteration randomly re-distributed relevant variables into 2 simulated data sets, performed SNF and identified variables with different distributions between simulated clusters. Simulation 2: each iteration randomly subsampled 70% of our cohort into a simulated data set, performed SNF, and determined the percent of patients in the simulated data set that had identical clustering to our original SNF patient clusters.

Results: Our study included 104 undifferentiated SID patients. SNF revealed 2 clusters in our cohort. Cluster 1 (n= 72) had a median age of symptom onset of 5.7 years old and cluster 2 (n= 32), 6 years old. Overall, cluster 2 consisted of patients with more severe SID features compared to cluster 1. Specifically, elevated levels of IgG antibodies and the presence of hepatitis, autoantibodies, anemia, and macrophage activation syndrome characterized cluster 2 and were

normal/absent in cluster 1 (p< 1x10-7. [Figure 1] The majority of variables that differentiated the clusters in our cohort were laboratory features. Simulation 1 demonstrated that the same features were consistently significant in defining clustering (> 946 times out of 1000). Simulation 2 illustrated that 95% of cluster 1 patients (69/72) and 82% of cluster 2 patients (26/32), consistently clustered together over 1000 SNF iterations.
Conclusion: SNF successfully identified 2 robust, patient clusters from a heterogeneous SID cohort. Simulation studies showed that 89% of the patients consistently clustered together and that laboratory variables primarily determined these clusters. Future work will incorporate genetic data into SNF to identify shared genetic and inflammatory pathways within clusters.

TOUR7C

Direct Health Care Costs Differ by SLE Autoantibody Machine Learning Clusters in an International Inception

May Choi (University of Calgary, Calgary); Karen Costenbader (Brigham and Women's Hospital, Boston); Marvin Fritzler (University of Calgary, Calgary); Ann Clarke (University of Calgary, Calgary); SLICC The Systemic Lupus Erythematosus International Collaborating Clinics

Objectives: Using machine learning, we identified 4 patient clusters, based on longitudinal autoantibody profiles in an international SLE inception cohort, which were predictive of disease outcomes including mortality. [1] We now compare direct and indirect costs between these SLE clusters to elucidate healthcare utilization patterns in SLE.
Methods: Patients fulfilling the 1997 Revised ACR SLE Classification Criteria from 33 centres (11 countries) were enrolled within 15 months of diagnosis and clustered by k-means using longitudinal 29 ANA patterns and 20 autoantibody profiles. Data were collected annually on healthcare use (i.e., hospitalizations, medications, dialysis, and selected procedures, as well as antibodies, organ involvement, activity [adjusted mean SLEDAI-2K], and medication use), supplemented by data on additional resource use and lost work-force/non-work-force productivity in a patient subset. Multiple imputations predicted all missing values for the patients in the full cohort who did not provide direct/indirect costs for all observations. Healthcare use was costed using 2023 Canadian prices and lost productivity using Statistics Canada age-and-sex specific wages. Average annual costs over follow-up were compared between clusters using multivariable regressions, adjusting for significant predictors for direct and indirect costs.
Results: 805 subjects were included in the SLE clusters and provided cost data. The mean follow-up time for the entire cohort was 12.3 years (2.9-21.6 years) and similar across clusters. There were no clear differences in direct and indirect costs and component costs between clusters 1 (high frequency of anti-Sm/anti-U1RNP, predictive of high cumulative disease activity and immunosuppressant/biologic use), 2 (low autoantibody reactivity, predictive of low disease activity and immunosuppressant/biologic use), and 4 (multiple autoantibody reactivities, predictive of high disease activity). Thus, these 3 clusters were combined and compared with cluster 3 (the highest frequency of all five antiphospholipid antibodies predictive of seizures and mortality) using multivariable regressions. Cluster 3 had higher total direct costs than clusters 1, 2, and 4 combined ($9288 vs $7061; adj. diff. $2852 [95%CI $196,$5510]), particularly for hospitalizations ($2134 vs $1320; adj. diff. $1158 [95%CI $455,$1860]) (Table). Cluster 3 had significantly more hospitalizations for thrombotic/cardiovascular (CVD) events compared to combined clusters (two-sample test of proportions, 22.7% vs. 4.1%, diff. 18.6% [95%CI 6.0%,31.3%]).
Conclusion: Machine learning identified an SLE cluster with high antiphospholipid antibody

frequency that incurred the most substantial direct costs, a high proportion driven by hospitalizations due to thrombosis/CVD-related events. Even clusters with severe SLE did not incur such high costs, suggesting thrombotic and antiphospholipid-related complications are important contributors to the economic burden of SLE. References: [1.] Choi MY [etal] ARD.2023Jul;82(7):927-936.

TOUR8A

Reduced Statin Use in Patients With Autoimmune Myopathies and Systemic Lupus Erythematosus Compared to Rheumatoid Arthritis and Non-Inflammatory Diseases

Shane Cameron (University of Manitoba, Winnipeg); Liam O'Neil (University of Manitoba Faculty of Health Sciences, Winnipeg); Christine Peschken (Departments of Medicine and Community Health Sciences, University of Manitoba, Winnipeg); Annaliese Tisseverasinghe (University Of Manitoba, Winnipeg)

Objectives: Rheumatic diseases such as autoimmune myopathy (AIM), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA) confer an increased risk for atherosclerotic disease. The 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) inhibitors, or statins, play an important role in cardiovascular (CV) protection. However, concerns for muscle-related adverse effects may deter statin use in patients with AIM. We evaluated the prevalence of statin use in patients with AIM and a statin-indicated condition and compared it to patients with SLE, RA, and noninflammatory conditions followed at a single centre.

Methods: We conducted an electronic chart review of patients seen between January 2016 and June 2023 at The Arthritis Centre (TAC) in Winnipeg, the primary rheumatology referral centre for Manitoba. Patients diagnosed by a rheumatologist with an AIM and ≥1 statin-indicated condition as per the 2021 Canadian Cardiovascular Society Guidelines were included. Those with necrotising autoimmune myositis (NAM) associated with statin use or anti-HMGCR antibodies were excluded. Age and sex-matched comparator groups were identified at a 1:1 ratio for SLE, RA, and non-inflammatory conditions (predominantly osteoarthritis). Categorical group differences were analyzed by chi-square test. Multivariable regression models were constructed to assess whether these conditions and other clinical factors are associated with current statin use (prescription fill within 4 months of last follow-up in the provincial prescription database).

Results: Of the 201 patients with AIM followed at TAC, 40 met the study criteria: 62% female, mean age 68+/-11 (range 41-86) years. Statin indication reflected secondary prevention (e.g. coronary artery disease) in 19 of the AIM patients versus 14 of the non-inflammatory group. Only 40% (16/40) with AIM were on a statin (an additional 3 on an alternative lipid-lowering agent) compared with 70% (28/40) of the non-inflammatory group ($p = 0.007$). Compared to the noninflammatory group, the odds of current statin use were significantly lower in patients with AIM [adjusted OR 0.27 (95% Confidence Interval 0.10-0.68)] and SLE [0.28 (0.10-0.69)], but not RA [0.56 (0.22-1.41)], whereas age, sex, and number of statin-indicated conditions (1 vs. > 1) were not associated with statin use. Within the AIM cohort, serum CK, disease duration (≤ 3 vs. > 3y), DMARD use, prednisone use, and concurrent cancer were not significantly associated with statin use.

Conclusion: Despite a clinical indication, statin use was significantly lower among patients with AIM and SLE versus non-inflammatory conditions. Future studies should evaluate other deterrents to statin use in these high CV risk populations including comorbidities, pill burden, and primary care access. Best Abstract on Research by a Rheumatology Resident

TOUR8B

Successful Treatment of Necrotizing Autoimmune Myositis With Subcutaneous

Immunoglobulins

Nikola Wilk (Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa); Nancy Maltez (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Catherine Ivory (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa)

Background: Intravenous immunoglobulin (IVIg) is commonly used in the management of idiopathic inflammatory myositis (IIM). However, there remains challenges including accessibility, high costs, side effects profile and need for frequent hospital visits for infusions. [1] As an alternative, it has been shown in observational studies that subcutaneous immunoglobulins (SCIg) can have similar effectiveness as IVIg. [2] We expect that SCIg can be useful in the treatment of IIM and may improve patient experience and health-related quality of life. [3]

Case: We present the case of a 68-year-old male with hypertension, dyslipidemia, and diabetes mellitus type II who presented with a two-year history of progressive proximal bilateral lower extremity weakness. He had been treated with atorvastatin for two years, then with rosuvastatin until discontinued in 2016. He was referred to rheumatology in 2018 for suspected myositis. Physical examination revealed no rash, but proximal weakness with a Medical Research Council Manual Muscle Testing (MRC) score of 4-/5 of his bilateral hip flexors and deltoids, and elevated creatinine kinase (CK) (1644 U/L, 3304 U/L in 2016). Electromyography revealed a generalized myopathic disorder with proximal predominance. A muscle biopsy of the right quadriceps showed myopathic features with increased internal nuclei and rare necrotic and regenerating fibers. Serum HMG-CoA reductase antibody was high-titer positive. Cancer screening was negative.

Due to delayed diagnosis and concern of corticosteroids use in this comorbid patient, IVIg for induction therapy was considered. The patient lived in a rural community far from any centre to receive IVIg. He was unable to drive to a treatment centre given his weakness and did not have any alternative transportation. Therefore, we opted for a trial of SCIg initiated three times a week for a total dose of 56g (0.5g/kg/week). Within a month his CK decreased to 520 U/L and his weakness improved with MRC score 5/5. He reported no adverse effects. SCIg monotherapy continued with a slow taper over three years and the patient remains in remission off therapy since 2021.

Conclusion: We describe a case of HMG-CoA reductase necrotizing autoimmune myositis successfully treated with SCIg monotherapy as induction and maintenance therapy. To our knowledge, this is the first case report describing successful treatment of this entity with SCIg as first-line treatment. Although this case presents a safe and effective alternative to IVIG, larger studies are required to confirm its effectiveness in inflammatory myositis and to provide guidelines for dosing recommendation, monitoring parameters and suggestions for tapering.

References: [1.] Guo, Y., et al., Adverse Effects of Immunoglobulin Therapy. Front Immunol, 2018. 9: p. 1299. [2.] Cherin, P., et al., Long-term subcutaneous immunoglobulin use in inflammatory myopathies: A retrospective review of 19 cases. Autoimmun Rev, 2016. 15(3): p. 281-6. [3.] Nicolay, U., et al., Health-related quality of life and treatment satisfaction in North American patients with primary immunedeficiency diseases receiving subcutaneous IgG self-infusions at home. J Clin Immunol, 2006. 26(1): p. 65-72.

TOUR8C

Knowledge Gaps in Treatment and Biomarkers for Melanoma Differentiation-Associated Gene 5 Dermatomyositis With Rapidly Progressive Interstitial Lung Disease

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Background: Melanoma Differentiation-Associated Gene 5 (MDA5) dermatomyositis (DM) is an idiopathic inflammatory myopathy (IIM) subtype associated with a poor prognosis, specifically when accompanied by rapidly-progressive interstitial lung disease (RP-ILD) [1,2]. There is a gap in the literature regarding biomarkers to accurately identify patients at risk of developing RP-ILD, and to monitor disease activity in these patients.
Case: We report a case of a previously healthy 69-year-old male admitted to the ICU after presenting with a five-week history of dry cough, proximal leg weakness, Gottron's papules of bilateral elbows, shawl sign, V-sign, and heliotrope rash. On presentation, he had an elevated CK of 880 U/L, CRP of 17.6 mg/L, and ferritin of 608 µg/L. He had a positive ANA of 1:80 (homogeneous and speckled nuclei (AC-2), and midbody (AC-27)), and a low-positive anti-MDA5 antibody (signal intensity 28, upper limit of normal 10). Other myositis-specific autoantibodies were negative. Krebs von den Lungen-6 (KL-6), an alveolar glycoprotein and established marker of pulmonary inflammation and fibrosis in ILD, [1] was 48 U/mL (upper limit of normal 300). MRI revealed evidence of proximal myositis in his thighs, and high-resolution computed tomography (HRCT) of his chest revealed subpleural ground glass opacification with bibasilar confluence. Biopsies of Gottron's papules exhibited parakeratosis and orthokeratosis with inflammatory cell infiltration in the dermis. Pulmonary embolism and infection were ruled out.
Despite pulse corticosteroids, rituximab, tofacitinib (5 mg twice daily) and intravenous immunoglobulin (IVIg), his respiratory status progressively worsened, ultimately requiring intubation and ICU admission. Remarkably, anti-MDA5 antibody seroconverted to negative. His course was complicated by *Pneumocystis jirovecii* infection, pneumothorax with pneumomediastinum, a large volume aspiration event, *Staphylococcus epidermidis* bacteremia, and *Pseudomonas* ventilator-associated pneumonia. Though infectious complications prohibited continuation of corticosteroids, rituximab, and tofacitinib, he received one further dose of IVIg. His pulmonary status worsened during the remainder of his admission, and after 17 days in ICU, he was transitioned to care with palliative intent.
Despite worsening clinical and radiographic status, his CK had fallen to 343 U/L and his CRP remained normal. Curiously, KL-6 had only risen to 95 U/mL. An autopsy revealed punctate exudates, especially in the right lower lobe, and parenchymal fibrosis in the left lower lobe.
Conclusion: This case illustrates the complex and often fatal course of MDA5-associated DM with RP-ILD. In Calgary, to address knowledge and clinical practice gaps, we have started developing a patient registry to identify local cases to better understand practice patterns and outcomes. Furthermore, we hope to identify novel biomarkers to help better identify patients at risk for development of RP-ILD, and to better monitor disease progression. References:
[1.] Wang Y, Chen S, Lin Z, Lin J, Xie X, Lin Q, Du G, Huang X, Matucci-Cerinic M, & Furst DE. Clin Rheumatol 2019;38(5):1433-36. [2.] Choi MY, Minoru S, & Fritzler MJ. Curr Opin Rheumatol 2023;35(6):383-94.

TOUR8D

Idiopathic Inflammatory Myopathies and Malignancy Screening: A Survey of The Current Practices Amongst Canadian Neurologists and Rheumatologists

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Toronto); Ophir Vinik (Toronto); Angelo Papachristos (St. Michael's Hospital, Toronto); Rosane Nisenbaum (St. Michael's Hospital, Toronto)
Objectives: To better understand and characterize the current gaps and uncertainties amongst neurologists and rheumatologists in Canada with regards to malignancy screening in patients with idiopathic inflammatory myopathies (IIM).
Methods: An online survey was created consisting of 18 multiple-choice questions related to IIM malignancy screening practices. The survey contained questions pertaining to respondent characteristics, malignancy screening practices, and concerns surrounding these practices. The survey was distributed to adult neurologists and rheumatologists practicing in Canada. Data analysis was both descriptive and quantitative. Quantitative analysis was performed using statistical software programs.
Results: The majority of respondents (96%, n= 69) performed malignancy screening, however, there was variability in practice including delegation and choice of screening tests, influence of patient-specific factors, and time and duration of repeat testing. Only 18% of respondents were confident in their malignancy screening practices. The most significant perceived knowledge gap was the lack of consensus or guidelines on the choice and frequency of malignancy screening. Between neurologists and rheumatologists, rheumatologists saw a higher proportion of IIM patients and were more likely to consider more patient risk factors and order more investigations, while neurologists were more likely to repeat testing.
Conclusion: Several knowledge gaps and variability exist amongst neurologists and rheumatologists with regard to malignancy screening in IIM patients. There is a lack of consensus and confidence in the choice and timing of investigations, with neurologists and rheumatologists differing in their approach to malignancy screening. Further research is required to better understand the relationship between IIM and malignancy to create expert-led consensus guidelines.

TOUR9A

Gla:d® to Be Walking Better: Change in Self-Reported Difficulty Walking After Exercise Therapy and Education in Persons With Knee Osteoarthritis

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Objectives: Difficulty walking is a primary reason that individuals with knee osteoarthritis (OA) seek care, including joint replacement. It is also a precursor to disability and is associated with an increased risk of cardiovascular disease, diabetes, and all-cause death. Good Life with osteoArthritis in Denmark (GLA:D®) is an 8-week group-based hip and knee OA education and

exercise program that has been implemented worldwide, including Canada. We examined the change in self-reported difficulty walking after participating GLA:D® and assessed patient factors associated with improvement in difficulty walking.
Methods: This was a registry-based cohort study of individuals with knee OA who enrolled in GLA:D® in Denmark. Assessments were administered at baseline, at program completion (~3 months), and 12 months. Our pre-specified primary outcome was change in self-reported difficulty walking assessed using the EuroQol 5-dimension 5-level walking item. Exposures of interest were variables hypothesized to affect perceived ability to walk, drawing on a biopsychosocial model of difficulty walking, and included sociodemographic factors, measures of OA illness severity, comorbidities, and psychological factors. We assessed the proportion of participants within each level of difficulty walking (no problems, slight problems, moderate problems, and severe problems/unable to walk) at baseline, 3 months and 12 months overall and after stratifying by age, sex, and baseline knee pain intensity. In those with baseline moderate/severe difficulty walking, we used a multivariable logistic regression model with participants nested within clinics to assess the relationship between exposures of interest and improvement to no/slight difficulty walking.
Results: We included 5,262 participants. Of 2,178 (41%) individuals with baseline moderate/severe difficulty walking, 51% and 58% reported no/slight difficulty walking at 3 and 12 months, respectively. [Figure 1] Similar improvement in difficulty walking was observed in younger (≤ 65 years) and older (> 65 years) participants, in those who were male vs female, and those with higher (VAS > 60/100) vs lower (VAS ≤ 60/100) baseline knee pain intensity. (Figure 1) Greater self-efficacy, younger age, female sex, lower BMI, less intense knee pain and better function at baseline were associated with a greater likelihood of improvement in difficulty walking; severe difficulty walking at baseline and back pain intensity were associated with decreased likelihood of improvement.
Conclusion: More than half of those with baseline difficulty walking experienced meaningful improvement after completing GLA:D® and this improvement was maintained at 12 months. Several patient factors were associated with the outcome suggesting that some Individuals may require additional support and extended treatment.

TOUR9B

Degenerative Disc Disease in Young Adults With Psoriatic Arthritis

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Objectives: Degenerative Disc Disease (DDD) may occur in young adults. This study aimed to define the prevalence of DDD in patients with Psoriatic Arthritis (PsA) younger than 50 years of age and to describe predictors of its development. The association between axial imaging findings and inflammatory and mechanical types of back pain (IBP and MBP) was also examined.
Methods: Patients with PsA were recruited from a prospective observational PsA cohort. Radiographs of the hands, feet, pelvis, and spine were obtained every 2 years. DDD was defined as intervertebral space narrowing, spinal canal stenosis, bony spur formation, facet joint

degeneration, and/or antero- or retrolisthesis on X-rays of the spine. We identified patients younger than 50 with DDD and compared them with patients without DDD of the same age group, in terms of their demographic features and disease characteristics at the baseline visit (clinic entry). For predictors of the development of DDD [Table 1], multivariate Cox regression was used to model the time to event. Generalized estimating equations (GEE) were used for testing the association between axial imaging findings and the type of back pain experienced (IBP vs. MBP). For this analysis, we divided the cohort into 4 groups based on radiographs: Isolated DDD, isolated inflammatory axial disease (sacroiliitis and/or syndesmophytes), mixed features of both, and normal spine radiographs.
Results: Of the 814 patients included in the study, 316 (38.8%) had some degree of DDD on radiographs of the spine. Of these, 182 patients (57.6%) had DDD at their baseline visit, whereas 134 (42.4%) developed it during follow-up. In the Cox regression models, the following factors were found to be predictive of the development of DDD: Age at clinic entry (HR= 1.08, p< 0.001), female sex (HR= 0.65 for male, p= 0.022), peripheral erosions (HR= 1.51, p= 0.049), inflammatory back pain (HR= 2.13, p< 0.001), and biologic use (HR= 1.48, p= 0.044). Having ever been a smoker was found to be protective (HR= 0.61, p= 0.012). Presence of enthesophytes and BMI were associated with higher risk of developing DDD (HR= 1.46, p= 0.056 and HR= 1.02, p= 0.058, respectively) although not significant at the 5% level. In the GEE analysis, none of the 3 abnormal imaging categories was significantly associated with having back pain. After censoring the visits where no back pain was described, none of the imaging categories was significantly associated with MBP or IBP.
Conclusion: DDD is common in young patients with PsA. IBP and MBP do not reliably distinguish between axial disease and DDD.

TOUR9C

Assessing Responsiveness of ICOAP Pain Measure in Patients With Knee Replacement

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Objectives: The WOMAC pain subscale, commonly used in OA research, assesses pain with activity. Thus, WOMAC pain scores are highly correlated with measures of hip/knee function. To address this limitation, the OARSI-OMERACT Intermittent and Constant Osteoarthritis Pain (ICOAP) scale was developed to evaluate the pain experience of people with OA. ICOAP assesses the intensity and impact of constant and intermittent pain on sleep, mood, and quality of life, and has been shown to be reliable, valid, and responsive to treatment effects. Since development, two intermittent knee pain subscales were introduced to assess knee pain predictability; they assess the frequency with which intermittent knee pain arises 'without warning' and 'following a trigger', e.g., activity. The current study assessed the responsiveness of ICOAP, with and without the predictability subscales, to patient-reported symptom improvement in OA patients undergoing total knee arthroplasty (TKA).
Methods: We used data from a prospective cohort study that recruited individuals with primary knee OA from provincial arthroplasty clinics in Alberta. Participants completed the ICOAP pre- and 12 months post-TKA, 11-point pain intensity NRS, and WOMAC pain measures. ICOAP intermittent and constant scores were summed to create the ICOAP total score. An ICOAP overall score was calculated as the mean of the four subscale scores. Scale scores were standardized from 0-100 (higher scores worse). The standardized response mean (SRM) was calculated for ICOAP, NRS and WOMAC pain (mean change/SD change). Relative efficiency of measures (ratio of SRMs) was calculated with ICOAP total as the comparator. Finally, Spearman

correlations between measure change scores were assessed.
Results: 1269 participants were included (60.8% females, mean age 66.0 years [SD 12.6]). As expected for TKA, all measures, including the ICOAP predictability subscales, demonstrated large effects (Table). For ICOAP, SRMs ranged from 1.07 to 1.66; SRM for ICOAP total was 1.66 compared with 1.60 for the ICOAP overall score. Based on RE, WOMAC pain and NRS pain detected greater change than ICOAP (RE > 1). The Spearman correlations for change in ICOAP scores with change in WOMAC pain ranged from 0.43 to 0.68. For NRS pain, the Spearman correlations ranged from 0.44 to 0.59.
Conclusion: ICOAP intermittent pain predictability subscales are responsive to changes in OA knee pain following TKA, but their incorporation with the intermittent and constant subscale scores did not enhance responsiveness. Moderate correlations of ICOAP change scores with changes in WOMAC pain and NRS indicate they measure different knee pain constructs.

TOUR9D

Validation of Clinical Criteria to Diagnose Knee Osteoarthritis

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Objectives: The NICE guideline on osteoarthritis (OA) recommends that adults aged ≥45 should be diagnosed with OA clinically, without investigations, if they have activity-related joint pain and either no morning joint-related stiffness or morning stiffness that lasts no longer than 30 minutes. While the NICE criteria are frequently used as diagnostic criteria for OA, they have not been validated. The objective of this study was to validate the NICE criteria for knee OA.
Methods: This was a diagnostic test study embedded within a larger study of people with type 2 diabetes. We recruited participants from clinics at three academic hospitals in Toronto, Canada. We invited individuals aged ≥45 years with and without self-reported knee pain to participate (aiming for 50% with/without). We excluded individuals with a history of inflammatory rheumatic disease. Participants first self-completed a questionnaire to identify the presence of activity-related knee pain and morning joint stiffness ≤30 min (NICE criteria for OA). As history and physical exam are considered the gold standard for making an OA diagnosis, an experienced rheumatologist, blinded to the questionnaire responses, conducted a standardized clinical assessment to identify the presence of knee OA (yes, no, possible). A second rheumatologist completed a subset (n= 11) of assessments in duplicate for validation of the rheumatologist's assessment. We calculated the sensitivity (sens), specificity (spec), likelihood ratio positive (LR+), and likelihood ratio negative (LR-) of the NICE criteria to detect symptomatic knee OA (yes or possible).
Results: Our study included 91 participants with type 2 diabetes: mean age was 65.9 (SD 8.1) years, 50.6% women, mean BMI 29.1 (SD 6.6) kg/m2. 50 (54.9%) fulfilled the NICE criteria with a spectrum of illness severity: median (range) pain numeric rating score (0-10) was 5 (1-9). Gold standard assessment identified 51 (56.0%) participants with symptomatic knee OA (yes: n= 48, possible [suspected to be early knee OA]: n= 3). The sens, spec, LR+, and LR- of NICE criteria for symptomatic knee OA were 86.3%, 85.0%, 5.75, 0.16, respectively. Activity-related knee pain alone, without combination with morning stiffness, improved operating characteristics (88.2%, 90.0%, 8.82, 0.12). [Table 1] There was high rheumatologist inter-rater reliability for OA diagnosis (kappa = 0.84).

Conclusion: The NICE criteria have high sensitivity and specificity for detecting symptomatic knee OA. A simplified version, assessing self-reported activity-related knee pain in individuals age ≥45 years, performed slightly better and may be a preferable OA diagnostic tool. This should be validated in other settings. Best Abstract on Research by Young Faculty Award

TOUR10A

Safety and Health Care Use Following Vaccination With BNT162b2 in Youth and Children with Juvenile Idiopathic Arthritis (JIA) – A Population-Based Study

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Objectives: To evaluate among Ontario children and youth (< 16 years old) with JIA, whether COVID-19 vaccines were associated with adverse events of special interest (AESIs), emergency department (ED) visits, hospitalizations, and/or specialist visits.

Methods: Using Ontario health administrative databases, all children/youth with JIA billing/hospitalization diagnosis codes were identified, from Nov. 2020 - Dec. 2021. Those receiving at least 1 COVID-19 vaccine through Ontario's vaccination program were followed from 6 months before their first COVID vaccine until 6 months following their last COVID vaccine. The study's end date was August 31, 2022. Self-controlled case series analyses were used to determine the relative incidence rates (RIR) of events in any 3-week period (for AESI, ED visits, hospitalizations) and in any 1-month period (for rheumatologist visits) post-vaccine compared to control periods. AESIs evaluated included Bell's palsy, idiopathic thrombocytopenia, acute disseminated encephalomyelitis, myocarditis, pericarditis, Guillain-Barre syndrome, transverse myelitis, myocardial infarction, anaphylaxis, stroke, deep vein thrombosis, pulmonary embolism, narcolepsy, appendicitis, and disseminated intravascular coagulation, febrile seizures, and Kawasaki disease. Monovalent BNT162b2 (Pfizer BioNTech) was the only COVID-19 vaccine approved for Ontario children/youth in this period.

Results: A total of 1629 JIA patients were included, of whom 60.8% (n= 991) were female. The median age at first COVID-19 vaccine was 12.0 years (IQR:10.0-14.0), with 964 (n= 59.2%) being > 12 years old. Median JIA duration was 4.3 years (IQR: 2.0-7.5). Sixty-seven percent (n = 1093) of patients received 2 COVID-19 vaccine doses and 24.1% (n= 393) received 3 doses. In the risk periods, there were no AESIs reported. Relative to control periods, JIA patients demonstrated similar rates of hospitalizations [RIR after dose 1: 0.76 (95%CI: 0.25-2.33), RIR after dose 2: 0.28 (95%CI: 0.04-1.87)], ED visits [RIR after dose 1: 1.11 (95%CI: 0.77-1.59), RIR after dose 2: 1.31 (95%CI: 0.95-1.80)], and rheumatologist visits [RIR after dose 1: 1.06 (95%CI: 0.89-1.26), RIR after dose 2: 0.98 (95%CI: 0.82-1.18)].

Conclusion: Overall, this study demonstrates the safety of the BNT162b2 vaccine in children/youths with JIA, with no significant increase in AESI or healthcare use following COVID-19 vaccination.

TOUR10B

Safety & Immunogenicity of Covid-19 Vaccines in Systemic Immune-Mediated Inflammatory Diseases (SUCCEED): Preliminary Results on Severe Adverse Events

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Western Hospital and Division of Rheumatology, Department of Medicine, University of Toronto, Toronto); Maggie Larché (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Vancouver); Gilles Boire (Université de Sherbrooke, Sherbrooke); Ines Colmegna (The Research Institute of the MUHC, Montreal); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver); Nadine Lalonde (COVID-19 Global Rheumatology Alliance, London); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Janet Gunderson (Canadian Arthritis Patient Alliance, Glaslyn); Dawn Richards (Canadian Arthritis Patient Alliance, Toronto); Hugues Allard-Chamard (Université de Sherbrooke, Sherbrooke); Sophie Roux (Université de Sherbrooke, Sherbrooke); Ayesha Kirmani (Arthritis Research Canada, Vancouver); Sumiya Lodhi (University of Ottawa, Faculty of Medicine, Ottawa); Lauren Heesels (McMaster University, Faculty of Health Sciences, Hamilton); Ante Markovinovic (University of Calgary, Calgary); Luck Lukusa (Research Institute of the McGill University Health Centre, Montreal); Daniel Pereira (University Health Network, Toronto); Jennifer Lee (RI-MUHC, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Division of Clinical Epidemiology, Montreal); SUCCEED Investigators Safety and immUnogenicity of Covid-19 vaCcines in systEmic immunE mediated inflammatory Diseases (Montreal)

Objectives: SUCCEED was funded by the Canadian government's COVID Immunity Task Force to study SARS-CoV-2 vaccination in participants with immune-mediated inflammatory diseases (IMID). One of our primary objectives was to describe vaccine safety, particularly severe adverse events (SAE) defined as events associated with emergency department (ED) visits and/or hospitalizations.

Methods: In Vancouver, Calgary, Winnipeg, Montreal, Quebec City, Sherbrooke, Toronto, and Hamilton, data were collected from adults with rheumatoid arthritis (RA), ankylosing spondylitis/spondyloarthritis (SpA), systemic lupus erythematosus (SLE), psoriasis/psoriatic arthritis (PsA) and inflammatory bowel disease (IBD), who received SARS-CoV-2 vaccination. Participants filled out questionnaires reporting SAE experienced within 31 days following each vaccine dose.

Results: About two-thirds (63%) of 1556 participants were female; mean age was 52.5 years. BNT162b2 (Pfizer) vaccine accounted for 75% of first/second doses, 67.8% of third doses, 63.3% of fourth doses and 62% of fifth doses. mRNA-1273 (Moderna) was the second most common vaccine. Forty-nine percent of participants had IBD, 27.4% had RA, 14.3% had PsA, 5.3% had SpA, and 4% had SLE. There were 12 (0.8%) self-reported SAEs leading to ED visit or hospitalization, occurring in 11 participants; one participant reported 2 SAEs. There were 6 ED visits (including one Bell's Palsy that occurred 31 days after the first vaccine) and 6 hospitalizations (including one Guillain-Barré syndrome that occurred 15 days after the first vaccine). Other causes for ED visits included an allergic reaction of hives, an episode of labyrinthitis, a case of severe menstrual bleeding and a case of pericarditis. There was only one serious disease flare in an SLE patient who presented to ED with pericarditis. Other reasons for hospitalizations included one new-onset migraine with aura, a case of idiopathic thrombocytopenia purpura, one case of atrial fibrillation, one transient multifactorial renal failure, and one diverticulosis flare. There were two additional hospitalizations not specifically labelled by the participant as vaccine-related: one case of shingles and a case of epiploic appendagitis. Among the 12 self-reported vaccine-related SAEs, 7 were experienced by participants < 65 years old. Three events occurred after the first vaccine dose, 3 after the second

dose, 5 after the third dose, and 1 after the fourth dose. No deaths occurred in the 31 days after vaccination.
Conclusion: In the 31 days after SARS-CoV-2 vaccination in IMID, there were relatively few serious AEs, and no deaths. Additional analyses will consider all other non-severe AEs that did not require an ED visit or hospitalization (including flares).

TOUR10C

When Should I Get My Next Booster? Active Surveillance of Covid-19 Breakthrough Infections in Canadian Patients With Immune-Mediated Inflammatory Diseases

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Objectives: Breakthrough COVID-19 infections are still a risk after vaccination and may be more common in patients with immune-mediated inflammatory diseases (IMIDs) than in the general population. Previous studies on breakthrough infections in IMID relied on retrospective databases; however, these are subject to limitations on COVID-19 test availability, making it hard to determine true infection prevalence as asymptomatic cases may have gone untested. We performed active surveillance of breakthrough COVID-19 infections, analyzing saliva samples via quantitative polymerase chain reaction (qPCR), in vaccinated individuals with IMIDs (systemic lupus erythematosus, rheumatic arthritis, psoriatic arthritis, spondylarthritis, inflammatory bowel disease, and scleroderma).
Methods: Adults with IMID were recruited from Canadian clinics and registries between September 2022 and March 2023, and asked to self-collect saliva samples monthly. Samples underwent batch qPCR testing, with each sample being tested twice, to qualitatively detect SARS-CoV-2 nucleic acids indicators (N1 and N2).
Results: 202 patients have been enrolled, providing 458 valid samples (Table 1). Most (66.2%) were on immunomodulatory medications and the majority (78.8%) had received 3 or more vaccine doses. Only 5% of participants (n= 10/202) met the N1 and N2 thresholds required to confirm COVID-19 positivity. Given the small number of positive results, we were unable to ascertain significant differences between demographic factors, including age, sex, immunosuppression, or vaccination status. However, participants who tested positive had a median time since their last vaccination that was considerably longer (278 days) than those who tested negative (165 days) (95% CI for difference,18-205). The majority (three-quarters) of positive saliva samples occurred in patients who were beyond 217 days of their last vaccine.
Conclusion: A 5% COVID-19 breakthrough infection rate aligns with that of a Canadian population-based cohort where break-through infections occurred in 5.4-6.5% of fully vaccinated IMID patients. [1] In our sample, those with break-through infections had a longer median time since vaccination (by 112 days), corroborating the currently held belief that protection against COVID wanes in the 3-4 months post-vaccination and beyond. Most infections occurred 7-8

months after the last vaccine dose. These findings will help patients, clinicians, and other stakeholders with decision-making in 2023-2024 and beyond. References: [1.] Widdifield J. Lancet Rheumatol 2022;4(6):e430-40.

TOUR11A

Evaluating Treat-to-Target Benchmarks Amongst Older Adults With Gout Initiating Urate Lowering Therapy in Ontario, Canada

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Objectives: Treatment to target (T2T) serum uric acid (SUA) levels in patients with gout on urate-lowering therapy (ULT) is associated with decreased flares and tophi reduction. In this study of older adults with gout, we evaluated the percentage of patients and factors associated with achieving SUA < 360 µmol/L in the first year after initiating ULT, incorporating key covariates including SUA monitoring, ULT dose titrations, and ULT adherence.

Methods: This population-based retrospective cohort study used Ontario health administrative databases, including patients aged ≥66 with gout newly dispensed ULT between January 1, 2010 and March 31, 2019. Achieving an SUA on target (< 360 µmol/L) within 12 months after ULT dispensation was assessed overall, annually, and by specialty. Multi-level logistic regression clustered by ULT prescriber evaluated factors associated with reaching target SUA.

Results: Among 44,438 patients (mean (SD) age 76.0±7.3 years; 64.4% male), prescribed ULT between 2010 and 2019, 35.4% of patients overall achieved a SUA on target within a year of treatment initiation, ranging from 25.7% in 2010 to 45.8% in 2019 ($p < 0.0001$). Rheumatology patients were significantly more likely to be treated to target with improvements across all specialties over time. [Figure 1] In the logistic regression model, independent factors associated with reaching SUA target were febuxostat use (OR 11.30, 95% CI 5.83–21.92), ULT adherence (OR 5.17, 95% CI 4.93–5.41), allopurinol starting doses > 50 mg (OR 2.53, 95% CI: 2.21–2.91), > 2 ULT dose titrations (OR 1.48, 95% CI:1.17–1.88), co-prescription of colchicine/oral corticosteroids (OR 1.24, 95% CI: 1.16–1.32), hypertension (OR 1.09, 95% CI: 1.02–1.18), cancer (OR 1.21, 95% CI: 1.06–1.37) and increasing patient age (OR 1.01, 95% CI 1.01–1.01). Compared with rheumatologists, patients of family physicians (OR 0.37, 95% CI: 0.34–0.41), internists (OR 0.45, 95% CI: 0.40–0.51), nephrologists (OR 0.34, 95% CI: 0.28–0.40) and other specialties (OR 0.46, 95% CI 0.40–0.54) were less likely to achieve SUA target. Patients of younger/newer physicians (OR 0.87, 95% CI: 0.81–0.93) and male patients (OR 0.66, 95% CI: 0.63–0.70) were less likely to meet SUA targets as were patients in the lowest income quintile, with other comorbidities and concomitant diuretic, anti-platelet and losartan use.

Conclusion: Despite improvements over time, this study found that 64.6% of patients did not achieve an optimal SUA level within 1 year of ULT initiation, suggesting room for improvement in gout management in Canada and potential strategies to address care gaps.

TOUR11B

Improving Pre-Conception Counselling and Family Planning in General Rheumatology: A Quality Improvement Study

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Hamilton)
Objectives: The objective of this study is to utilize quality improvement (QI) methodology to improve the rates of family planning discussions in a high-volume general rheumatology clinic in Hamilton, Ontario. Multiple international guideline bodies recommend routine pre-conception counselling for patients with rheumatologic diseases (1-3). Pre-conception counselling is a fundamental component of effective general rheumatology care and should be routinely offered to patients given obstetrical complications associated with rheumatologic disorders and their treatment.
Methods: A retrospective chart review was completed to determine baseline frequency of documented family planning discussions for female patients aged 18-45 in the preceding 1-year period between September and May 2023. We concurrently performed purposive sampling of patients and rheumatologists to describe local practice patterns in family planning and contraception counselling. Interviews were conducted with two rheumatologists and four patients to identify physician, patient and organizational factors of relevance to the local context. Using this information, a fishbone diagram was constructed. A reminder-based approach intended to prompt the physician with editable macros for documentation was designed as the initial intervention. This was applied to all visits with eligible female patients aged 18-45. Frequency of documented discussions was tracked and depicted in a run chart for graphical representation and analysis.
Results: The baseline frequency of documented discussion of family planning prior to the start of the intervention was 19%. After the start of the intervention, the frequency of documented discussions on family planning averaged 34.7% (range, 0 to 100%). The number of patients seen in clinic eligible for family planning discussion ranged from 2 to 5 per clinic half day.
Conclusion: We report interim results of a quality improvement initiative aimed at increasing rates of family planning discussions in a general rheumatology clinic in Hamilton, Ontario. The frequency of discussions around family planning is currently low. Interviews with clinic physicians and administrative staff will provide further insight into required changes to the intervention. Iterative improvement cycles are currently in progress on a monthly cycle.
References: [1.] Russell MD, Dey M, Flint J, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). Apr 03 2023;62(4):e48-e88. doi:10.1093/rheumatology/keac551 [2.] Keeling SO, Alabdurubalnabi Z, Avina-Zubieta A, et al. Canadian Rheumatology Association Recommendations for the Assessment and Monitoring of Systemic Lupus Erythematosus. J Rheumatol. Oct 2018;45(10):1426-1439. doi:10.3899/jrheum.171459 [3.] Sammaritano LR, Bermas BL, Chakravarty EE, et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Rheumatol. 04 2020;72(4):529-556. doi:10.1002/art.41191.

TOUR11C

Predictors of Adherence to Cervical Cancer Screening Guidelines Among Patients With Systemic Lupus Erythematosus

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Objectives: Women with systemic lupus erythematous (SLE) are at increased risk for cervical dysplasia and cervical cancer. While cervical cancer screening guidelines in Nova Scotia recommend that average-risk women aged 25-69 years undergo Pap tests every 3 years, annual

screening is recommended for immunocompromised women, which includes patients with SLE. However, the uptake of these recommendations in clinical practice is unclear. In this retrospective cohort study, we aimed to describe rates of adherence to cervical cancer screening guidelines among SLE patients, and to identify demographic and clinical predictors of adherence to screening.

Methods: Demographic and clinical data was extracted for women with SLE aged 25-69 years, living in Nova Scotia, and followed in the Dalhousie Lupus Clinic Registry between January 2014 and December 2019. Exclusion criteria included prior total hysterectomy, HIV infection, organ transplant, or history of cervical dysplasia/cancer. Adherence with general population (Pap test once every 3 years) and SLE-specific (Pap test annually) cervical cancer screening guidelines was measured. Two separate analyses were conducted, with follow-up divided into one- or three-year eligibility periods. For each analysis, adherence was defined as the proportion of time periods where ≥1 Pap test was performed. Pre-specified demographic and clinical variables were evaluated as predictors of adherence to screening guidelines using generalized estimating equation (GEE) models.

Results: Analysis included 131 SLE patients contributing 557 one-year eligibility periods, and 98 SLE patients contributing 154 three-year eligibility periods. Patient characteristics are summarized in Table 1. Pap tests were performed in 125/557 (22.4%) of 1-year eligibility periods, and 79/154 (51.3%) of 3-year eligibility periods. Mean adherence rates were 49.5% for general population (q3year) screening guidelines and 23% for SLE-specific (q1year) guidelines. In univariable analysis, SLE-related renal disease was associated with higher rates of adherence to annual screening (OR 1.64, 95% CI 1.0-2.8; p= 0.049), while a history of cigarette smoking (OR 0.59, 95% CI 0.35-0.99; p= 0.046) was associated with lower adherence. Older age (per year: OR 0.97, 95% CI 0.95-0.99; p= 0.002; OR = 0.96, 95% CI 0.93-0.99; p= 0.018, respectively) and longer SLE disease duration (per year: OR 0.97, 95% CI 0.94-1.0; p= 0.032; OR = 0.96, 95% CI 0.92-1.0; p= 0.048, respectively) were associated with lower rates of adherence to both general population and SLE-specific screening guidelines.

Conclusion: Adherence to general population and SLE-specific cervical cancer screening guidelines was suboptimal in SLE patients. Future work should aim to identify barriers to cervical cancer screening in this population.

TOUR11D

Evaluation of Methods for Ascertainment and Categorization of Race and Ethnicity for Clinical Research: An Umbrella Review

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Objectives: Race and ethnicity are concepts that are increasingly being evaluated in rheumatology research due to their influence on health outcomes, yet there remains heterogeneity and confusion in the interpretation of these concepts. Informed use of these concepts is essential to address racial and ethnic disparities in rheumatic diseases, thus we conducted an umbrella review to identify: (1) how race/ethnicity have been conceptualized, (2) methods used to ascertain race/ethnicity, and (3) methods of racial and ethnic categorization in clinical research.

Methods: An umbrella review was conducted compliant with Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). We searched MEDLINE, Embase, CINAHL, and Sociological Abstracts from January 2002 to October 2023 using search terms related to: (1) race and ethnicity, (2) conceptualization, (3) genetics, and (4) clinical research. Relevant English language review articles published in peer-reviewed journals were selected for inclusion by two independent reviewers. Titles and abstracts were reviewed for potentially relevant articles, then full text articles for final inclusion. References of selected articles and grey literature were examined to identify additional articles. Data relevant to the research questions were extracted.
Results: Our preliminary search yielded 2236 articles from MEDLINE for inclusion and 11 review articles were selected for final inclusion to date. Race and ethnicity have historically been conceptualized as biologic entities, with more recent literature citing these as socially constructed concepts. We identified 5 methods for the ascertainment of race: (1) self-report, (2) social assignment, (3) name-based ethnic classification, (4) geocoding, and (5) genetic analysis (Table 1). Systems of race and ethnic categorization vary by geography, reflect social context, and range from 3 to 15 categories.
Conclusion: The constructs of race and ethnicity are evolving, with the more recent interpretation of these constructs as socio-political measures rather than biologic entities. There are also several methods of ascertainment and categorization or race and ethnicity, with self-report considered the gold standard. There is no international recommendation for the categorization of race or ethnicity, given that these are influenced by social context. This synthesis of methods can be used to inform the conduct of clinical research in rheumatic diseases. References: [1.] Tricco, AC, Lillie, E, Zarin, W, O'Brien, KK, Colquhoun, H, Levac, D, Moher, D, Peters, MD, Horsley, T, Weeks, L, Hempel, S et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med. 2018,169(7):467-473. doi:10.7326/M18-0850.

TOUR12A

Phenotype of Musculoskeletal Manifestations in a Canadian Inception Cohort of Pediatric Patients With Inflammatory Bowel Disease

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Objectives: Musculoskeletal (MSK) manifestations, including arthritis and arthralgia, are among the most common extraintestinal manifestations (EIMs) of inflammatory bowel disease (IBD). While patterns of MSK EIMs have been well-characterized in adults, there remains limited pediatric data. The purpose of this study was to determine the frequency of MSK EIMs in a contemporary cohort of Canadian pediatric IBD (pIBD) patients and describe their phenotype in this population.
Methods: This was a prospective longitudinal cohort study using existing data from the inception cohort of CIDsCaNN (Canadian Children IBD Network), which was established in

2013 and includes patients from 12 academic centers. The inception cohort encompasses patients aged 2 to 17 enrolled at diagnosis and followed prospectively. Frequency of MSK EIMs was calculated for the entire cohort, as well as for subgroups based on age, sex, and IBD type. For patients with MSK EIMs, phenotype was described by analyzing case report forms for specific EIM features as reported by treating physician.
Results: A total of 1330 pIBD patients were included. 81 (6.1%) were reported to have MSK EIMs at IBD diagnosis or any point during follow-up. There was no significant difference in MSK EIM frequency between sex or age groups. Patients with Crohn's disease were more likely to have MSK EIMs than those with ulcerative colitis or unspecified IBD (7.6% vs 3.6%, p= 0.002). 47 patients (58.0%) had MSK EIMs at or prior to IBD diagnosis while 34 developed them > 4 weeks after. There was no difference in time to MSK EIM development by age or ethnicity. However, females were more likely to develop MSK EIMs after IBD diagnosis than males (p= 0.047). Of MSK EIM patients, 59 (74.7%) were evaluated by a rheumatologist. Peripheral MSK disease (arthritis, enthesitis, and dactylitis) was reported in 51 patients (63%). Data regarding axial disease (sacroiliitis and ankylosing spondylitis) were only available in 37 patients, 19 (51.3%) of whom reported this distribution. Peripheral and axial MSK symptoms followed the course of bowel disease in 40.3% and 28.1% of patients respectively, which was not significantly different.
Conclusion: MSK EIMs affect 6.1% of a contemporary cohort of Canadian pIBD patients. This is less than reported in literature, which may relate to physician-reported nature of our data. Their phenotype is variable, with peripheral disease more frequent than axial disease across IBD types. Our next step is to compare patients with MSK EIMs to a matched group without bowel disease-related outcomes and medication exposures.

TOUR12B

(Dis)Association Between Physical Examination and Ultrasound Findings in Rheumatoid and Psoriatic Arthritis

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Objectives: Ultrasound (US) has emerged as a sensitive method, especially when compared to clinical examination, for evaluating disease activity and damage in Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA). Several studies have shown discrepancies between the physical examination and US to detect inflammation. This study investigates and compares the frequencies of PE and US findings on a joint level, using heat map analysis and agreement between the PE and US based on the joint and disease.
Methods: The Ottawa Rheumatology CompreHEnSive TReatment and Assessment Clinic (ORCHESTRA) is a prospective cohort that includes all patients with inflammatory arthritis starting a new advanced therapy at the Ottawa Hospital Rheumatology Division. A standardized protocol is followed, including a comprehensive US scan. We analyzed the results of the PE and US of RA and PsA patients. The B-mode and Doppler findings were scored according to the OMERACT definitions on a scale between 0-3 per joint and ³ 2 was used as a threshold of positivity for this analysis. In addition to the heat map analysis, we have also tested the

agreement between the PE and US using kappa testing.
Results: There were 64 RA and 24 PsA patients with 2293 and 1051 joints being analyzed, respectively. The mean (SD) age was 59.2(14.9), with a median (IQR) disease duration of 10 (20.8) years. Thirty-six RA patients (56.3%) and 13 PsA patients (54.2%) were bio-naive at baseline. Overall, on the heatmap, same joints had higher degrees of involvement, regardless of the modality (fig1). The joint distribution for the physical exam seemed comparable for RA and PsA, whereas the Bmode findings were less prevalent for PsA than RA. US positivity was present more often in swollen joints, rather than tender joints. The agreement between PE and US was none-to-slight for most of the joints, only with a few joints having fair agreement (data not given).
Conclusion: The agreement between the US and PE is not consistent in all joints and only slight to fair in half of the comparisons. The large discrepancy between the US and PE needs further research to understand the role of each modality on the patients' care.

TOUR12C

Expert Consensus Recommendations for Musculoskeletal Ultrasound Education in Canadian Rheumatology Residency Training Programs

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Objectives: To establish expert consensus on the MSUS competencies that can be incorporated into Canadian rheumatology residency programs.
Methods: We used a 3-stage consensus design to identify MSUS competencies for Canadian rheumatology residents. We defined consensus a priori as agreement > 70%. We identified all study participants using non-probability sampling and snowball technique. In stage 1, we invited 13 MSUS experts to participate in an online meeting using a modified nominal group technique (NGT) to identify a prioritized list of MSUS competencies. In stage 2, we invited 18 individuals (MSUS experts, rheumatology residents, and rheumatology program directors) to participate in a MSUS working group. We invited members of the MSUS working group to complete three rounds of online surveys using a modified Delphi technique to establish consensus on the items that should be included for each of the prioritized MSUS competencies identified during the modified NGT. Items not reaching consensus were re-addressed in a maximum of two subsequent rounds of surveys. In stage 3, we invited MSUS experts to attend a structured online focus group to review the final list of competencies.
Results: Ten of the 13 (77%) invited experts attended the online meeting using a modified NGT,

in which experts reached consensus on a prioritized list of 31 competencies. In stage 2, members of the MSUS working group included individuals from 7/12 Canadian rheumatology programs (English stream) and two MSUS experts from the United States. There was a 100% response rate for all three rounds of the modified Delphi technique. The first round of surveys addressed 83 items derived from the prioritized competencies identified in stage 1. After 3 rounds of surveys, the MSUS working group reached consensus on all but 5 items, recommending 42 items be mandatory and 39 be optional. Members of the MSUS working group recommended that it is mandatory for all Canadian rheumatology residents to learn basic ultrasound skills; perform a focused MSUS exam of the hands, wrists, and feet for features of inflammatory arthritis including effusion, synovitis (grey scale and power Doppler), bone erosion versus osteophyte, and tenosynovitis; use MSUS to identify double contour sign in the metatarsophalangeal (MTP) joint; and perform a limited MSUS exam of the knee and ankle to identify a joint effusion (Table 1).

Conclusion: We report the expert consensus for the minimum MSUS training recommendations in Canadian rheumatology residency programs. Rheumatology programs can use these recommendations to guide development of MSUS curricula.