

WORKSHOP1F_01

Autoantibodies to 14-3-3 η : A Novel Diagnostic Biomarker for Axial Spondyloarthritis

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Methods: Serum samples (n=160) from the Bath Spondyloarthritis Biobank were selected based on availability. All patients had rheumatologist-confirmed diagnoses and met criteria for r-axSpA (n=55), nr-axSpA (n=54), or MBP (n=51). 14-3-3 η autoantibody levels were measured using a multiplex assay. Nominal regression modeled the relationship between predictors and diagnosis, generating a probability-based linear score for three models: 1) axSpA (n=109), 2) r-axSpA, and 3) nr-axSpA versus MBP. Predictors included age, sex, CRP, and HLA-B27. The r-axSpA vs MBP model was also applied to healthy controls (n=100) for comparison. Statistical significance was set at $p < 0.05$.

Results: Mean age (SD) was 55 (23) yrs for r-axSpA, 42 (14) yrs for nr-axSpA, and 30 (14) yrs for MBP. Male percentages were 67%, 41%, and 59%, respectively. Disease duration averaged 13 years for r-axSpA and 5 years for nr-axSpA. HLA-B27+ rates were 69% (r-axSpA), 72% (nr-axSpA), and 18% (MBP). ROC AUCs for the 14-3-3 η AAb model were 0.77 (all axSpA), 0.78 (r-axSpA), and 0.73 (nr-axSpA). At ~90% specificity, sensitivities were 42%, 47%, and 38%, with PPVs of 88%, 83%, and 83% - all exceeding the SPARTAN target of 33.3%. Adding age and sex to the model improved the diagnostic odds ratio (DxOR) from 5.4 to 18.4, rising to 23.4 with CRP and 63.7 with HLA-B27 (Table 1). Scores for healthy controls matched MBP ($p > 0.99$).

Conclusion: Autoantibodies to 14-3-3 η AAb differentiates radiographic and non-radiographic-axSpA from MBP, achieves a high PPV and its discrimination improves when age, sex, CRP, and HLA-B27 are added. Alongside of these clinical variables, auto-antibodies to 14-3-3 η may reduce the diagnostic delay at primary care, and complement HLA-B27.

WORKSHOP1F_02

Acyl-Alkyl-Phosphatidylcholine C40:6 is Potentially a Causal Biomarker for Obesity-Related Knee Osteoarthritis: Data from Four Independent Cohorts

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Methods: Four cohorts were included: the Newfoundland Osteoarthritis Study (NFOAS) as discovery, the Tasmanian Older Adult Cohort Study (TASOAC) and Longitudinal Evaluation in the Arthritis Program: Osteoarthritis Study (LEAP OA) as replications, and the Multicenter Osteoarthritis Study (MOST) for assessing longitudinal prediction. OB+OA+ was defined as either end-stage or radiographic knee OA with BMI \geq 30 kg/m². Plasma metabolomic profiling and genome-wide genotyping were performed. Regression models were used to identify biomarkers for OB+OA+ and MR for assessing causal relationships.

Results: Metabolome-wide association analysis of 310 OB+OA+ and 99 OB-OA+ patients from the NFOAS identified that acyl-alkyl-phosphatidylcholine C40:6 (PC ae C40:6) was associated with OB+OA+ at metabolome-wide significance ($P=1.80\times 10^{-6}$), which was replicated in the TASOAC including 102 OB+OA+ and 254 OB-OA+ and the LEAP OA including 118 OB+OA+ and 114 OB-OA+ ($P\leq 7.78\times 10^{-3}$) (Figure 1A). MR analyses showed causal relationships of PC ae C40:6 with knee OA and obesity (Figure 1B). Our longitudinal data showed that the baseline PC ae C40:6 predicted overweight status and BMI at 10-year follow-up in the TASOAC ($n=159$; $P<0.02$) and incidence radiographic and symptomatic knee OA at 5-year follow-up in the MOST ($n=337$; $P<0.03$) in subjects with baseline normal weight (Figure 1C and D). Furthermore, structural equation modeling analysis in the NFOAS ($n=526$) revealed that PC ae C40:6 had a significant indirect via obesity and a direct effect on knee OA (all $P<0.001$).

Conclusion: Our data suggested a causal relationship between PC ae C40:6 and OB+OA+. PC ae C40:6 could be a promising biomarker for monitoring OB+OA+ disease progression and a novel target for developing new therapies.

WORKSHOP1F_03

Clinical and Genetic Spectrum of Familial Mediterranean Fever in Adult Patients: Insights from a Canadian Autoinflammatory Clinic

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Methods: Patients over age 18 years meeting the Tel HaShomer diagnostic criteria for FMF were recruited from an Autoinflammatory Clinic in Toronto. Clinical records and data were analyzed. Gene panel testing was performed with Next Generation Sequencing at the Hospital for Sick Children. Variants were classified as per the American College of Medical Geneticists criteria. All patients provided written consent to be included in a case series.

Results: A total of 37 patients were included (38% male). The cohort was composed of a variety of ethnicities, predominantly including Middle Eastern (35%), Caucasian (27%) and West Asian (10%). The median age at enrollment was 43 years, symptom onset was 15 years, and diagnosis was 35 years. Thirteen patients had first symptom onset after age 18. The median diagnostic delay was 7 years. Specific triggers for flares were reported in 51% of patients; the most common being stress (42%). The most common symptoms were abdominal pain (97%), fever

(83%), and arthritis (73%). CRP was elevated during flares in 80% of patients. Of 36 patients with genetic data; 17 (47%) were homozygous/compound heterozygous, 13 (36%) were heterozygous, and 6 (17%) had no detectable variants in MEFV. The most common variants were V726A (9/36), E148Q and M694V (both in 8/36), and M680I (4/36). All were classified as variants of uncertain significance, or likely/pathogenic. Six patients did not carry any MEFV variants. A positive response to colchicine was observed in 88%, though 33% reported intolerances. IL-1 inhibitors were requested for 11 patients; all applications were denied under public funding, but compassionate access resulted in universal clinical improvement.

Conclusion: FMF remains under-recognized in adults, with significant diagnostic delay (maximum 60 years in our cohort). Colchicine intolerance limits therapy for some, and restricted IL-1 access remains a major barrier. This study adds to the limited Canadian data on adult FMF and highlights the need for greater awareness and advocacy for equitable access to evidence-based biologic therapy. Further studies are needed also to investigate the potential causes of mutation negative FMF.

WORKSHOP1F_04

ANA-Reactive IgG Memory B Cells Differentiate and Proliferate Abnormally Via T-Dependent Stimulation in Patients with SLE

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Methods: We isolated peripheral blood mononuclear cells from whole blood obtained from healthy individuals (n=6) and patients with SLE (n=7). We selected patients with SLE with clinically inactive disease, defined as a clinical SLEDAI of 0. Using a previously developed assay to identify autoreactive cells, we isolated ANA+ and ANA- IgG memory B cells using fluorescence-activated cell sorting and cultured them in vitro with CD40L and IL-21.[3] Plasmablast differentiation and immunoglobulin production were subsequently assessed using flow cytometry and IgG ELISA, respectively. Statistical analyses were performed using paired t-test with $p < 0.05$ being significant.

Results: We observed statistically significant group differences in response to T-dependent stimulation with CD40L and IL-21 between ANA+ and ANA- memory B cells in healthy individuals and patients with SLE. ANA+ cells from healthy individuals had significantly less plasma cell differentiation compared to ANA- cells, but this difference was not seen in patients with SLE ($p=0.0046$ and $p=0.7371$, respectively) [Figure 1a]. Comparable findings were seen in IgG immunoglobulin production between healthy individuals and patients with SLE ($p=0.0231$ and $p=0.9961$, respectively) [Figure 1b]. Mean age of patients with SLE was 41.0 +/- 14.6 years and mean disease duration was 13.1 +/- 5.8 years. Mean SLEDAI was 1.86 +/- 2.04, mean SDI was 0.29 +/- 0.48, and mean PGA was 0.37 +/- 0.46. 85.7% (6/7) of patients with SLE were female and 57.1% (4/7) of patients with SLE had serological activity. All patients with SLE were on hydroxychloroquine and 28.6% (2/7) of patients required either immunosuppressive medications or corticosteroids. All healthy controls were ANA negative by Hep-2 IFA testing.

Conclusion: We demonstrate a regulatory checkpoint in healthy individuals which inhibits differentiation of ANA+ IgG memory B cells into plasmablasts using a model of T-dependent

stimulation. This checkpoint is not seen in patients with SLE. This abnormality may partially explain the production of deleterious antibodies in patients with SLE.

WORKSHOP1G_01

Extremely High Maternal Anti-Ro/la Antibody Titers Predict Non-Cardiac Neonatal Lupus Erythematosus Manifestations

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Methods: Participants were identified from the SickKids NLE clinic, born between 2012 and 2019, to mothers with positive anti-Ro Ab titers within 1 year and 6 months of their child's birth. We included the first child seen in the NLE clinic per mother. Clinical details were extracted from the NLE database supplemented by retrospective chart review of both infants and mothers. Ab titers were measured using enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CIA), classified as high (ELISA: 8-100 U/mL, CIA: 20-1685 CU anti-Ro52, 20-1375 CU anti-Ro60) or extremely high (anti-Ro/La titer exceeded upper limit of detection). We excluded infants with cardiac NLE, and tested associations between maternal titer and infant NLE manifestations, jointly adjusting for infant sex, ethnicity, maternal HCQ use during pregnancy, extremely high anti-La Ab titer, and maternal rheumatic disease status.

Results: We identified 282 infants; 59% of mothers had extremely high anti-Ro titers. Hepatitis (27%) was the most prevalent NLE manifestation, followed by cytopenias (24%), rash (12%), and macrocephaly (4%). We excluded 24 infants with cardiac NLE. We observed a significant association between extremely high anti-Ro Ab titer and presence of any non-cardiac NLE manifestations (OR: 1.78, 95% CI: 1.06-3.00, P=0.028; Table), and extremely high anti-La Ab titer and cutaneous NLE (OR: 4.17, 95% CI: 1.68-10.15, P=0.002), in multivariable adjusted models.

Conclusion: Extremely high maternal anti-Ro Ab titer was significantly associated with non-cardiac NLE, and anti-La Ab titer with cutaneous NLE. These associations were significant after adjusting for extremely high titers of the alternate autoantibody and other potential risk factors for NLE. Our findings have important clinical implications, informing family counselling and improving care for infants at risk of NLE and their families.

WORKSHOP1G_02

the Interplay Between Functional Status, Quality of Life, and Productivity: a Rheum4U Precision Health Registry Study

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Methods: A cross-sectional analysis of data prospectively captured in the Rheum4U Precision Health Registry. Adults with IA attending rheumatology clinics in Calgary completed Patient-reported Outcomes Measures (PROMs), including the Clinical Health Assessment Questionnaire for functional disability (ClinHAQ; score range 0-3, no to severe disability), EQ-5D-5L for HRQoL (utility range -0.148 to 0.949, worst to perfect health), and Work Productivity and Activity Impairment instrument (WPAI domains: absenteeism, presenteeism, work impairment, and activity impairment; 0-100%, higher scores = greater impairment). Spearman rank correlations assessed associations overall and by IA type at the first registry visit with complete PROMs data (very weak (0–0.19), weak (0.2–0.39), moderate (0.40–0.59), strong (0.6–0.79), and very strong (0.8–1)). [1] Partial correlations adjusted for age and sex.

Results: A total of 1,336 patients were included, 68% were women, the median age was 52 [IQR 39-62] years. Among diagnoses, 51% had rheumatoid arthritis, 16% ankylosing spondylitis, and 15% psoriatic arthritis. The median time since diagnosis was 7.3 [IQR 2.8-13.2] years. Higher ClinHAQ scores (greater disability) were significantly associated with lower EQ-5D-5L utilities (poorer HRQoL) and higher WPAI scores (greater work and activity impairment). Absenteeism ($r=0.32$) showed weak associations, while presenteeism ($r=0.58$) and overall work impairment ($r=0.57$) were moderately correlated with disability. The strongest effects were between disability and both activity impairment ($r=0.7$), and EQ-5D-5L utilities ($r= -0.75$). EQ-5D-5L utilities were negatively associated with all WPAI domains, with weak relationship for absenteeism ($r= -0.31$), moderate for presenteeism ($r= -0.62$) and work impairment ($r= -0.61$), and strong for activity impairment ($r= -0.74$). Results were consistent across IA types and remained stable after adjusting for age and sex.

Conclusion: The Rheum4U Precision Health Registry uniquely enabled deciphering the interrelationship of key domains impacted by IA in a large Canadian cohort. Greater disability was associated with poorer HRQoL and increased productivity loss. Similarly, lower HRQoL was related to greater work impairment. The results emphasize the multidimensional, interconnected burden of IA. Day-to-day physical limitations have a more direct impact on participation than missed work alone, highlighting the importance of early, function-preserving interventions. These may yield meaningful benefits across multiple domains of patient well-being.

WORKSHOP1G_03

Ethnic Disparities in Mental Health Screening and Outcomes in Youth with Childhood-Onset Systemic Lupus Erythematosus

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Methods: We completed a retrospective study of patients with cSLE (diagnosed <18 years of age) followed in the SickKids Lupus clinic from Jan 2022-Dec 2024. Self-reported ethnicity was categorized by Canada census groups. We reviewed electronic medical records for documented MH questionnaire completion, referrals to MH providers, and identified issues at MH visit. Elevated depression and anxiety symptoms were identified by positive screens on the Patient Health Questionnaire 9-item (PHQ-9 score ≥ 10) and Generalized Anxiety Disorder 7-item (GAD-7 score ≥ 10). We tested the association between ethnicity and ever completing MH screening and ever screening positive in univariate and multivariable logistic regression models, adjusted for demographic and clinical factors (age, sex, marginalization score, duration of follow-up, neuropsychiatric SLE [NPSLE], lupus nephritis, disease damage) (significance $P < 0.05$).

Results: Our study included 138 cSLE patients; 85% were female with a median age at SLE diagnosis of 13 years (IQR 10-15). The majority of patients were of East Asian (28%), White/European (24%), and South Asian (20%) ethnicity. A total of 107 (78%) patients completed both the PHQ-9 and GAD-7; 28% screened positive on the PHQ-9 and 27% on the GAD-7. In logistic regression models, there was no significant difference in MH screening between ethnic groups. In adjusted models, Black patients had a significantly lower odds of screening positive on the PHQ-9 (OR = 0.07, CI: 0.01-0.57, $P = 0.01$). Increased marginalization (OR = 4.77, CI: 1.26-22.61, $P = 0.02$) and NPSLE (OR = 5.98, CI: 1.12-42.77, $P = 0.04$) were significantly associated with screening positive on the PHQ-9. No significant associations were found between demographic or clinical factors and GAD-7 outcomes (Table 1). For patients that screened positive on the PHQ-9 and/or GAD-7, 89% were referred to a MH provider, with the most commonly identified issue at MH visit being low mood (39%).

Conclusion: In this multiethnic cSLE cohort, there was no difference in MH screening between ethnic groups. However, Black patients had a significantly lower odds of screening positive on the PHQ-9, after adjusting for marginalization and NPSLE. Patients with cSLE experience many MH issues, especially low mood. This study highlights the need to re-evaluate the performance of MH questionnaires in assessing depression and anxiety between ethnic groups, as well as the importance of addressing MH as part of routine care.

WORKSHOP1G_04

Transition to Adulthood Through Coaching and Empowerment in Rheumatology (Tracer): Patient-Reported Outcomes of a Feasibility Randomized-Controlled Trial

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Methods: This feasibility RCT recruited youth aged 17-18 years with a pediatric-onset rheumatic disease seen at their last pediatric rheumatology visit at McMaster Children's Hospital and Children's Hospital in London. Participants were randomized to receive a Youth Transition Roadmap (YTR) only (standard of care), or YTR plus TCI - 8 monthly virtual coaching sessions covering topics from the YTR. At baseline, 8 months and 11 months, collected patient-reported

outcomes included measures of transition readiness (Transition-Q, max 100) and PROMIS® Self-Efficacy for Managing Chronic Conditions, which assesses activities of daily living (ADLs), symptoms, medications and treatments, emotions, social interactions, and informational supports.

Results: Of 65 patients approached, 31 (48%) consented and 25 went on to participate (n=12 TCI group). Over 95% of TCI appointments were attended, and 80% of patients completed 8-month follow-up questionnaires. Enrollment was split almost equally between sites. At baseline, 23% of participants in the control group reported being “definitely ready” for transition to adult care, compared to 31% in TCI. At follow-up, comparable values were 10% and 73%, respectively. Mean (SD) Transition-Q scores for the control group at baseline, 8- and 11-month follow-ups were 65.6 (15.9), 73.4 (21.8) and 80.8 (15.5) compared to 71.6 (17.5), 80.1 (12.2) and 90.0 (9.6) for the TCI group, respectively. PROMIS Self-Efficacy scores showed that the TCI group had overall improvements at each timepoint across all domains except for ADLs. The control group showed less consistent improvement, with initial stagnation at 8 months, followed by improvement at 11 months across all domains (Figure).

Conclusion: Our results suggest that TCI provides an opportunity to improve skills and confidence in youth transitioning from pediatric to adult rheumatology care. This will inform planning a multicentre RCT to assess effectiveness of a TCI program in supporting youth in their transition to adult care.

WORKSHOP2D_01

High-Resolution Thermography and Artificial Intelligence to Evaluate and Classify Rheumatoid Arthritis

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Methods: RA patients (n = 100) were recruited from an academic rheumatology clinic (Winnipeg, Canada). Healthy controls (n = 137) were recruited through advertising. Thermal images of the dorsal aspects of the hands and feet were captured with a Flir A700 camera. Regions of interest (ROI) were pre-identified as joints commonly affected in RA (Fig1A). ROIs were manually gated, and the maximum/minimum/average temperatures were extracted. Data analysis was performed in R to identify temperature differences between groups, followed by machine learning classification using ROI-restricted data. Thermograms were also analyzed using a deep learning model which deployed unsupervised feature extraction (DINOv2) and classification (ElasticNet) in Python.

Results: Principle components analysis using ROI thermogram data revealed clear separation between RA and HC (Fig1B). Differential analysis identified 56 of 114 temperature parameters that were significantly higher in RA patients. For example, the maximum temperatures of the right 5th PIP joint (adjusted $p=1.3\times 10^{-8}$) and right 4th PIP joint (adjusted $p=7.6\times 10^{-8}$) were higher in RA compared to controls. All thermogram parameters (minimum, maximum, average) were increased in joints that were tender or swollen on clinical examination in RA (Fig1C, all p-values <0.0001). Using thermogram ROI data, XGboost achieved an AUC of .869 to classify RA

from control. Rankings of variable importance by SHAP index included average temperatures of several hand joints including the Wrist and 3rd PIP. A computer vision model achieved high performance in classifying RA from controls using entire thermograms (without ROI information), with an AUC of 0.977 and recall of 0.909 (Fig1D). Principal components from this model were mapped to red, green, and blue channels to visualize thermographic differences between RA and control subjects (Fig. 1E).

Conclusion: Thermal imaging is a low-cost, accessible method for detecting synovitis in small joints and can distinguish RA patients from controls. It may enable early detection of subtle joint inflammation at the earliest stages of RA onset, such as in individuals with clinically suspect arthralgia.

WORKSHOP2D_02

Characterizing Publicly-Funded Medication Utilization and Expenditures for Individuals with Rheumatoid Arthritis of All Ages in Ontario

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Methods: Using a population-based repeated cross-sectional study design, we ascertained medication dispensation claims from the Ontario Drug Benefit (ODB) database from 2000 to 2022, among individuals with RA identified from the Ontario Rheumatoid Arthritis Database. For each year, RA individuals were required to be alive, 20 years or older, with Ontario Health Insurance Plan coverage, and contributed to annual RA population denominators from diagnosis until death, outmigration, or end of study. RA-related medication claims included biologic, conventional synthetic, or targeted DMARDs, NSAIDs, opioids, and systemic glucocorticoids. ODB funding programs included Seniors (for 65+), Ontario Disability Support Program, Trillium/Exceptional Access Program (for high-cost medications), Ontario Works (for unemployment), and a combination of other programs. Analyses included trends in annual number of RA medication claims and cumulative medication expenditures, stratified by funding program and age groups.

Results: From 2000 to 2022, the RA population increased from 60,781 individuals [34,394 aged <65; 26,387 aged 65+] to 154,675 individuals [74,182 aged <65; 80,493 aged 65+]. Among those under 65, the number of individuals with at least one ODB-related RA medication claim rose from 5,069 (15%) in 2000 to 13,121 (18%) in 2022. For RA individuals aged 65+, the number of individuals with at least one ODB-related RA medication claim increased from 22,476 in 2000 to 63,293 in 2022 (representing 78-86% of eligible RA seniors across all years). Trends in total claim volumes and expenditures by age groups are depicted in Figure 1. Total RA medication expenditures peaked in 2022 at \$256,907,248 for all ages (\$78M under 65, \$179M in 65+). Among funding sources, the ODB Seniors Program accounted for the largest share of claims, followed by the Disability and Trillium programs.

Conclusion: Ontario has seen a significant growth in publicly-funded RA medication utilization and spending over time. Among working-age individuals, nearly 1 in 5 had at least one RA medication claim, while most RA seniors consistently accessed treatment. The substantial increase in RA medication utilization and expenditures alongside the growing RA population underscores the need for more sustainable healthcare planning.

WORKSHOP2D_03

Preventable Hospital Admissions in Persons with Psoriatic Arthritis and Axial Spondyloarthritis: A Population-Based Study

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Methods: Linked administrative health datasets from the province of Alberta were used to create a combined incident cohort based on validated ICD codes for PsA and axSpA from years 2002-2023. Controls were selected in a 4:1 ratio matched for age and sex. We used the Canadian Institute for Health Information ACSC ICD-10-CA case definitions to identify hospitalizations from the Discharge Abstract Database as our outcome of interest.[1] We calculated incidence rate ratios (IRR) at 3 and 5 years from the date of the first PsA and/or axSpA diagnosis using a multivariable regression model adjusting for age, sex, location of residence, and socioeconomic status using the Pampalon Deprivation Index.

Results: There were 16,054 individuals with incident PsA and/or axSpA over the study period (45% male, mean age 59 years, 78% urban, 31% with both material and social deprivation). Of these, 40.3% (n=6,467) had at least 1 hospital admission for any reason, with a total of 22,516 unique hospitalizations, compared to 27.2% (n=18,665) of controls with 48,350 unique hospitalizations. ACSC hospitalizations accounted for 6.4% (n=1,433) of all admissions in persons with PsA/axSpA, compared to 8.0% (n=3,856) of all admissions in controls. In both cohorts, chronic lower respiratory diseases were the most frequent reasons for an ACSC admission (40% in cases, 41% in controls). After adjusting for age, sex, location of residence, and socioeconomic status, the IRR for an ACSC hospitalization was increased at 3 years (IRR 1.35, 95%CI 1.16, 1.57) and 5 years (IRR 1.23, 95%CI 1.10, 1.38) in those with PsA and/or axSpA compared to controls. Among individual ACSCs, the IRR for a diabetes-related admission was increased by 65% (IRR 1.65, 95%CI 1.14, 2.39) and angina-related admissions nearly 3 fold higher (IRR 2.74, 95%CI 1.58, 4.75) at 5 years relative to controls.

Conclusion: People with PsA and/or axSpA are at a higher risk of being hospitalized for ACSCs compared to the general population, with a signal for higher diabetes and angina related admissions in established disease. An enhanced focus on risk reduction is indicated.

WORKSHOP2D_04

Ultrasound-Detected Enthesitis Response to Advanced Therapies in Psoriatic Arthritis: a Real-World Study Highlighting Greater Improvement with IL-17 Inhibitors

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Methods: At the ORCHESTRA (Ottawa Rheumatology CompreHENsive TRreatment and Assessment) Clinic, PsA patients initiating a new AT undergo a protocolized ultrasound (US) examination, at baseline and 3 months post therapy assessing 14 entheses for elementary lesions: hypoechogenicity, thickening, and power Doppler signal (inflammatory features), as well as erosions, calcifications, and enthesophytes (damage features), each graded on a 0–3 scale (none, mild, moderate, severe). These were summed to calculate per-patient inflammation and damage scores. Patients were categorized into three groups by treatment mechanism: anti-TNF agents (TNFi), JAK inhibitors (JAKi), and IL-17 inhibitors (IL17i). Due to sample size limitations, JAKi or TNFi were combined when analyzing bio-naïve and bio-experienced subgroups. Baseline and three-month disease activity indices and US scores were compared.

Results: Sixty-two patients who had 3 months follow-up were included, 27 of whom (43.5%) were AT-naïve. 20 patients (32.3%) initiated TNFi, 10 patients (16.1%) initiated JAKi, and 32 patients (51.6%) initiated IL17i. Baseline disease activity and US findings were similar across groups. However, US-enthesal inflammation scores differed at follow-up ($p = 0.025$), with lower scores in patients receiving IL17i compared with JAKi (2 [0–6.5] vs. 6.5 [3.5–12]; $p = 0.036$) and a trend of higher reductions in patients receiving IL17i compared with JAKi or TNFi (table). Among biologic-experienced patients, despite having similar baseline clinical and US scores, follow-up enthesal inflammation scores were lower with IL17i (1 [0–4] vs. 7 [4.5–11.5]; $p = 0.001$) with higher reduction at 3 months than others (4 [0–8] vs. 0 [–4–4]; $p = 0.049$). More IL17i recipients demonstrated reduced enthesal Doppler signal (7 [31.8%] vs. 0 [0%]; $p = 0.031$) (Table). Same differences were not seen in bionnaïve patients (data not shown).

Conclusion: In this real-world cohort of PsA patients initiating AT, IL17i were associated with greater improvement in US-detected enthesal inflammation compared with JAKi and TNFi, particularly among biologic-experienced patients. These findings support a potential preferential effect of IL-17 blockade on enthesal inflammation, consistent with its pathogenic role. US proved a sensitive tool for detecting early treatment-related changes, highlighting its value in evaluating therapeutic response in PsA.

WORKSHOP3F_01

Adverse Pregnancy Outcomes Within the Lupus in Pregnancy (Legacy) Cohort: Anti-Phosphatidylserine/prothrombin Igg Antibodies Are Stronger Predictors than Lupus Anticoagulant

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Methods: LEGACY includes Systemic Lupus International Collaborating Clinics in Canada, South Korea, Peru, and Mexico. Pregnant SLE women are consecutively enrolled <17 weeks' gestation and followed at pre-defined visits throughout pregnancy and postpartum. At enrolment, plasma was tested for aPS/PT, using ELISA (Werfen, San Diego), with positivity cutoffs for IgG and IgM as >30 chemiluminescent units. LAC testing was performed at each site using validated assays. The present analysis includes the first 98 pregnancies with aPS/PT results. APO were a composite outcome of either: 1) fetal death >20 weeks, 2) neonatal death, 3) placenta-mediated preterm delivery <36 weeks, and/or 4) small for gestational age (<5th percentile). We performed multivariable hazards models with frailties and gestational age as the time axis to assess associations between APO and aPS/PT IgG and/or IgM versus LAC. Maternal covariates at enrolment included age, body mass index, prior nephritis, SLE Pregnancy Disease Activity Index, and medications. We used Harrell's C-index to assess model discrimination.

Results: Among 98 SLE pregnancies, 9 (9%) were aPS/PT IgG-positive, 25 (26%) were aPS/PT IgM-positive, and 11 (11%) were LAC-positive (Table1). Eight pregnancies (8%) were positive for both aPS/PT (IgG and/or IgM) and LAC. Thirteen pregnancies (13%) experienced APO, including 5/9 (56%) in the aPS/PT IgG-positive group and 5/11 (46%) in the LAC-positive group. In multivariable analysis, aPS/PT IgG positivity was strongly associated with APO (HR 12.2, 95%CI 1.7-87.2), whereas IgM and/or overall aPS/PT positivity showed non-significant trends [HR 1.9 (95%CI 0.3-11.2) and HR 2.2 (95%CI 0.4-11.2), respectively]. LAC positivity was also associated with a substantially higher APO risk (HR 7.8, 95%CI 1.7-35.1), though less strongly than aPS/PT IgG. Discriminative performance was slightly higher for aPS/PT IgG (adjusted C-index 0.80, 95%CI 0.65-0.95) compared with LAC, aPS/PT IgM, and combined aPS/PT IgG and/or IgM models (0.78, 95%CI 0.68-0.89; 0.72, 95%CI 0.59-0.85; and 0.73, 95%CI 0.61-0.86, respectively).

Conclusion: In this preliminary analysis of the LEGACY cohort, aPS/PT IgG demonstrated a stronger independent association with APO and slightly better discriminative performance than LAC. These findings suggest that aPS/PT IgG may outperform LAC in predicting APO and could improve risk stratification in SLE pregnancies. **Supported by a CIORA grant.**

WORKSHOP3F_02

Characterizing Immune Cell Subsets and Interferon in the Kidneys of Lupus Nephritis Patients

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Methods: We optimized an IMC panel to simultaneously evaluate IFI-P expression and characterize immune cell subsets directly within kidney tissue. Paraffin-embedded biopsies from LN patients in the Lupus Nephritis New Emerging Team and University of Toronto Lupus Clinic cohorts were analyzed. A pseudo-tissue composed of IFN-stimulated and unstimulated peripheral blood mononuclear cells in a clot that was embedded paraffin was used as a positive and negative control for antibody specificity. The panel includes 34 metal-conjugated antibodies to detect renal resident cells, infiltrating immune cells (T cells, B cells, monocytes, macrophages, dendritic cells), IFI-Ps, and fibrosis.

Results: The IMC panel successfully detected renal and immune cell subsets, as well as distinct patterns of IFI-P expression in various renal compartments (Figure 1A). IFI-P expression demonstrated a moderate to strong correlation between the different kidney compartments (Figure 1B). Preliminary analysis of 10 LN biopsies revealed a trend to increased IFI-P staining intensity in all of the renal compartments of non-responders when compared to responders (Figure 1C). This achieved statistical significance ($p < 0.05$) for IFNAR1, MX1, and PKR in the glomerulus and PKR in the non-proximal tubules, consistent with the concept that elevated renal levels of IFN are associated with poorer response to treatment.

Conclusion: This study establishes a validated IMC-based approach for high-resolution spatial profiling of interferon signatures and immune cell subsets in LN kidney biopsies. Preliminary data suggest that elevated IFI-P expression is associated with non-response to therapy, supporting further investigation of IFI-Ps as predictive biomarkers. Application of this panel to larger LN cohorts may enable early patient stratification and guide precision treatment strategies to improve renal outcomes.

WORKSHOP3F_03

Non-IgG Anti-Double-Stranded DNA Antibodies in Systemic Lupus Erythematosus: Biomarkers of Extrarenal Disease Activity

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Methods: We studied 87 adult (≥ 18 years) SLE patients from a Canadian cohort without current LN, all with detailed clinical phenotyping. Serum IgG, IgM, and IgA anti-dsDNA levels were measured by ELISA. Extrarenal disease activity was quantified using the clinical SLEDAI-2K (cSLEDAI; range 0–12). Associations between individual isotypes and isotype ratios (IgM/IgG, IgM/IgA) and cSLEDAI were examined using Spearman's correlation. Group comparisons across predefined activity categories were performed with Mann-Whitney U tests (two groups) or Kruskal-Wallis tests with post hoc multiple-comparison correction (>2 groups).

Results: Of 87 non-LN SLE patients, 51 (58%) were clinically active (cSLEDAI ≥ 1). In this

active subgroup, IgM anti-dsDNA levels were inversely correlated with disease activity ($r = -0.34$, $p = 0.016$), whereas IgG and IgA anti-dsDNA levels showed no significant correlation with cSLEDAI. A lower IgM/IgA anti-dsDNA ratio was also associated with higher disease activity ($r = -0.30$, $p = 0.033$), while the IgM/IgG ratio was not. Patients with high disease activity (cSLEDAI >6) had significantly lower IgM anti-dsDNA levels than those with mild/moderate activity ($p = 0.0028$). When disease activity was categorized as inactive (cSLEDAI 0), mild/moderate (1-7), and high (≥ 8), IgM anti-dsDNA levels remained lowest in the high-activity group, with significant differences between inactive vs high ($p = 0.046$) and mild/moderate vs high ($p = 0.0278$).

Conclusion: In non-LN SLE, lower IgM anti-dsDNA levels and a reduced IgM/IgA ratio are associated with higher extrarenal disease activity, whereas IgG and IgA anti-dsDNA alone do not track clinical activity. These findings support a potential protective/regulatory role of IgM anti-dsDNA and suggest that IgG-only testing may miss clinically relevant isotype patterns.

WORKSHOP3F_04

Feasibility of Saliva-Based Autoantibody Detection in Systemic Lupus Erythematosus

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Methods: Paired serum and saliva samples were collected from SLE patients and healthy controls. Serum was collected by venipuncture and stored at -80°C . Saliva was collected by 1) swab brushing of the gingival crevicular fluid on the gum line, enhancing IgG capture, or 2) passive drooling. Saliva was stored at -20°C . Antinuclear antibodies (ANA) were detected by conventional indirect immunofluorescence on HEp-2 cells (NOVA Lite, Werfen; cut-off $\geq 1:80$), and for a subset of participants, SLE-related antibodies were quantified by QUANTA Lite ELISA for dsDNA ($n=6$ SLE, $n=3$ healthy controls), and FIDIS Connective Luminex 100 (Biosynx, Theradiag) for the remaining antibodies, anti-U1-RNP, histone, Jo-1, Pm-Scl, PCNA, Ro62/TROVE2, Ro52/TRIM21, SSB/La, Sm, Sm/RNP, Scl-70, ribosomal P, and centromere B ($n=18$ SLE, $n=6$ healthy controls).

Results: We included 19 SLE patients and 6 healthy controls. Among these participants, 16 SLE patients (84.2%) and one (16.7%) healthy control were serum-positive for ANA. With gum line brushing, ANA positivity was observed in 10/16 (62.5%) of serum-positive SLE cases (Figure 1), and in one (100%) serum-positive healthy control. End-point ANA titers were reduced in saliva-positive cases relative to serum, with an average change of two dilution factors. When expert-level ICAP ANA patterns were included, 4/10 (40%) were congruent. There was a trend towards moderate correlation in anti-dsDNA titres between serum and saliva ($r=0.65$, $p=0.06$). For the remaining autoantibodies, where the presence or absence of any antibody in the ENA panel was considered a positive or negative ENA, 8/14 (57.1%) of the serum/saliva samples were in agreement. None of the passive drooling samples were ANA, anti-dsDNA, or ENA positive.

Conclusion: Saliva collected by brushing the gum line represents a promising matrix for autoantibody detection in SLE, particularly for ANA screening and anti-dsDNA titers. This

minimally invasive approach can be self-administered and easily transported to laboratories equipped for diagnostic testing. Ongoing studies aim to optimize autoantibody detection and further validate the method in larger cohorts.