

## 1

### **Long Term Safety of Rituximab in Rheumatoid Arthritis Clinical Trials: A 10-Year Follow-Up Study**

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**Objective:** To assess rituximab (RTX) long-term safety in rheumatoid arthritis (RA) patients (pts) in clinical trials.

**Methods:** Safety data from a global clinical trial programme were pooled and analyzed to evaluate safety in moderate-to-severe active RA pts treated with RTX plus methotrexate (MTX). Pts received either 2x1000 mg or 2x500mg of RTX (IV infusions, 2 weeks apart), preceded with IV methylprednisolone (100 mg). All pts received stable doses of MTX weekly (10-25mg). RTX retreatment was offered based on physician's decision of clinical need, including active disease evidence.

**Results:** As of September 2011, 3595 pts had been treated with RTX, for a total exposure of 14 008 pt-years (pt-yrs). The analysis contained >10 yrs of follow-up with up to 19 courses of RTX. Baseline demographics and disease characteristics were similar across the long-term, the all-exposure, and the pooled placebo populations, although the former patients had a longer mean RA disease duration and a greater number (n=2.4) of previous disease modifying anti-rheumatic drugs, not including MTX. The safety profile of RTX was comparable to the pooled placebo population, with the exception of infusion-related reactions (IRR), which occurred after the first infusion of the first course (22%), with 0.5% reported as serious (over all courses). Generally, rates of adverse events (AEs), serious AEs (SAEs), and serious infectious events (SIEs) remained stable over time. SIE rates in the RTX all-exposure, RTX long-term, and pooled placebo populations were 3.80, 2.76, and 3.79 events/100 pt-yrs, respectively. SAEs that occurred in >1% of pts comprised osteoarthritis, pneumonia, falls and exacerbations of RA. Lower respiratory tract infections were the most frequent serious infections, with pneumonia being predominant (2%). Serious opportunistic infections were rare, with a rate comparable to the placebo population (0.05 vs. 0.09 events/100 pt-yrs, for all-exposure vs. placebo respectively). The most frequent cardiac AE was myocardial infarction, with a rate of 0.40 events/100 pt-yrs consistent with rates in the general RA population (0.48-0.59 events/100 pt-yrs). No evidence of an increase in malignancy over time or RTX course was found.

**Conclusion:** Data from long-term follow-up of RA pts treated with RTX in clinical trials indicate that RTX continued to be well tolerated over time and over multiple courses, with safety profiles similar to that of the placebo population and consistent with published data on pts with moderate-to-severe RA. No new safety signals were observed with increasing duration of exposure, including inpatients with >5 yrs of follow-up.

## 2

### **Patient Demographics, Disease Parameters, and Cardiovascular Risk Factors of Rheumatoid Arthritis Patients at Tocilizumab Initiation: The Umbrella Study**

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**Objective:** Efficacy of tocilizumab in RA has been demonstrated in numerous controlled clinical trials. Post-marketing observational studies assessing real-life effectiveness and safety are essential to demonstrate true population-based benefits. This analysis describes the baseline profile of Canadian patients enrolled in ACT-UP, a multi-national non-interventional study in patients with moderate-to-severe RA treated with tocilizumab.

**Methods:** ACT-UP is an ongoing, multi-national, non-interventional study with tocilizumab. To date, 1,046 patients have been enrolled from 14 countries. In this analysis, baseline data from the 200 Canadian patients participating in ACT-UP were used.

**Results:** Of 200 patients included, 70.0% had inadequate response to biologic DMARD(s) (Biologic-IR), 27% were DMARD-IR, and 3% had missing data. Among Biologic-IR patients, 48.9% had been treated with one prior biologic, 24.8% with two and 26.3% with  $\geq 3$ . Prior biologics were: etanercept (49.6%), infliximab (35.3%), adalimumab (32.4%), abatacept (24.5%), certolizumab (20.1%), rituximab (10.1%) and golimumab (10.1%). Mean (range) age at baseline was 55.5 (19.3-80.3) years (Biologic-IR vs. DMARD-IR: 55.4 vs. 55.8 years;  $P=0.847$ ) with disease duration of 12.4 (0.0-50.0) years (13.5 vs. 9.8 years;  $P=0.025$ ). 65.2% were rheumatoid factor positive (61.8% vs. 72.3%;  $P=0.273$ ), and 51.5% had evidence of structural joint damage (56.8% vs. 37.0%;  $P=0.016$ ). Tocilizumab was used as monotherapy in 37.2% of patients (35.8% vs. 39.6%;  $P=0.620$ ). Concomitant methotrexate [mean dose=19.9 mg/week], NSAID(s), and steroids [mean prednisone dose=9.6 mg/day] was reported for 31.0%, 37.0%, and 18.0% of patients, respectively. Mean disease parameters at baseline were: patient global = 63.1 mm (Biologic-IR vs. DMARD-IR: 63.9 vs. 60.6 mm;  $P=0.349$ ), pain = 63.2 mm (64.6 vs. 60.7 mm;  $P=0.303$ ), fatigue = 63.3 mm (63.9 vs. 61.5 mm;  $P=0.550$ ), morning stiffness = 58.9 mm (61.9 vs. 52.6 mm;  $P=0.011$ ), physician global = 61.3 mm (61.6 vs. 60.7 mm;  $P=0.349$ ), CRP = 18.0 mg/L (17.4 vs. 20.0 mg/L;  $P=0.599$ ), TJC28 = 12.6 (12.2 vs. 13.9;  $P=0.136$ ), SJC28 = 9.3 (9.2 vs. 9.8;  $P=0.455$ ), HAQ-DI = 1.55 (1.57 vs. 1.48;  $P=0.443$ ), and DAS28-CRP = 5.3 (5.4 vs. 5.3;  $P=0.723$ ). The most common cardiovascular risk factors were hypertension (36.0%), hyperlipidemia (20.5%), smoking (18.5%), diabetes (13.0%), and family history of premature CAD (10.0%). No significant differences were observed between Biologic-IR and DMARD-IR patients.

**Conclusion:** One quarter of patients initiating tocilizumab in Canada do so before failing treatment with other biologics. Longer disease duration and higher rate of structural damage were observed at baseline in Biologic-IR compared to DMARD-IR patients but disease activity parameters were comparable.

### 3

#### **Retention Rates and Effectiveness of Abatacept at 12 Months: A Subgroup Analysis of the Canadian Population from the ACTION Study**

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**Objective:** To evaluate real-world usage and outcomes with intravenous abatacept, as monotherapy and in combination with DMARDs, in Canadian patients with RA who were enrolled in the ACTION (AbataCepT In rOutiNe clinical practice) study.

**Methods:** ACTION is a non-interventional, prospective cohort of patients with RA treated with intravenous abatacept in Europe and Canada. The study was initiated in May 2008; patients were biologic naïve or had an inadequate response to prior biologics. This analysis included all Canadian patients followed-up in ACTION at the data cut-off on February 28, 2012 (1 year of follow-up interim analysis). Retention rates (Kaplan–Meier estimator), core components and patient-reported outcomes at 12 months are reported (as-observed analysis).

**Results:** The Canadian analysis comprised 229 evaluable patients from 36 sites in 8/10 Canadian provinces. At abatacept initiation, mean (standard deviation [SD]) age was 57.5 (12.3) years, RA duration was 9.9 (8.9) years, tender joint count/28 was 13.61 (7.42), swollen joint count/28 was 10.83 (6.25) and Health Assessment Questionnaire-Disability Index was 1.58 (0.59); 57 (24.9%) patients were biologic naïve, 80 (34.9%) had received 1 previous anti-TNF and 87 (38.0%)  $\geq 2$  previous anti-TNFs. A total of 43 (18.8%) patients initiated abatacept monotherapy and 186 (81.2%) initiated combination therapy; 110/229 patients were on treatment and had data available at 12 months. The overall retention rate (95% CI) in this Canadian population was 69.0% (62.3, 74.8) at 12 months and did not differ in the monotherapy and combination therapy groups (65.4% [48.6, 77.9] vs 69.8% [62.3, 76.1]). Overall, abatacept demonstrated numerical improvement in clinical outcomes at 12 months for mean (SD) change from baseline in swollen joint count (–5.76 [6.84], n=103), physician global assessment of disease activity (visual analogue scale [VAS] 100 mm: –25.32 [23.93], n=53) and patient global assessment of pain (VAS 100 mm: –17.84 [26.86], n=76). Overall mean (SD) patient global assessment of satisfaction of current RA treatment (VAS 100 mm) at 12 months was 68.64 (24.25), n=69.

**Conclusion:** In a Canadian real-life setting, abatacept had similar retention rates at 12 months when used as monotherapy or in combination with DMARDs. In a previous analysis of the entire ACTION cohort, monotherapy was not a prognostic factor of abatacept discontinuation. Despite low patient numbers, this subgroup had similar baseline characteristics to the entire cohort, although abatacept was initiated after fewer previous biologics. Abatacept monotherapy can be successfully used in RA subpopulations in whom biologic monotherapy may be considered.

#### 4

##### **Predictors of ACR/EULAR Boolean and SDAI Remission in Patients with Established Rheumatoid Arthritis Treated with Anti-TNF: An Analysis from the Prospective, Observational Registry, BioTRAC**

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**Objective:** Early achievement of remission is associated with improved clinical, functional and

radiographic outcomes<sup>1</sup>. Recent recommendations of the Canadian Rheumatology Association dictate that treatment target should be remission or, when not possible, low disease activity. The aim of this analysis is to define the predictive factors of time to disease remission in established rheumatoid arthritis (RA) patients treated with infliximab.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab or golimumab as first biologics or after having been treated with a biologic for < 6 months. RA patients treated with infliximab who were enrolled between 2002-2012 and had  $\geq 1$  follow-up assessment were included. Remission was defined according to the ACR/EULAR Boolean criteria ( $TJC28 \leq 1$ ,  $SJC28 \leq 1$ ,  $CRP \leq 1$  mg/dL, and  $PtGA \leq 1$ ) or  $CDAI \leq 2.8$ . Independent predictors of remission were identified by multivariate Cox regression considering as potential confounders parameters showing a statistical trend ( $P < 0.150$ ) in univariate analyses.

**Results:** A total of 671 patients were included of whom 494 (73.6%) were female. At baseline, mean (SD) age was 56.0 (13.5) years and mean (SD) disease duration was 10.3 (10.1) years. Median time to CDAI and Boolean remission was 47.3 and 54.1 months, respectively. In univariate analysis, the following factors showed a statistical trend in their association with longer time to CDAI remission: earlier enrolment period ( $P=0.117$ ), increased age ( $P=0.070$ ), longer disease duration ( $P=0.008$ ), female gender ( $P=0.143$ ), and increased baseline disease activity as indicated by TJC28 ( $P < 0.001$ ), SJC28 ( $P < 0.001$ ), morning stiffness ( $P=0.003$ ), pain ( $P < 0.001$ ), PtGA ( $P < 0.001$ ), MDGA ( $P < 0.001$ ), HAQ-DI ( $P < 0.001$ ), and CDAI ( $P < 0.001$ ). Rheumatoid factor (RF) status, number of previous DMARDs, and initial (first 6 months) treatment with DMARD(s), NSAID(s) or steroid(s) did not predict achievement of remission. In multivariate analysis, baseline CDAI [HR (95%CI): 0.97 (0.96, 0.98);  $P < 0.001$ ] and disease duration [0.98 (0.97, 1.00);  $P=0.018$ ] were identified as independent predictors of time to CDAI remission. Similarly, multivariate survival analysis showed that increased disease duration [0.98 (0.96, 1.00);  $P=0.047$ ] and increased pain [0.98 (0.98, 0.99);  $P < 0.001$ ] at baseline were associated with a lower chance of achieving ACR/EULAR Boolean remission.

**Conclusion:** Upon adjusting for potential confounders, increased disease duration before anti-TNF initiation is an independent predictor of longer time to remission. The results of these real-world Canadian data support findings that earlier initiation of anti-TNF agents may be associated with increased remission rates when stringent definitions of remission are considered.<sup>1</sup> Smolen JS et al. Ann Rheum Dis. 2009; 68:823-7.

## 5

### **Corticosteroid Use in Rheumatoid Arthritis Patients on Infliximab: Treatment Implications and Impact on Durability of Response Based on a Real-World Canadian Population**

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**Objective:** Examine the effect of chronic systemic corticosteroids (CS) treatment at different

doses on the incidence of infections in RA patients treated with IFX in a real-life setting. The impact of CS use on the sustainability of remission was also assessed.

**Methods:** BioTRAC is an ongoing, Canadian, prospective, registry of rheumatology patients initiating treatment with IFX or golimumab as first biologics or after having been treated with a biologic for less than 6 mos. RA patients treated with IFX enrolled between 2002 and 2012 were included. Cox regression was used to examine the time-dependent association between systemic CS dose (no CS,  $\leq 5$  mg,  $> 5$  mg) and the incidence of first infection, while adjusting for possible confounders, and to assess the sustainability of remission.

**Results:** 838 RA patients were included in the analyses. Mean (SD) age of the patient cohort was 56.6 (13.5) yrs and mean (SD) duration since diagnosis was 10.5 (9.8) yrs. At initiation of treatment, 38.2% of patients were treated with a systemic CS. After a mean (SE) follow-up of 51.3 (1.7) mos, 310 infections were reported for 19.7% of patients (19.6 /100 PYs). Among these, the majority (90.0%) were non-serious infections. Multivariate survival analysis using Cox regression showed that, upon adjusting for enrolment period, age, disease duration, number of steroid administrations, and HAQ-DI, the hazard ratio (HR) (95%CI) for acquiring an infection was 2.48 (1.24-4.98) in patients treated with high dose ( $> 5$  mg) CS compared to patients not receiving CS. Treatment with low dose CS was also associated with an increased hazard for infection (HR (95%CI) = 2.12 (0.97-4.66)) which did not reach statistical significance. Consistent with previous studies, increased HAQ-DI (HR (95%CI) = 1.51 (1.15-1.92)) and disease duration (HR (95%CI) = 1.01 (1.00-1.03)) were also identified as significant predictors. CS use was continued in 15% of cases despite the achievement of remission (DAS28-CRP: 15.2%; CDAI: 15.7%). Survival analysis did not show a significant positive effect of steroid use on sustainability of remission [HRDAS28-CRP (95%CI) = 1.40 (0.95-2.06); HRCDAI (95%CI) = 1.19 (0.75-1.88)].

**Conclusion:** Treatment with systemic CS was associated with an increased hazard ratio for acquiring an infection upon adjusting for possible confounders. Despite the achievement of remission, steroid use was continued in 15% of cases without having an impact on sustainability of remission. Treatment with systemic CS is an independent predictor of infection in patients treated with anti-TNF agents and the use of concomitant medications should be considered in the interpretation of safety data.

## 6

### **Variability in Patient Characteristics and Outcomes in Rheumatoid Arthritis upon Infliximab Treatment Based on the Size of Biologic Treatment Registry Site**

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**Objective:** Efficacy of TNFi in the management of rheumatoid arthritis (RA) has been

demonstrated in numerous controlled clinical trials. Variations with respect to patient (pt) profile, extent of physician familiarization with TNFi agents, and pt management may affect real-world outcomes. This analysis compared the pt profile and outcomes of RA patients (pts) treated with infliximab under routine practice in biologic treatment registry sites of different sizes.

**Methods:** BioTRAC is an ongoing, prospective registry of pts initiating treatment for RA with infliximab or golimumab as first biologics or treated with a biologic for < 6 mons. Pts with RA treated with infliximab who were enrolled between 2002-2012 were included in the analysis (N=832). The number of pts enrolled in BioTRAC at each site was used as the measure for the size of the registry site, resulting in the classification of 3 sizes of registry sites - Group A=sites enrolling 1-15pts; Group B=sites enrolling 16-35pts; Group C=sites enrolling>35 pts. The total number of pts enrolled in each type of rheumatology practice site was; Group A:n=324, Group B:n=239, Group C:n=269.

**Results:** Mean age of the cohort was 55.8yrs with 76% of pts being female and 74% RF+. Pts seen at larger sites had significantly shorter disease duration (Group A:11.9yrs, Group B:10.9yrs, Group C:7.5yrs;  $P < 0.001$ ) and had been treated with a smaller number of previous DMARDs (2.5, 2.5, 1.6, respectively;  $P < 0.001$ ). Furthermore, a trend towards lower disease activity at infliximab initiation was observed in larger sites as indicated by the decreased physician global assessment (7.0 vs. 6.4 vs. 6.2;  $P < 0.001$ ), DAS28-CRP (5.6 vs. 5.3 vs. 5.3;  $P=0.023$ ), CDAI (38.1 vs. 34.5 vs. 35.0;  $P=0.019$ ), and SDAI (40.9 vs. 36.3 vs. 36.9;  $P=0.009$ ). Significant differences were also observed with respect to pt management with a significantly greater proportion of pts in larger sites being treated with concomitant DMARD (87.3% vs. 89.5% vs. 95.2%;  $P=0.004$ ) and lower proportion being treated with corticosteroid (23.5% vs. 22.6% vs. 15.6%;  $P=0.044$ ). Upon adjusting for baseline disease activity, DAS28-CRP remission ( $P=0.013$ ) and minimal clinically meaningful improvement in HAQ-DI ( $\Delta \geq 0.25$ ;  $P=0.025$ ) over 24 mons was significantly greater among pts seen in larger sites.

**Conclusion:** Consistent with findings from a Canadian early RA registry<sup>1</sup>, results of this study demonstrate that significant variation in disease characteristics, pt management and outcomes exist within the registry based on the size of the site. A trend towards earlier infliximab initiation and improved outcomes was observed with larger enrolment sites.

## 7

### **Correlation of Individual HAQ Questions with Outcome Measures in Rheumatoid Arthritis: Implications for Instrument Reduction**

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**Objective:** Despite the importance of HAQ in assessing patient-reported functional status, it was originally developed primarily for research studies. As a result, HAQ has been critiqued for being time-consuming, not easily scored, and, thus, not contributing to decisions in routine care, and being influenced by comorbidities. (1) The objectives of this analysis were to describe the

correlation of individual HAQ questions with outcome measures used in Rheumatoid Arthritis (RA) and to examine whether the instrument could be reduced to better reflect routine clinical practice.

**Methods:** BioTRAC is an ongoing, prospective registry of RA, AS, or PsA patients initiating infliximab or golimumab as first biologics or after < 6 months of biologic treatment. Data from RA patients treated with infliximab in 2002-2011 were used. Parameter correlation was described with the Pearson's correlation coefficient. The impact of each question on aids/devices/help use was assessed with logistic regression. Factor analysis was used to assess the variability in HAQ score due to each question.

**Results:** 877 patients with 4,180 complete HAQ assessments were included. Higher pain, patient global assessment (PtGA), tender joint count (TJC-28) and, to a lesser extent, swollen joint count (SJC-28) were associated with increased functional impairment. In correlation analysis, individual HAQ questions correlated at different extents with each outcome measure. Q5B, "Are you able to take a tub bath?", showed the lowest correlation with the patient outcomes while the questions related to "Rising" (Q2A, "Stand up from an armless straight chair?"; Q2B, "Get in and out of bed?") showed the highest overall correlation. All individual questions were significantly associated with the use of aids/devices/help within their corresponding category with the exception of Q3B, "Lift a full cup or glass to your mouth?" and Q8B, "Get in and out of car?". In factor analysis, "Dressing & Grooming" was found to account for 66.5% of the matrix variance suggesting that the ability to dress/groom alone may be the main driver of HAQ.

**Conclusion:** Variability exists in the correlation of individual HAQ questions with patient-reported and clinical outcomes. Pain and joint tenderness are significantly associated with the individual functions of HAQ while SJC is less important. The ability to dress/groom alone was the main driver of HAQ variability which may have implications from an occupational health perspective and in the design of self-report instruments for daily activities. References: AC&R 2011;63:S486-S490; The Rheumatologist. Jan 2013.

## 8

### **Development of Cardiovascular Quality Indicators (QIs) for Rheumatoid Arthritis (RA): Defining the Evidence Base and Identifying Candidate QIs**

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**Objective:** Rheumatoid arthritis (RA) causes a significantly increased risk of death compared to those without RA, primarily due to premature cardiovascular disease (CVD). Yet, risk reduction strategies for CVD are rarely employed in Rheumatology clinics. To address this clinical gap, we are developing CV quality indicators (QIs) for use in clinical practice.

**Methods:** A systematic review of the literature on CVD risk reduction, based on predefined inclusion criteria, was conducted to identify all existing guidelines and QIs in the rheumatology and general preventive care literature. Four medical databases (EMBASE, MEDLINE, CINAHL

and Web of Science) were searched over a 10-year period ending April 2013. A Grey literature search was also conducted. In total 16,165 abstracts were screened and 40 guidelines and nine QI sets were identified. Recommendations and indicators were abstracted in the following areas: CVD risk assessment, hypertension, lipids, obesity and diabetes screening, lifestyle measures, smoking, aspirin use, corticosteroid use, and CV safety of NSAIDs. The resultant set of 12 QIs and evidence monographs were presented to a Canadian expert panel of two cardiologists and four rheumatologists. Input on the scope, audience, specification and wording of the indicators was received and an iterative process was used to revise the indicators and achieve consensus.

**Results:** From the initial set of 12 draft QIs, a final set was selected consisting of 11 QI's addressing the following themes: communication to primary care physicians (PCPs) about increased CV risk in RA, CV risk assessment strategies, defining smoking status and providing cessation counselling, screening for hypertension and communicating findings to PCPs, measurement of a fasting lipid profile, screening for diabetes, exercise recommendations, BMI screening and weight loss counseling, minimizing corticosteroid use and communicating to patients at high risk of CV events about the risks/benefits of NSAIDs.

**Conclusion:** Eleven process QIs for primary prevention of CV events in RA patients have been developed. Importantly, the theme of shared care between PCPs and rheumatologists is emphasized.

## 9

### **A Systematic Review of Best Practices for Cardiovascular Disease Prevention in Persons with Rheumatoid Arthritis**

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**Objective:** Cardiovascular disease (CVD) is the major cause of excess mortality for persons with rheumatoid arthritis (RA). The aim of this study was to conduct a systematic review of the literature to identify all guidelines and quality indicators (QIs) pertaining to CVD primary prevention in patients with RA and in the general population so as to identify best practices that could be applied to patients with RA and ultimately develop CVD QIs for RA.

**Methods:** EMBASE, MEDLINE, CINHALL and Web of Science were searched from 2003 until April 2013 using MeSH terms and keywords pertaining to the following themes: guidelines, QIs, and QIs from the past 10 years were identified, only guidelines published within 5 years were ultimately included due to the rapidity of advances in the topic.

**Results:** 16,165 unique abstracts were screened and 716 underwent full text review (10-year data). From these, 44 guidelines underwent AGREE II rating. The grey literature review added 33 guidelines. After quality rating, a total of 40 guidelines and nine QI sets were selected for inclusion. Ten guidelines provided recommendations for CVD prevention in patients with RA but only four RA-specific CVD QIs were identified (three European: one on general comorbidity screening, one on formal CVD risk estimation, one on exercise and one American one on



minimizing steroid use). The most commonly reported recommendation for RA patients was screening for CVD risk factors including hypertension, smoking, and dyslipidemia. The frequency of screening for modifiable risk factors and the treatment of risk factors were not consistently described in the RA literature.

**Conclusion:** CVD prevention is an important part of routine care for patients with RA.

Unfortunately existing RA-specific CVD QIs do not adequately address risk factor screening or treatment in the following areas: smoking cessation, diabetes, dyslipidemia and hypertension screening, obesity, safety of NSAIDs, or frequency of CVD risk screening. A comprehensive set of CVD QIs in RA is essential to better measure and identify gaps in CVD screening and improve CVD care for persons with RA.

RA and CVD. A Grey literature search was also conducted. Abstracts were screened for inclusion and rated using the Appraisal of Guidelines for Research & Evaluation (AGREE) II instrument. The inclusion criteria were: English language, relevance to primary CVD prevention, endorsement by a medical society, and high quality by AGREE II rating. Although guidelines

## 10

### **Identification of Psoriatic Arthritis Putative Biomarkers in Synovial Fluid by Quantitative Mass Spectrometry**

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**Objective:** There is a high prevalence of undiagnosed psoriatic arthritis (PsA) in patients seen in dermatology clinics. Identifying soluble biomarkers for PsA will help in screening psoriasis patients for appropriate referral to a rheumatologist as well as provide further insight into disease pathogenesis. However, identification of novel protein biomarkers in peripheral blood is difficult and unreliable. Potential PsA biomarkers are likely to originate in sites of inflammation such as inflamed joints and subsequently enter systemic circulation. We hypothesize that quantitative proteomic analysis of synovial fluid (SF) obtained from PsA patients, will generate a comprehensive list of proteins specific to PsA, facilitating the identification of potential PsA screening biomarkers.

**Methods:** SF was obtained from swollen knee joints of PsA patients, and age/sex matched early osteoarthritis controls. Using strong cation exchange chromatography, followed by liquid chromatography and tandem mass spectrometry, we extensively characterized the proteomes of pooled SF from ten PsA and ten controls. Extracted ion current (XIC) intensities were used to calculate protein abundance ratios, and were utilized to identify upregulated proteins (PsA/OA ratio > 2). Selected reaction monitoring (SRM) assays were developed to quantify potential markers an independent set of samples with PsA and controls.

**Results:** We identified and quantified 443 proteins from both groups (False Discovery Rate < 0.05), and 44 of these represented upregulated proteins in PsA SF ( $p < 0.05$ ). These were investigated using two publicly available databases (Ingenuity Pathway Analysis and DAVID Bioinformatics Resources 6.7) to identify disease relevant proteins. Gene ontology (GO) analysis classified these proteins into categories pertaining to five main biological processes: complement activation, defense response, immunoglobulin mediated response, response to wounding, and extracellular matrix remodelling, all of which are attributes of PsA. Application of subsequent filtering criteria yielded approximately 17 proteins, which served as putative PsA biomarkers. SRM validation confirmed that 12 proteins were indeed elevated in the 10 PsA SF samples, and these included positive controls, MMP3, S100A9, and CRP.

**Conclusion:** We have developed and utilized a high-throughput proteomics platform using LC-MS/MS to delineate the SF proteome from PsA patients and controls. Proteins that were differentially expressed were validated using targeted mass-spectrometric assays. Using these methods we have identified several candidate PsA biomarkers. In the future, these proteins will be verified using highly specific immunoassays in patient serum, in order to identify their clinical utility in PsA patients.

## 11

### **Electronic Consent Processes for Rheumatology Research**

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**Objective:** Informed consent is based on the right of research participants to be fully informed in order to exercise full autonomy in health decision-making. Traditionally, consent to research has been expressed in writing. Technological advances and increasingly complex research questions have created a potential environment where consent may be collected and managed electronically. Participants have begun to expect the same online functionality currently existing in other areas including banking and social media. There is an emerging need to evaluate ethical and legal challenges that will be created by using technologies to obtain consent. In collaboration with ethics and legal researchers, the Canadian Consortium of Rheumatology Cohort, analyzed international policy and Canadian legislation regarding consent and using electronic consent (e-consent) for rheumatology research.

**Methods:** A systematic review of international published and grey legal literature was conducted using established methods. We examined the Model Law on Electronic Commerce (United Nations Commission on International Trade Law), the Electronic Commerce Directive and European Union Signature Directive and the Food and Drug Administration regulations (US), which clarify the legal framework surrounding electronic transactions including electronic signatures and contracts. Subsequently, an evaluation of the Canadian legislation was performed to determine the conditions that permit e-consent in medical research nationally and in select provinces. Finally, we examined perceived impacts of the Ethical, Legal and Social Issues (ELSI) that may emerge as consent moves from a paper-based format to electronic.

**Results:** An international review revealed that there are few governing standards specific to e-consent in health research. Conditions examined within Canadian legislation for research consent included. 1) Integrity: ensuring an electronic document has not been altered. 2) Electronic signature: verifying the identity of a person and creating a connection with their document. 3) Accessibility: requiring that electronic documents remain accessible for subsequent reference. 4) Retention: requiring that electronic documents be protected and retained for subsequent reference. ELSI considerations identified potential benefits and challenges in the use of e-consent. Challenges include lack of guidance regarding interactions with and feedback to participants, and creating appropriate mechanisms for participants that do not use e-consent. Finally, potential electronic privacy and confidentiality issues were identified.

**Conclusion:** The Canadian legal framework currently allows the consent process to be completed electronically, if certain conditions are met. However, this legal framework was developed for e-consent in e-commerce and does not address the requirements of consent in the context of health research. Consequently, we will develop a Canadian consensus based guidance

framework.

## 12

### **Effect of Certolizumab Pegol Over 48 Weeks on Signs and Symptoms in Patients with Psoriatic Arthritis with and without Prior Tumor Necrosis Factor Inhibitor Exposure**

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**Objective:** Previous reports of RAPID-PsA demonstrated efficacy and safety of certolizumab pegol (CZP), over 24 weeks (wks) in psoriatic arthritis (PsA) patients (pts), including pts with prior TNF inhibitor therapy. We report the clinical efficacy and safety of CZP in PsA pts to Wk48.

**Methods:** The RAPID-PsA trial is double-blind and placebo (PBO)-controlled to Wk24 and dose-blind to Wk48. 1 Pts had active PsA and had failed  $\geq 1$  DMARD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W) continued on their assigned dose in dose-blind phase; PBO pts entering dose-blind phase were re-randomized to CZP loading dose followed by CZP 200mg Q2W or CZP 400mg Q4W. Primary endpoints were ACR20 response at Wk12 and change from baseline (BL) in modified Total Sharp Score (mTSS) at Wk24. Other pre-planned endpoints included PASI75/90 and ACR20/50/70, change from BL HAQ-DI, PsAQoL, pain and fatigue at Wk24 and 48, and mTSS at Wk48. Post-hoc analyses evaluated minimal disease activity (MDA) at Wk24 and 48, and compared ACR response rates to Wk48 in pts with and without prior TNF inhibitor exposure.

**Results:** 409 pts were randomized, of which 273 received CZP from Wk0. 54 (19.8%) combined CZP pts (200mg Q2W + 400mg Q4W) had prior TNF inhibitor exposure. Of CZP-randomized pts, 91% completed to Wk24 and 87% to Wk48. ACR20/50/70 and MDA response rates were maintained from Wk24 to Wk48, and similar ACR response rates to Wk48 were observed in pts with and without prior TNF inhibitor exposure. Change from BL in HAQ-DI, PsAQoL, pain and fatigue were maintained to Wk48. In pts with  $\geq 3\%$  skin involvement at BL (60.8% CZP pts), PASI75 and PASI90 responses were maintained from Wk24 to Wk48. Radiographic progression in CZP-treated pts remained low (LS mean mTSS change from BL: Wk24, 0.00; Wk48, 0.13). In the safety set (N=393), adverse events (AEs) occurred in 304 pts (77.4%; event rate [ER] per 100 pt-yrs=394.6), serious AEs in 39 (9.9%; ER=15.3). Serious AEs included 8 infections (2.0%; ER=3.0), 1 case of tuberculosis (0.3%; ER=0.3), and 3 deaths in the 48-week period (0.8%), including 1 death (0.3%) between Wk24 and 48 (breast cancer).

**Conclusion:** Clinical efficacy of CZP was maintained over 48 wks in pts with PsA, including pts with and without prior TNF inhibitor exposure. Low radiographic progression and improvements in PASI were maintained to Wk48. Safety profile was in line with that observed for CZP in RA

## 13

### **Apremilast, an Oral Phosphodiesterase 4 Inhibitor, is Associated with Long-Term (52-Week) Improvements in Enthesitis and Dactylitis in Patients with Psoriatic Arthritis: Pooled Results from Three Phase 3, Randomized, Controlled Trials**

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California at San Diego, San Diego); Adewale Adebajo (University of Sheffield, Sheffield); Juan Gomez-Reino (Hospital Clinico Universitario, Santiago); Jürgen Wollenhaupt (Schön Klinik Hamburg Eilbek, Hamburg); Maurizio Cutolo (University of Genova, Genova); Georg Schett (University Erlangen-Nuremberg, Erlangen); Eric Lespessailles (University of Orléans, Orléans); Kamal Shah (Celgene Corporation, Warren); ChiaChi Hu (Celgene Corporation, Warren); Randall Stevens (Celgene Corporation, Warren); Christopher Edwards (University Hospital Southampton, Southampton); Charles Birbara (University of Massachusetts Medical School, Worcester)

**Objective:** The PALACE 1-3 trials compared the efficacy and safety of apremilast (APR) with placebo in patients with active psoriatic arthritis (PsA) despite prior DMARDs and/or biologics.

**Methods:** Patients were randomized 1:1:1 to placebo, APR 20 mg BID (APR20), or APR 30 mg BID (APR30) stratified by baseline DMARD use (yes/no). At week 16, patients with < 20% reduction from baseline in swollen or tender joint counts qualified for protocol-defined early escape; those on placebo were re-randomized to APR20 or APR30 and those on APR remained on their initial APR dose. At week 24, all remaining placebo patients were re-randomized to APR20 or APR30 through week 52. Patients taking concurrent DMARDs were allowed to continue stable doses (methotrexate, sulfasalazine, leflunomide, or a combination). Data were pooled across PALACE 1, 2, and 3.

**Results:** APR administration resulted in statistically significant and clinically meaningful improvement in ACR20 response (primary endpoint) in all 3 PALACE trials. In patients originally randomized to APR and with enthesitis (n=634) or dactylitis (n=428) at baseline, APR was associated with improvements in the severity of enthesitis and dactylitis over 52 weeks, as evidenced by reductions in Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) and dactylitis count. At week 24, mean change in MASES in patients receiving placebo, APR20, and APR30 were -0.8, -1.2, and -1.4 (P=0.0159), respectively. In those patients originally randomized to APR and completing 52 weeks of study, median change in MASES was -66.7% with both APR20 and APR30 (baseline median: 4.0). A MASES score of 0, indicating no pain at any of the entheses assessed, was achieved by 41.4% of APR20 and 37.4% of APR30 patients. At week 24, mean change in dactylitis count in patients receiving placebo, APR20, and APR30 were -1.2, -1.5, and -1.8 (P=0.0121), respectively. At week 52, both APR doses resulted in a median 100% decrease in dactylitis count (baseline median: 2.0). Dactylitis count decreased to 0 in 66.9% of APR20 and 65.9% of APR30 patients. Patients randomized to APR at weeks 16 and 24 demonstrated results consistent with those initially randomized to APR at baseline. No new safety findings were identified; the incidence of patients experiencing any AE was comparable over the 0-≥24- and 0-≥52-week periods.

**Conclusion:** Over 52 weeks, APR demonstrated efficacy in the treatment of PsA, including improvements in enthesitis and dactylitis. APR demonstrated an acceptable safety profile and was generally well tolerated for ≥52 weeks.

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**Objective:** Assessment of functional (dis)ability in rheumatoid arthritis (RA) is subject to patient judgment when appraising their ability to do daily activities. The aim of this analysis was to describe the impact of specific joint involvement on patient reported outcomes (PROs) - functional activity, pain and patient global assessment of disease activity (PtGA) - and to identify joints most resistant to treatment over time.

**Methods:** Biologic Treatment Registry Across Canada (BioTRAC) is an ongoing, prospective, registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. In this analysis, data were included from RA patients treated with infliximab between 2002 and 2012 or with golimumab between 2010 and 2012. Based on joint involvement seven groups were created: shoulder(s), elbow(s), metacarpophalangeal (MCP), wrist(s), proximal interphalangeal (PIP), knee(s), and thumb(s). The impact of specific joints on patient outcomes was assessed with the independent-samples t-test. Linear regression was used in order to produce adjusted estimates.

**Results:** A total of 935 RA patients with 4,854 assessments were included. Swelling, tenderness, and swelling and/or tenderness in all joint groups were associated with significantly ( $P < 0.001$ ) higher HAQ-DI, PtGA, and pain. Upon adjusting for age, gender and the total number of swollen (SJC28) and tender (TJC28) joints, swelling in all joint groups but the thumb(s) had a significant impact on PtGA, pain and HAQ. Similarly, tenderness in all joints but PIP(s) had a significant impact on these parameters. Overall, swelling and/or tenderness at specific joints - shoulders, wrists, knees and elbows - had the greatest impact on HAQ-DI, PtGA, and pain ( $P < 0.001$ ). Swollen and/or tender PIP(s) did not have a significant effect on any PRO. At baseline, the MCP joint(s) and the wrist(s) were the most commonly swollen (86.4% and 67.9% of patients, respectively) or tender (82.9% and 73.1%, respectively) joints. Upon 12 months of treatment, the MCP joints were the joints most resistant to treatment, still remaining affected.

**Conclusion:** Significant variability in PROs exists based on the presence of swelling and/or tenderness in specific joint groups. Swelling/tenderness of shoulders, wrists, knees and elbows were the main drivers of HAQ-DI, PtGA and pain. The results have important implications for the achievement of disease remission and suggest that the joint type in addition to the number of affected joints has unique impact on PROs.

## 15

### **Are there Gender Specific Differences in Patient Reported Outcomes at Initiation of Golimumab Treatment in Rheumatoid Arthritis?**

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Windsor); Michel Zimmer (CH Maisonneuve-Rosemont, Montreal); Sanjay Dixit (McMaster University, Hamilton); Michael Starr (McGill University, Montreal); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Francois Nantel (Janssen, Toronto); May Shawi (Janssen Inc., Toronto); Susan Ottawa (Janssen Inc., Toronto); Allen Lehman (Janssen Inc., Toronto)

**Objective:** The prevalence of RA is 2-4 times higher in women compared to men. Furthermore, RA incidence in women increases from the age of menarche peaking around menopause, while it is rare in men younger than 45 years (1). Several studies have shown that treatment outcomes are worse in women (2). This analysis examined gender-specific differences with respect to disease parameters at initiation of the first anti-TNF agent for RA treatment in a Canadian routine clinical practice setting.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. In this analysis, data were assessed from RA patients treated with golimumab subcutaneous as a first biologic who were enrolled between 2010 and 2012.

**Results:** 121 RA patients were included with mean (SD) disease duration of 9.3 (9.6) years. Eighty-nine patients (73.6%) were female. In the overall population, rheumatoid factor positivity was observed in 67% of patients and 17.5% were smokers, without any significant differences between genders. Patient reported disease parameters differed significantly between genders. Despite the younger age (56.6 vs. 62.0 years;  $P=0.051$ ), female patients reported significantly higher pain (56.6 vs. 44.5 mm;  $P=0.045$ ), patient global assessment (PtGA: 6.0 vs. 4.7 cm;  $P=0.034$ ), tender joint count (10.2 vs. 6.8;  $P=0.022$ ), and functional disability (HAQ-DI: 1.43 vs. 1.06;  $P=0.024$ ). In addition, a statistical trend towards higher morning stiffness in female patients was observed (55.7 vs. 38.9;  $P=0.063$ ). However, physician assessment of global disease activity (MDGA: 5.7 vs. 5.5;  $P=0.581$ ), SJC (7.9 vs. 8.5;  $P=0.641$ ), DAS28-ESR (5.3 vs. 4.7;  $P=0.086$ ), CDAI (29.7 vs. 24.5;  $P=0.120$ ) and SDAI (32.1 vs. 30.2;  $P=0.675$ ) were statistically comparable between genders.

**Conclusion:** Objective measures (SJC, CRP/ESR), MDGA and composite outcomes were similar for male and female patients at golimumab initiation, with the exception of TJC being higher in women. Patient reported outcomes (PROs: pain, PtGA, HAQ-DI), however, were worse at baseline for female patients at biologic treatment initiation. These findings are similar to our previous research on patients initiating anti-TNF IV therapy (3). Overall, the results may suggest gender bias in the interpretation and use of PROs during the treatment decision making process in Canadian RA patients. References 1. Wilder RL. J Rheumatol Suppl. 1996 Mar;44:10-2.2. Forslund K. et al. Ann Rheum Dis. 2007 Jan;66(1):46-52.3. Bensen W. et al. J Rheumatol Suppl. 2013 Jun;40:1020-1

## 16

### **What are the Implications of Concomitant and Pre-medication on Infusion Reactions to Infliximab: Results from “RemiTRAC Infusion”, a Prospective Real-World Community Registry**

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**Objective:** Infliximab (IFX) is a therapeutic monoclonal antibody targeting TNF $\alpha$  indicated in the treatment of a number of chronic inflammatory diseases. IFX is administered by intravenous infusion and may be associated with infusion reactions (IRs).

**Methods:** RemiTRAC Infusion is a prospective observational registry conducted in 12 Canadian sites from 2005-2012. IFX infusions were followed to document IRs and their management, pre-medication use and adverse events. An IR was defined as any AE occurring during the infusion or within 1 hour post-infusion.

The effects of concomitant medication and pre-medication prior to infusions on the incidence of IRs were evaluated by propensity score adjusted analysis using a multilevel logistic regression model with the following variables as predictors: Patient age, weight and gender; prior enrolment use of IFX, any prior biologic use; indication; season and year of infusion; patient eligibility; dose; time since the last infusion and number of previous IRs.

**Results:** 1,632 patients were enrolled and 24,852 infusions were recorded. The majority (63%) of patients in this cohort are treated with IFX for rheumatologic conditions such as RA (40%), AS (18%) and PsA (6%). 201/1632 (12.3%) patients reported at least one IR. Of 24,852 infusions, 322 resulted in an IR (1.3%) and most IRs were mild to moderate in severity (95%). The most common IR was pruritus, occurring in 19.9% of IRs. Flushing (9.9%) and dyspnoea (6.2%) are the only other infusion AEs occurring in  $\geq 5\%$  of IRs. Four serious IRs (fever, itching/flushing, chest pain, flushing) and no serious anaphylactic reactions occurred. Neither immunosuppressive agent overall ( $p=0.5487$ ), nor do MTX ( $p=0.5473$ ) or corticosteroids ( $p=0.3106$ ) had any effect in reducing the incidence of IRs. In contrast, pre-medication with anti-histamines ( $p=0.0129$ ), used alone or in combination with steroids ( $p<0.001$ ) were associated with a significant increase in the incidence of IRs. Only the use of acetaminophen monotherapy was associated with a significant reduction in the incidence of IRs ( $p=0.0426$ ).

**Conclusion:** This registry shows that in community-based infusion clinics, IR to IFX are uncommon and largely mild to moderate in nature. Anti-histamines, intravenous steroids and acetaminophen have been widely used to decrease the odds of IRs. However, the results of this registry demonstrate that anti-histamines and steroids are ineffective as prophylactic pre-medication.

## 17

### **Change Over Time in the Profile of Ankylosing Spondylitis Patients Treated with Infliximab in Canadian Routine Care**

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**Objective:** Canadian provincial reimbursement policies in regards with infliximab coverage status have evolved in the last decade. The objective of this study was to describe and compare over time the demographics and disease parameters at infliximab treatment initiation and to assess the effectiveness of treatment at 6 and 12 months in Canadian AS patients.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. People with AS treated with infliximab who were enrolled between 2002 and 2013 were included in this analysis ( $N=303$ ) and stratified to two groups (2005-2007:  $n=135$ ; 2008-2013:  $n=168$ ) based on the year of enrolment in the registry.

**Results:** Patient demographics were comparable in the two cohorts with a mean (SD) age of 45.72 (11.74) years and the majority being males (62.4%). A significant change in the geographic distribution of patients enrolled in the BioTRAC registry was observed ( $P=0.001$ ) and more patients with provincial coverage were enrolled in 2008-2013 compared to 2005-2007 ( $P=0.012$ ). A trend towards earlier initiation of

infliximab was observed in more recent years as indicated by the shorter disease duration (11.12 vs. 8.24 years;  $P=0.013$ ) and the lower number of prior traditional DMARDs used (0.83 vs. 0.59;  $P=0.078$ ). Furthermore, overall, patients recruited in 2008-2013 had lower disease activity compared to those enrolled in 2005-2007. ESR (29.96 vs. 19.91 mm/hr;  $P<0.001$ ), physician global assessment (MDGA; 6.99 vs. 6.26;  $P=0.001$ ) were significantly lower in the 2008-2013 cohort while a statistical trend was observed in morning stiffness (78.96 vs. 70.11 minutes;  $P=0.064$ ) and ASDAS (3.90 vs. 3.70;  $P=0.103$ ). Treatment for 6 months resulted in a greater proportion of patients in the 2008-2013 cohort achieving inactive disease ( $ASDAS<1.3$ ) without reaching statistical significance (20.7% vs. 34.9%;  $P=0.140$ ).

**Conclusion:** The results of this analysis show that the profile of the AS patient population in the BioTRAC registry has changed over time towards lower disease activity and earlier initiation in the patient management process. These results may reflect differences in patient management over time or may be related to earlier access to care. Irrespective of enrolment period, 6-month treatment with infliximab was effective in reducing disease activity in Canadian AS patients.

## 18

### **Differential Relative Contribution of Individual Components on DAS28 Over Time. An Analysis from the Prospective, Observational Registry, BioTRAC**

Denis Choquette (Institut de Rhumatologie de Montréal, Montreal); Dalton Sholter (124 Street Medical Group, Edmonton); Isabelle Fortin (Rimouski); Michael Starr (McGill University, Montreal); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Milton Baker (University of Victoria, Victoria); Regan Arendse (Saskatoon); Philip Baer (Scarborough); Michel Zumner (CH Maisonneuve-Rosemont, Montreal); Jude Rodrigues (Clinical Research and Arthritis Centre, Windsor); Andrew Chow (Credit Valley Rheumatology, University of Toronto, McMaster University, Mississauga); Maqbool Sheriff (Nanaimo Regional General Hospital, Nanaimo); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Francois Nantel (Janssen, Toronto); Allen Lehman (Janssen Inc., Toronto); Susan Ottawa (Mississauga); May Shawi (Janssen Inc., Toronto)

**Objective:** DAS28 is an important outcome for clinical research and practice assisting with therapeutic decisions. The main contributors to DAS28 are joint tenderness and acute-phase reactants. A simulation analysis showed that, due to its logarithmic transformation in the DAS28 formula, the ESR contribution is greater in the lower than in the higher DAS28 range. This analysis assessed the relative contribution of individual DAS28 components and examined its clinimetric properties in rheumatoid arthritis (RA) patients treated with infliximab in a Canadian real-world setting.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab or golimumab as first biologics or after treatment with a biologic for  $<6$  months (M). RA patients treated with infliximab between 2002-2012 and with  $\leq 60$ M of follow-up were included. The association between treatment duration and parameter improvement was assessed using linear regression. Slope correlation was assessed with the Pearson's correlation coefficient.

**Results:** 832 patients evaluated over 4,002 visits were included. Longer treatment duration was associated with significant ( $P<0.001$ ) improvements in DAS28, TJC28, SJC28, PtGA, ESR, and CRP. Correlation analysis of the rate of change over time showed a high correlation (0.7-0.9) of DAS28 with TJC28, SJC28, and PtGA but low correlation with ESR ( $r=0.418$ ) and CRP ( $r=0.411$ ). Overall, the relative contribution of TJC28, SJC28, PtGA, and ESR in DAS28-ESR was 22%, 9%, 12%, and 57%, respectively. For DAS28-CRP, the relative TJC28, SJC28, PtGA, and CRP contributions were 25%, 10%, 12%, and 20%. Over 60M



of treatment, the mean relative contribution of TJC28 (M0:31%, M60:17%), SJC28 (M0:15%, M60:5%), and PtGA (M0:15%, M60:9%) significantly ( $P < 0.001$ ) decreased whereas the weight of ESR contribution increased (M0:39%, M60:69%). Similar results were obtained with DAS28-CRP although the CRP contribution was lower compared to ESR. Increased DAS28-ESR was associated with higher relative contributions (per unit of DAS28-ESR increase) of TJC28 [parameter estimate ( $B$ ) = 5.3], SJC28 ( $B$ =2.1), and PtGA ( $B$ =0.7) but lower ESR contribution ( $B$ =-8.1). Similarly, increased DAS28-CRP was associated with lower relative CRP contribution ( $B$ =-2.0).

**Conclusion:** This analysis shows that TJC28 and acute-phase reactants have a greater weight than SJC28 and PtGA within DAS28. Furthermore, the relative contribution of acute-phase reactants is greater with lower DAS28, due to their logarithmic nature. These findings suggest that biologic variability and variability in laboratory techniques may have significant impact on classifying remission or DAS28 changes among patients with low DAS28 and on therapeutic plan changes.

## 19

### **Methotrexate Use at Infliximab Initiation and Impact on Treatment Outcomes: An Analysis from the Canadian Registry, BioTRAC**

Denis Choquette (Institut de Rhumatologie de Montréal, Montreal); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Division of Rheumatology, University of British Columbia, Vancouver); Michel Zimmer (CH Maisonneuve-Rosemont, Montreal); Michael Starr (McGill University, Montreal); Maqbool Sheriff (Nanaimo Regional General Hospital, Nanaimo); William Bensen (St Josephs Hospital and McMaster University, Hamilton); Andrew Chow (Credit Valley Rheumatology, University of Toronto, McMaster University, Mississauga); Philip Baer (Scarborough); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Francois Nantel (Janssen, Toronto); Allen Lehman (Janssen, Toronto); Susan Ottawa (Mississauga); May Shawi (Janssen Inc., Toronto)

**Objective:** Clinical trials have shown that concurrent methotrexate therapy enhances the efficacy of infliximab<sup>1</sup>. Data on the benefits of combination therapy with methotrexate and infliximab in real-life are scarce. The aim of this analysis is to describe changes in the use of methotrexate at infliximab initiation in patients enrolled in Canadian routine clinical practice between 2002-2011 and to assess the impact of methotrexate dose on the real-life effectiveness of infliximab.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab as first biologics or after treatment with a biologic for < 6 months. In this analysis, data from RA patients who were treated with infliximab between 2002-2011 were analysed. Patients were stratified based on the methotrexate use (0mg of methotrexate - infliximab monotherapy-,  $\leq 10$ mg/week, 10.1-24.9mg/week,  $\geq 25$ mg/week) or the 3-year enrolment period (01/2002-06/2005, 07/2005-06/2008, 07/2008-06/2011). Cox regression was used to examine the time-dependent association between disease remission and methotrexate dose.

**Results:** 790 RA patients were included with a mean age of 55.75 years and mean disease duration of 10.15 years. Concomitant use of methotrexate at infliximab initiation increased across enrolment periods (66.5% vs. 73.3% vs. 77.6%;  $P=0.022$ ) which was associated with decreased baseline disease activity. Concomitant use of azathioprine (5.2% vs. 0.2%;  $P < 0.001$ ) and leflunomide (46.1% vs. 14.5%;  $P < 0.001$ ) at baseline, and past use of methotrexate (77.8% vs. 65.7%;  $P=0.001$ ) was more frequent in patients not treated with methotrexate at baseline than those treated. Among patients treated with methotrexate at baseline the most common methotrexate dose category was 10-25mg/week (66.3%). However, a trend towards higher methotrexate doses was observed over time with significantly more patients treated with

>25mg/week in more recent years. Upon adjusting for baseline disease activity, use of methotrexate over time was associated with increased hazard [HR(95%CI)] of attaining DAS28-CRP [1.35 (1.06-1.71)], CDAI [1.33 (1.02-1.72)], and SDAI [1.62 (1.14-2.32)] remission. This effect was observed across all methotrexate dose categories although for DAS28-CRP and CDAI the >25mg/week dose category did not reach statistical significance.

**Conclusion:** The results of this analysis shows that clinical practice has changed over time with physicians using concomitant methotrexate at infliximab initiation more frequently in recent years despite lower disease activity compared to earlier years. The data support improved outcomes among patients treated with infliximab in routine clinical care when receiving concomitant methotrexate. This is consistent with the current label and recent recommendations of the CRA<sup>2</sup>.1. Arthritis Rheum 1998;41:1552–63.2. J Rheumatol 2012;39:1559-1582.

## 20

### **Addressing Emotional Aspects of Living with Osteoarthritis as a Standard of Practice in the Osteoarthritis Therapeutic Education Program**

Diane Tin (Southlake Regional Health Centre, Newmarket); Lorna Bain (Southlake Regional Health Centre, Newmarket); Sue Charette (Southlake Regional Health Centre, Newmarket); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Hyeon Kang (Toronto); Janet Jeffrey (Southlake Regional Health Centre, Newmarket)

**Objective:** Literature suggests emotional aspects associated with osteoarthritis (OA) are often neglected by primary health care providers. In the Osteoarthritis Therapeutic Education Program (OAThEP) we administer outcome measures including; Western Ontario and McMaster University Arthritis Index (WOMAC), Modified Health Assessment Questionnaire (MHAQ), Hospital Anxiety and Depression Scale (HADS) and a Knowledge Questionnaire. The HADS is used as a screening tool to identify patients at risk for anxiety and/ or depression. In Cohort One, May 2012 to Feb 2013, occupational therapist (OT) made targeted phone contact with patients having abnormal HADS scores. Our pilot review in Jan 2013 found only 48% of those with abnormal HADS scores were successfully contacted due to practice restraints and constraints on resources. A new process was piloted starting Mar 2013, identified as Cohort Two, where OT returned scored HADS to all patients during the lifestyle management session. We hypothesize that patients who are aware and informed of their personal scores will attain validation of their emotional status and be empowered to consider treatment options. This study aims to explore the clinical utility of HADS in both the old and new format within OAThEP

**Methods:** We use a descriptive-correlational design. Retrospective chart review was conducted for 271 patients attending OAThEP from May 2012 to May 2013. HADS is administered pre-class and at 6 months; WOMAC, MHAQ and Knowledge Questionnaire are administered at pre-class and end of class. Results from HADS, WOMAC, MHAQ and the Knowledge Questionnaire are included in analysis using Chi-square, paired and independent t-tests, and RM-ANOVA

**Results:** Of the 202 patients in cohort one, 87% attended the lifestyle management session, or intervention class, and of the 69 patients in cohort two, 87% also attended this session. There were 50 patients (73%) who received their individual HADS score assessments in cohort two. Throughout the study period 20 patients, representing 8.7% (20/229 who completed HADS) were referred to the social worker.

**Conclusion:** This study demonstrated a novel design of an osteoarthritis patient education program. The new algorithm piloted in cohort two confirmed the feasibility of using HADS as a standard practice to detect and triage issues related to anxiety and depression. We were able to reach a greater number of patients in providing their personal HADS score in the new method. The number of self-referrals to the social worker in cohort two supports our hypothesis that patients are demonstrating self-management and

empowerment in seeking treatment options.

## 21

### **Pseudohypoparathyroidism... a Possible Insight into the Pathophysiology of Ankylosing Spondylitis**

Edith Garneau (McMaster University, Hamilton); Raj Carmona (McMaster University, Hamilton)

**Case Report:** Objective: Ankylosing Spondylitis (AS) is a chronic systemic inflammatory disorder characterized by axial skeleton and enthesial involvement. The disease process involves new bone generation leading to formation of syndesmophytes. At this time, however, the pathophysiology of AS remains poorly understood, although familial studies suggest there is a genetic component to the risk of developing AS. Studies have shown that the HLA-B27 allele is involved in the pathophysiology; however, it is not absolutely necessary for the disease process to occur; as a result, other genetic factors must be involved. Methods: We report a 40 year old male with a past medical history significant for pseudohypoparathyroidism who presented with multiple years of pain in his hips and back. His pseudohypoparathyroidism was previously diagnosed on the basis of hypocalcemia, elevated PTH level, and hyperphosphatemia, along with stereotypical physical features including round facies, short stature, obesity, short metacarpal bones, and developmental delay. Results: Clinically, the patient's spine was fused and his range of motion was quite restricted, with an occiput-to-wall distance of 14.5cm and a Schober test of 0.5cm. A review of his blood work revealed hypocalcemia (1.46mmol/L), hyperphosphatemia (1.53mmol/L), elevated PTH (peaked at 357pg/mL), low vitamin D (26.3nmol/L), as well as an elevated alkaline phosphatase (159U/L). It was also noted that the patient was HLA-B27 negative. Upon further testing, imaging revealed the presence of a "bamboo" spine and complete fusion of his sacro-iliac (SI) joints bilaterally, thereby confirming the diagnosis of AS. The earliest x-rays available to us, taken in his early 30s, already revealed extensive syndesmophytes in the thoracic spine and fusion of his SI joints. This, combined with his description of past symptoms, suggests that spinal fusion began in his teenage years or early 20s. Conclusion: We therefore report a case of a patient with pseudohypoparathyroidism type 1a with a rapid progression of AS, suggesting that a common pathway may link these two diseases. Pseudohypoparathyroidism type 1a is a rare genetic disorder characterized by PTH resistance that is caused by a mutation in the exons of the GNAS1 gene, which encodes the alpha-stimulatory subunit of the intracellular G protein. We speculate that AS may be partly mediated by abnormalities in GNAS1 expression leading to impaired adenylyl cyclase activation. The link may be either through direct or indirect pathways and more research will need to be done to clarify this question.

## 22

### **Hypergammaglobulinemic Purpura of Waldenstrom... an Underdiagnosed Condition with a Distinctive Clinical Rash**

Edith Garneau (McMaster University, Hamilton); Melissa Deamude (McMaster University, Hamilton); William Bensen (St Josephs Hospital and McMaster University, Hamilton)

**Case Report:** Objective: Hypergammaglobulinemic Purpura of Waldenstrom is a rare syndrome in which patients develop recurrent purpura mainly in the lower extremities and dorsum of the feet. Usually benign and more common in women, this condition may be associated with an underlying connective tissue disorder or hematologic malignancy. The petechiae may develop after long periods of standing or walking, tight-fitting garments, or heat. The pathogenesis of this disease is still unclear; however, increased production of polyclonal immunoglobulins is thought to be the cause. Methods: We report two cases of young females with Hypergammaglobulinemic Purpura of Waldenstrom. The first is a 35 year old

previously healthy female who presents with recurrent purpura on her lower extremities for the past year. She denies beginning any new medications and denies use of recreational drugs. There was no report of constitutional symptoms, arthritis, sicca symptoms, or Raynaud's phenomenon. She denies any headache, oral ulcers, or photosensitivity. The second patient presented in 1982 at 40 with arthritis in the feet and a distinctive intermittent rash over the lower legs. Over time she developed Sjogrens Syndrome, and more recently, a currently well controlled B cell lymphoma. Results: Clinically, the first patient looked well systematically but had purpura on her lower extremities. A review of her blood work revealed a positive ANA (with a titer of 1:640, speckled pattern with positive SS-A52, SS-A60, SS-B, and RNP A). She also had an elevated rheumatoid factor (547U), and markedly increased IgG level (48.2 g/L; normal 5.64-17.65) and IgA level (5.16g/L; normal 0.85-3.85). ANCAs, cryoglobulins, cryofibrinogen, hepatitis serologies, as well as cold agglutinins were all negative. A skin biopsy was done which was consistent with a leukocytoclastic vasculitis. The second patient also looked well on presentation but with the purpurial rash over her legs and arthritis in her ankles. Her rheumatoid factor was strongly positive, her ANA weakly positive, and both IgG and IGA were twice the normal limits of the lab at that time. Biopsy was consistent with a vasculitis. At one time, cryoglobulins were also positive. Since treatment of the B cell lymphoma, the rash is rare. Conclusion: We report two cases of patients presenting with leukocytoclastic vasculitis and elevated IgG levels, consistent with Hypergammaglobulinemic Purpura of Waldenstrom. This is a chronic disease which seems to be under-recognized in our practices but exhibits a distinctive rash. Physicians should be more aware of this uncommon and overlooked condition.

## 23

### **Protective ERAP1 Variants Lead to Decreased Natural Killer Cell Conjugation and Chemokine Suppression**

Hasan Abdullah (University of Toronto, Toronto); Zhenbo Zhang (Toronto Western Research Institute, Toronto); Robert Inman (University of Toronto, Toronto); Nigil Haroon (University of Toronto, University Health Network, Toronto)

**Objective:** Ankylosing Spondylitis (AS) is an inflammatory arthritis affecting the axial and peripheral joints. Human Leukocyte Antigen (HLA)-B27 and Endoplasmic Reticulum Aminopeptidase (ERAP)1 genes are strongly associated with AS. An AS pathogenesis mechanism proposes that variant forms of HLA-B27 including B27 free heavy chains (FHC) can be recognized by Natural Killer (NK) cells through receptors like KIR3DL1. ERAP1 variants K528R and Q730E are strongly associated with AS. Decreased function results in higher HLA-B27 Free Heavy Chain (FHC) expression and can bind to the inhibitory receptor KIR3DL1 altering NK cell activation. The objective of this project is to elucidate effects of ERAP1 variants on KIR3DL1 interaction and NK cell activation.

**Methods:** C1R cells stably expressing HLA-B27 were transfected with ERAP1shRNA to silence the endogenous ERAP1 expression. These cells were transfected with either the common or one of the rare AS associated ERAP1 variants K528R / Q730E. The target cell line was co-cultured with both a KIR3DL1 expressing and a non-KIR3DL1 expressing YTS NK cell lines. Supernatants were analyzed for 64 cytokines and chemokines using a bead based assay. Separately, co-cultured cells were stained for intracellular chemokine CCL3. NK cells were labeled with a red linker dye before co-culture. Co-cultured cells were analyzed by flow cytometry at baseline and after 5 and 10 minutes of co-incubation, for NK cell-target cell conjugate formation.

**Results:** The presence of inhibitory KIR3DL1 receptor led to decreased conjugate formation and CCL3 production in all cell lines. Percentage reduction in conjugate formation with different target cells were: ERAP1 suppression - 32%; common variant - 21%, K528R - 28%; Q730E - 24%. Percentage reduction in CCL3 expression different target cells were: ERAP1 suppression - 68%; common variant - 78%; K528R -

83%; Q730E - 68%. However, CCL3 production by KIR3DL1 NK cells is independent of ERAP1 variant in target cells: ERAP1 suppression - 5.4%; common variant - 5.6%; K528R - 4.8%; Q730E - 6.5%.

**Conclusion:** We have previously shown that AS associated ERAP1 variants lead to increased surface HLA-B27 FHC in monocytes in comparison to the common variant. Here we show KIR3DL1, which is known to bind to HLA-B27 FHC, suppresses target cell conjugation and CCL3 chemokine expression. However the suppression of CCL3 production is to the extent that there are no significant differences with different ERAP1 variants.

## 24

### **Long-Term Safety and Efficacy of Certolizumab Pegol in Combination with Methotrexate in the Treatment of Rheumatoid Arthritis: 5-Year Results from a 52-Week Randomized Controlled Trial and Open-Label Extension Study**

Edward Keystone (Mount Sinai Hospital, Toronto); Robert Landewe (Amsterdam); Ronald van Vollenhoven (Karolinska Institute, Stockholm); Bernard Combe (Hôpital Lapeyronie, 34295 Montpellier); Vibeke Strand (Stanford University, Portola Valley); Phillip Mease (Swedish Medical Center and University of Washington School of Medicine, Seattle); Laura Shaughnessy (Raleigh); Brenda VanLunen (Raleigh); Désirée van der Heijde (Leiden University Medical Center, Leiden); Barb Phenix (UCB Canada Inc., Oakville)

**Objective:** In the RAPID1 randomized controlled trial certolizumab pegol (CZP) every 2 weeks (Q2W) plus MTX over 52 weeks (wks) provided rapid improvements in signs and symptoms and inhibition of radiographic damage in patients (pts) with active rheumatoid arthritis (RA). In this publication we examine the safety and efficacy of CZP plus MTX over 5 yrs in RA.

**Methods:** Eligible patients were treated in the open-label extension (OLE) with CZP 400mg Q2W, reduced to 200mg Q2W after  $\geq 6$  months, plus MTX. Primary objective of the OLE was to monitor safety; secondary objective was to assess efficacy. Combined safety data from RCT and OLE are presented to Wk334 (6.4 yrs) for all patients receiving  $\geq 1$  dose of CZP in RCT or OLE (Safety population, N=958). ACR20/50/70, DAS28(ESR) and HAQ-DI are reported to Wk256 (4.9 yrs) for CZP patients who completed the 52-wk RCT (CZP Completers, N=508) and for all patients randomized to CZP 400mg or 200mg in RCT (ITT population, N=783). Change from baseline in modified Total Sharp Score (mTSS) and % of patients with radiographic non-progression (defined as a change in mTSS from RCT baseline of  $\leq 0.5$ ) are reported to Wk148 (2.8 yrs) for CZP Completers. Kaplan-Meier analysis was used to estimate patient retention.

**Results:** Overall event rate per 100 pt-yrs (ER) of AEs was 290.4 and SAEs was 20.3 (serious infections=5.9; total exposure: 3,732 pt-yrs). The most common AEs were urinary tract infection (ER=7.9), nasopharyngitis (ER=7.3) and upper respiratory tract infection (ER=7.3). 177 pts (18.5%) experienced an AE leading to withdrawal (incidence rate per 100 pt-yrs [IR]=4.8). 21 (2.2%) experienced an AE leading to death (IR=0.6) (including 5 malignancies, 5 cardiac disorders, 3 infections). ACR20/50/70 response rates for CZP Completers and ITT population were maintained to Wk256 (74.4%/57.3%/39.6% and 59.0%/43.7%/28.8%, respectively), as were DAS28 (ESR) remission rates (25.2% and 20.3%), improvements in DAS28(ESR) (mean values: 3.43 and 3.83; mean change from baseline: -3.49 and -3.08) and HAQ-DI (mean values: 0.90 and 1.00; mean change from baseline: -0.77 and -0.66). The rate of radiographic progression in CZP-treated patients was not observed to change over time (mean change in mTSS from RCT baseline to Wk52: 0.27, from RCT baseline to Wk148: 0.77; proportion of patients achieving radiographic non-progression at Wk52: 76.5%, Wk148: 68.9%).

**Conclusion:** CZP plus MTX provided a favorable risk-benefit profile over 5 years of treatment in patients with active RA. No new safety signals were identified.

### **Does Ultrasound Examination Improve the Efficacy of Identifying PsA Patients with Erosive Arthritis?**

Amir Haddad (University of Toronto, Toronto); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Vinod Chandran (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

**Objective:** Identifying patients with erosive disease is important as it warrants the need for aggressive management to prevent further damage. The modified Steinbrocker scoring method defines 4 stages in joint damage where patients with juxta-articular osteopenia are reported with grade I damage. Some patients have severe osteopenia that could be elusive for big erosions. Ultrasound may be a better modality for studying these joints in particular. The aim of this study was to identify whether patients with marked osteopenia on X-rays involving the MTP joints have evidence of erosive arthritis using ultrasound exam.

**Methods:** Patients with PsA that have completed anteroposterior radiographs of the feet with evidence of marked osteopenia in at least one joint involving the MTP joints within at least 12 months, underwent an ultrasound exam for assessment of damage at the level of the MTP joints. The first and fifth MTP joints were scanned at a range of 180 degrees whereas the second, third and fourth MTP's were scanned from the dorsal and plantar aspects on both plantarflexion and dorsiflexion to optimize the scan using MyLab 70XVG scanner (Esaote) equipped with a 6–18 MHz linear transducer. Bone erosion was defined when a defect in the cortex was observed in two planes. The presence of cortical irregularity was also recorded. The scans were recorded in digital media and read at a separate location and later date after blinding for personal data. The sonographer was also blinded for the findings on X-rays. The intraobserver intraclass correlation coefficient for ultrasound reading was 0.9.

**Results:** 10 patients (6 were males with disease duration of 12.4 (9.9) and damaged joint count of 11.4 (3.5)) with a complete radiographic evaluation underwent an ultrasound exam. 8 patients were treated with DMARDs and 4 were on biologics. Using plain radiographs, 6 of the 100 MTP joints were recorded as normal, 15 with erosions and 79 with marked juxta-articular osteopenia. On ultrasound assessment, 50 joints were found normal, 14 had cortical irregularity and 26 had erosion. 27 of the 39 joints that were recorded with a juxta-articular osteopenia had an erosion and 12 had a cortical irregularity. However, 6 joints that had erosions on x-rays were not detected by Ultrasonography. Most of these joints had deformities that limited the scan.

**Conclusion:** Ultrasonography has a diagnostic value in identifying more patients with erosive arthritis, however, it has a low negative predictive value as 6/15 joints were not identified with an erosion.

### **Rituximab versus Abatacept in Rheumatoid Arthritis Patients with an Inadequate Response to Prior Biologic Therapy: A Retrospective Single-Center Study**

Edward Keystone (Mount Sinai Hospital, Toronto); Deborah Weber (The Rebecca MacDonald Center for Arthritis and Autoimmunity, Toronto); Juan Xiong (The Rebecca MacDonald Center for Arthritis and Autoimmunity, Toronto); Ye Sun (Mount Sinai Hospital, Toronto); Alex Grant (Mount Sinai Hospital, Toronto)

**Objective:** To evaluate the relative effectiveness of RTX and ABA in patients who failed at least one TNF inhibitor.

**Methods:** This was a retrospective chart review of patients from a single site (Rebecca MacDonald Center) with ACR-defined RA who initiated RTX or ABA after failure of at least one TNFi. The relative effectiveness of RTX and ABA was evaluated by analyzing drug survival distribution. Kaplan-Meier

survival curves were compared using the log rank test (p-values < 0.05 indicated statistical significance).

**Results:** The study cohort comprised 61 patients, of whom 37 and 24 were treated with RTX and ABA, respectively. In the RTX group, 10 patients had also received prior therapy with ABA. Demographics and disease characteristics were generally similar in the two groups, although RTX patients had higher disease activity compared with ABA patients (mean CDAI: RTX 32.5 vs. ABA 26.9) and had received more prior TNFi (1.8 vs. 1.7) and/or ABA (2.1 vs. 1.7). After excluding the RTX patients who had received prior ABA, survival rates over time were generally better with RTX vs. ABA. Estimated survival rates at time 1.0, 2.0, 3.0 and 4.0 years were 0.79, 0.68, 0.68, and 0.68 for RTX and 0.74, 0.54, 0.54, and 0.41 for ABA. Overall, survival distribution was not significantly different between the RTX and ABA groups (p=0.658); however, RTX patients who had also failed ABA had significantly reduced survival compared with those who had not received ABA (p=0.015). Stratification of survival data according to number of prior TNFi failures indicated that RTX (excluding patients with prior ABA) was superior to ABA among patients who had failed 3 TNFi. Survival was also numerically greater with RTX vs. ABA in patients who had failed 1 prior TNFi.

**Conclusion:** These results from real-life practice suggest that in RA patients who failed one or more TNFi, RTX may have better long-term survival than either ABA or an alternative TNFi. Prior ABA appears to reduce RTX efficacy. Further data are needed.

## 27

### **Efficacy of Ustekinumab in Patients with Active Psoriatic Arthritis : 9 Months Results**

Marie-Jeanne Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Eve Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Isabelle Fortin (Rimouski)

**Objective:** Psoriatic arthritis is characterised by arthritis, psoriasis, sacroilitis, enthesitis and dactylitis. The efficacy of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitor has been demonstrated in different controlled clinical trials and observational studies. However, some patients have inadequate response to TNF- $\alpha$  inhibitors and no alternative mechanism of action is available for those who failed more than one anti-TNF. Ustekinumab is an efficacious treatment for psoriasis and may be useful in patients with active psoriatic arthritis. The objective of this study was to assess in Canadian clinical practice the efficacy of ustekinumab in patients with psoriatic arthritis who failed to one or more TNF- $\alpha$  inhibitors agents.

**Methods:** Charts of patients taking ustekinumab at the Centre de Rhumatologie de l'Est du Québec were reviewed and detailed data including demographic information, disease characteristics, 28-joint disease activity score (DAS28-CRP), BASDAI, BASFI, SPARCC and Health Assessment Questionnaire-Disease Index (HAQ-DI) were collected. Descriptive statistics were used to describe patients initiating ustekinumab in this real-world setting.

**Results:** A total of 8 patients starting treatment with ustekinumab were enrolled in this study. Patients have failed an average of 3.63 anti-TNF agents. Overall, DAS28-CRP decreased from 3.86 at baseline to 2.86 at month 9. HAQ-DI decreased from 1.98 to 1.5. BASDAI decreased from 8.16 to 6.67. BASFI decreased from 7.18 to 5.37. SPARCC decreased from 2.38 to 2. Mean number of dactylitis decreased from 4.75 to 2. Finally, all patients have improved their psoriasis after 9 months.

**Conclusion:** The present study suggests that ustekinumab improved active psoriatic arthritis and may offer an alternative treatment for patients who failed to respond to their previous anti-TNF. The most impressive effect is the improvement of enthesitis and dactylitis. It is even more interesting that the response was good nevertheless the number who have failed to an anti-TNF. However, this is an exploratory study and a larger sample is needed for better interpretation.

## 28

### **Drug Survival of Biologics in Rheumatoid Arthritis Patients in a Canadian Patient Cohort**

Eve Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Marie-Jeanne Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Isabelle Fortin (Centre de santé et de services sociaux de Rimouski, Rimouski)

**Objective:** In recent years, major advances have been made in the treatment of rheumatoid arthritis (RA). The efficacy of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitor has been demonstrated repeatedly. However, some patients have inadequate response to TNF- $\alpha$  inhibitors and may switch to an alternative treatment. The objective of this study was to assess in Canadian clinical practice the survival rate in patients with RA treated with a TNF- $\alpha$  inhibitor such as etanercept (ETN) and adalimumab (ADA) and alternative treatments such as abatacept (ABA), tocilizumab (TCZ) and rituximab (RTX).

**Methods:** Charts of all RA patients taking ETN, ADA, ABA, TCZ and RTX at the Centre de Rhumatologie de l'Est du Québec were reviewed and detailed data including 28-joint disease activity score (DAS28-ESR), start and end date and motive for discontinuation were recorded. Survival estimation was explored using Kaplan-Meier analysis and the log rank test was used to check for differences between the Kaplan-Meier curves using the statistical software R.

**Results:** A total of 473 RA patients starting treatment with ETN, ADA, ABA, TCZ or RTX were enrolled in this study. 158 patients were on ETN, 128 patients were on ADA, 73 patients were on ABA, 53 patients were on TCZ and 61 patients were on RTX therapies. Overall, DAS28-ESR decreased from 4.37 at baseline to 2.80 at month 24 for ETN, from 4.37 to 2.98 for ADA, from 4.58 to 4.06 for ABA, from 5.31 to 3.24 for TCZ and from 4.65 to 2.97 for RTX. After 24 months, using Kaplan-Meier curves plotted for all treatments, 58% of patients are still on ETN, 41% of patients are still on ADA, 41% of patients are still on ABA, 58% of patients are still on TCZ and 74% of patients are still on RTX. However, for biologic-naïve patients, 57% of patients are still on ETN, 51% of patients are still on ADA, 67% of patients are still on ABA, 75% of patients are still on TCZ and 100% of patients are still on RTX (n=2) at month 24. Statistical tests of comparison between treatments revealed significant differences (log-rank: p=0.000125).

**Conclusion:** The present study suggests that the drug survival for biologic-naïve patients is higher than on patients who failed to respond to their previous biologic. It also suggests that RTX has a better survival rate than ETN, ADA, ABA and TCZ in second line treatment. Also, ADA, ABA and TCZ have a better profile when used as a first-line agent.

## **29**

### **The Rituximab Registry at the Centre de Rhumatologie de l'Est du Québec: Description of the Real World, Canadian Rural Patient Cohort**

Eve Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Marie-Jeanne Rioux (Centre de Rhumatologie de l'Est du Québec, Rimouski); Isabelle Fortin (Centre de santé et de services sociaux de Rimouski, Rimouski)

**Objective:** Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation, pain, stiffness and joint destruction. RA can lead to functional impairment, disability and poor quality of life in addition to higher rates of morbidity and mortality. Major advances have been made in the treatment of these diseases with tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitors. However, some patients have inadequate response to TNF- $\alpha$  inhibitors and may switch to an alternative treatment from a different class of drugs, such as rituximab (RTX). RTX, which is a chimeric monoclonal antibody, is indicated for use after the failure of a TNF- $\alpha$  inhibitor and approved in 2006 for the treatment of RA. The objective of this study was to assess in Canadian clinical practice the 36-month outcome in patients with RA treated with rituximab.



**Methods:** Charts of fifty RA patients taking RTX were reviewed and detailed data including demographic information, disease characteristics, rheumatoid factor (RF) and anti-cyclic citrullinated peptide status (ACCP), co-morbid medical condition, 28-joint disease activity score (DAS28), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Health Assessment Questionnaire-Disease Index (HAQ-DI) and adverse events were collected. Descriptive statistics were used to describe patients initiating RTX in this real-world setting. Predicted factors for response were studied with the  $\chi^2$  test such as RF, anti-CCP, gender and smoking status.

**Results:** Overall, DAS28-ESR decreased from 4.71 at baseline to 2.32 at month 36. 53% of patients are RF positive. No predicting factor for response was found in this cohort regarding RF, ACCP, and smoking status. The data from the present study suggest that RTX is as effective in active seropositive RA as in seronegative RA patients. After 36 months, 74% of patients are still on RTX. The safety profile was comparable and consistent with published data on patients with RA. However, the overall serious infection rate was 8.76/100 patient-years.

**Conclusion:** The present study suggests that RTX offers clinical benefits in RA patients and is well tolerated. Results are consistent with other registries such as the Belgian MIRA, AIR and ORA French Registries as well as published data based on clinical trials except for the effectiveness in seronegative RA. This is an explorative question to assess whether RA patients in Eastern Quebec may be different.

## 30

### **Construct Validity and Test-Retest Reliability of the OA GO AWAY, a Self-Management Intervention for Patients with OA of the Hip or Knee to Promote Exercise Adherence**

Gail Paterson (The Arthritis Society, Ottawa); Karine Toupin-April (Children's Hospital of Ontario, Ottawa); Catherine Backman (Arthritis Research Center of Canada, and Occupational Science and Occupational Therapy University of British Columbia, Vancouver); Anton Saarimaki (Ottawa Hospital Research Institute, Ottawa); Peter Tugwell (Institute of Population Health, University of Ottawa, and the Division of Rheumatology, Department of Medicine, University of Ottawa, Ottawa)

**Objective:** The purpose of this study was to determine the construct validity and test-retest reliability of the OA GO AWAY, a self-management tool that combines a monthly personalized self-evaluation 'journal', 'goals and action plan' and weekly 'exercise log'.

**Methods:** Fifty patients with OA of the hip and/or knee were recruited at The Arthritis Society in Ottawa. Participants completed the OA GO AWAY Journal and outcome measures commonly used in OA research to estimate aspects of construct validity using correlation coefficients: Short form Health Survey (SF-36); Pittsburgh sleep quality index (PSQI); and the measure of intermittent and constant osteoarthritis pain (ICOAP). They completed a second Journal page 4 to 7 days later, and the scores of the items were compared using Kappa and intraclass correlation coefficients (ICC) to assess test-retest reliability. Modifications were made to the OA GO AWAY to delete the items with poor construct validity ( $r < 0.50$ ) and test retest reliability ( $ICC < 0.40$ ). Five patients and five health care experts were then asked to review the revised OA GO AWAY to rate the relevance of each item to confirm face and content validity. Content validity ratios (CVR) of all items were calculated.

**Results:** OA GO AWAY pain scores correlated either moderately or strongly ( $r = 0.50-0.75$ ) with SF-36 bodily pain subscale scores and ICOAP total pain scores. OA GO AWAY sleep, mood and energy scores had moderate or strong correlations ( $r = 0.51-0.78$ ) with their respective PSQI and SF-36 subscale comparators. Since lower correlations were expected between the OA GO AWAY function scores and SF-36 subscales, function was retained even though correlations were low ( $r = 0.01-0.38$ ). Test-retest coefficients showed moderate to strong agreement ( $ICC 0.47-0.94$ ) except for the body mass index (BMI) and the FIT (frequency, intensity, time fitness score). The CVR was adequate for all items tested on the

revised OA GO AWAY except for ‘barriers’ and ‘confidence scale’ from the ‘Goals and Action Plan’ which were removed.

**Conclusion:** The majority of items on the OA GO AWAY had acceptable construct validity and test-retest reliability. This version of the OA GO AWAY had adequate face and content validity, except for two items. Further modifications were made based on patient and expert feedback. A future trial will determine if the OA GO AWAY is effective at motivating patients to adhere to physical activity recommendations.

## 31

### **Source and Quality of the Evidence used in the Development of the 2012 American College of Rheumatology (ACR) Knee and Hip Osteoarthritis Clinical Practice Guidelines**

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**Objective:** The 2012 American College of Rheumatology (ACR) clinical practice guidelines (CPGs) are the most recent CPGs developed to guide the pharmacologic and non-pharmacologic management of knee and hip osteoarthritis (OA). Evidence-based recommendations rely on a wide range of evidence, such as systematic reviews (SRs) (including Cochrane systematic reviews (CRs)), randomized controlled trials (RCTs), and observational studies. The objective of this study was to determine the source and quality of the evidence used in the development of the 2012 ACR CPGs for OA.

**Methods:** The best available evidence in the ACR CPGs was identified by searching for the most recent SR for each treatment comparison and patient important outcome (i.e. pain, function, adverse events, adherence, and withdrawals). If no SR was identified, the most recent RCT of sufficient quality was chosen. In the presence of uncommon and/or rare adverse events, observational studies were also searched. Evidence quality for each outcome was appraised using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) method which is based on study limitations, consistency of results, directness of evidence, imprecision and publication bias. We summarized the source and quality of the evidence using descriptive statistics.

**Results:** Eleven CRs were chosen as best available evidence for 4 of 14 non-pharmacologic interventions and 6 of 10 pharmacologic interventions. Sixteen non-Cochrane SRs were chosen for 7 of 14 non-pharmacologic and 4 of 10 pharmacologic interventions. Sixteen RCTs were chosen for 4 of 14 non-pharmacologic and 6 of 10 pharmacologic interventions. Fifteen observational studies were used as evidence for 2 adverse event outcomes of one pharmacologic intervention. GRADE scores were moderate or high for 94% of pharmacologic intervention outcomes and 56% of non-pharmacologic intervention outcomes. GRADE scores for outcomes were moderate or high for 92% of RCTs, 89% of CRs, and 51% of non-Cochrane SRs.

**Conclusion:** Cochrane Reviews, other systematic reviews and RCTs were used relatively equally as evidence for the development of the 2012 ACR OA CPGs. Evidence quality was generally higher for pharmacologic treatments compared to non-pharmacologic treatments and higher for CRs and RCTs compared with non-Cochrane SRs. The quality of the evidence was considered when developing the final CPG recommendations, making the ACR CPGs a trusted evidence-based resource to help health care professionals make daily clinical practice decisions for their patients with OA.

### **Improving Treatment Adherence Through Rapid Integrated Interdisciplinary Intervention after a Fragility Fracture: The OPTIMUS Initiative**

Marie-Claude Beaulieu (Université de Sherbrooke, Sherbrooke); François Cabana (Université de Sherbrooke, Sherbrooke); Michèle Beaulieu (Merck Frosst Canada, Kirkland); Nathalie Carrier (Université de Sherbrooke, Sherbrooke); Sophie Roux (Université de Sherbrooke, Sherbrooke); Gilles Boire (Université de Sherbrooke, Sherbrooke)

**Objective:** To assess persistence on osteoporosis (OP) treatment initiated after a fragility fracture (FF), to compare patient's self-reported adherence at 12 months with pharmacy refill records and to evaluate the impact of timing of treatment initiation after a FF on persistence.

**Methods:** The OPTIMUS initiative is a strategy implemented in orthopaedic fracture clinics to educate patients and empower Family Physicians (FPs) to diagnose and treat OP after a FF. Women and men over age 50 were screened for FF, individualized letters were sent to FPs, and patients were followed up (FU) by regular phone calls up to 48 months. During FU, dedicated personnel assessed side effects, evaluated the persistence and adherence to treatment, and suggested correctives when needed. At 12 months, pharmacists were contacted to confirm patients' 'adherence to treatment (> 80% drug delivery).

**Results:** 1213 patients with 262 hip FF, 19 vertebral FF and 932 other FF were included. At 12-month FU, 36 patients (3%) were deceased, 89 (7.3%) dropped out and 1088 (89.7%) remained active. At 12 months, 60% of patients were treated for OP (vs 27.4% at inclusion). Among initially untreated patients, treatment was started mainly within the first 6 months. At 12-month FU, adherence with oral bisphosphonates (BP) was self-reported as good in 92% and in 89% by the pharmacists. Patients who started OP treatment after a FF continued on treatment in 76.3% (72% with BP) with a median FU observation of 31 months. There was no significant difference in persistence rates of OP treatment (BP) at 12 months depending on the time of treatment initiation: 76.8% (70.6%) if treated at inclusion, 74.7% (73.1%) if treatment was started during the first 6 months, 75.7% (73.7%) when initiated from 6 to 12 months and 80.7% (77.6%) if started after 12 months. However, among patients who had stopped treatment for any reason, only 30.3% (19.3% for BP) initiated any alternative treatment during subsequent FU.

**Conclusion:** In our cohort, long-term persistence on OP treatments, and more specifically oral BP, was superior to previous reports, and the 1-year self-reported adherence was very similar to that reported by the pharmacist. Initial patient empowerment at the time of a FF may have contributed to the high adherence and persistence rates on OP treatment, including oral BP. Regular FU (phone calls or visits) and collaborative interdisciplinary interventions (nurse, pharmacist, FP, physiotherapist) are also important to improve adherence. Timing of treatment initiation after a FF does not impact persistence rates.

### **Which Patients with Low-Trauma Ankle Fractures are at Risk for Subsequent Fragility Fractures in the Optimus Cohort?**

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**Objective:** To analyze the characteristics of patients with low-trauma ankle fractures presenting recurrent fractures, along with the site of these recurrent FF.

**Methods:** The OPTIMUS study is an ongoing prospective cohort of men and women over 50 years of age, designed to assess a placebo-controlled intervention to increase the rate of initiation and persistence of

osteoporosis treatment after a FF leading to an orthopaedic consultation. The occurrence of any novel FF was collected during regular phone follow-ups, up to 48 months after inclusion. FRAX scores without BMD were calculated at the time of the ankle fracture, non-accounting for this fracture. Ankle x-rays were reviewed and classified as unimalleolar (lateral (Weber A, B or C) or medial), bimalleolar or trimalleolar. **Results:** 265 patients (190 women; median (IQR) age 61 (55-69); median (IQR) BMI 27.0 (24.6-30.1)) with low-trauma ankle fracture were included. 56% of ankle fractures were uni-, 21% bi-, and 23% trimalleolar with rates of recurrent FF of 1.1, 1.3, and 2.0 / 100 patient-years, respectively. Recurrent low-trauma fractures occurred in 10 (4.2%) patients over 775 patient-years of observation, and were localized at hip (1), vertebra (1), shoulder (2), wrist (2), and minor sites (4). Two additional patients had a recurrent ankle fracture. Of the 10 recurrent FF, 7 occurred in women (Relative Risk (RR) 0.92 [0.24-3.47], NS), 4 in patients with previous non-ankle FF (RR 5.88 [1.77-19.53], p=0.004) and 6 in patients at high risk according to pre-ankle fracture FRAX (RR 5.47 [1.60-18.74], p=0.007). The incidence of recurrent FF (per 100 patient-years) was highest in patients with FF prior to the ankle fracture (4.77), intermediate in patients without previous FF but with a High-risk FRAX score (2.46), and lowest in patients without previous FF and with Low or Moderate risk (0.53).

**Conclusion:** Some guidelines consider ankle fractures as fragility fractures (FF), while others do not. We observed that most recurrent fractures occurring in older individuals after low-trauma ankle fractures were at typical major and minor sites of FF. Recurrent fractures occurred at about 1.3 per 100 patient-years, with highest rates (4.77) in patients with previous FF, and lowest rates (0.53) in those without previous FF and with pre-fracture Low or Moderate risk according to FRAX. Gender, BMI and severity of bone damage were not predictors for recurrent fractures. Low-trauma ankle fractures represent clinical opportunities to identify patients with previous FF or with High FRAX score that need preventive treatment; those without these risk factors may not need treatment.

### 34

#### **Greater Trochanteric Enthesitis with Sacroiliitis and Hip Arthritis Presenting as Gait Abnormalities in Young Children: Report of 3 Cases**

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**Case Report:** Objective: We report three children with greater trochanteric enthesitis, sacroiliitis and hip arthritis who presented with atypical symptoms that delayed reaching an accurate final diagnosis. Methods: Retrospective case review of patients seen in the Pediatric Rheumatology clinic at British Columbia's Children's Hospital between 2009 and 2013. Cases: Case 1: A 6-year-old female of Chinese descent presented with two years of bilateral leg pain, and six months of buttock pain and an abnormal gait. There was a strong family history of ankylosing spondylitis. Initial examination did not reveal any obvious arthritis or enthesitis; however, she had a bilateral Trendelenberg gait. Case 2: A 9-year-old Caucasian female presented with bilateral leg pain for 3 years. Family history was positive for psoriasis in her father. Examination showed limited left hip movement, tenderness over both sacroiliac joints and a bilateral Trendelenberg gait. Case 3: An 11-year-old Caucasian male presented with right leg and buttock pain for 5 years. Family history was unremarkable. Examination showed positive Faber's test on the right side and a bilateral Trendelenberg gait. All three patients were initially seen by the Pediatric Neurology service, before rheumatology consultation, for evaluation of an abnormal gait. All had had two or more years of symptoms. None of the patients had peripheral joint arthritis apart from hip arthritis detected on imaging. HLA B27 was negative in all cases and ESR was elevated. MRI (with Gadolinium contrast) in all three

patients showed greater trochanteric enthesitis, sacroiliitis and hip arthritis. On further history, all three patients had poor growth and chronic gastrointestinal symptoms such as diarrhea or melena. The patients underwent endoscopy and were all ultimately diagnosed to have Crohn's disease. The final diagnosis in all three cases was inflammatory bowel disease related arthritis. Conclusion: Greater trochanteric enthesitis, sacroiliitis and hip arthritis seen on MRI facilitated the correct diagnosis of arthritis in these patients, who presented with an abnormal gait as a primary symptom. Greater trochanteric enthesitis has not been described as a prominent finding in either enthesitis related arthritis or the arthritis of inflammatory bowel disease. These cases highlight the importance of recognizing enthesitis and/or sacroiliitis as a cause of abnormal gait in young children, and this in turn should also alert for the possibility for such children to develop gastrointestinal signs and symptoms and possible inflammatory bowel disease.

### 35

#### **Quality Assurance Audit of the use of Liver Function Tests to Adjust Methotrexate Dosing in Rheumatology Patients**

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**Objective:** Methotrexate (MTX) is considered among the first lines agent used when treating patients admitted to the Sunnybrook Rheumatology Clinic. While effective, methotrexate is associated with notable side effects including possible liver, bone marrow and lung toxicities. Our focus is methotrexate-induced hepatotoxicity, which can progress to irreversible hepatic injury and necessitates diligent monitoring of liver function enzymes and appropriate dosing practices. Our objective was to identify correlations between methotrexate dosing and the liver function test (LFT) values of rheumatology patients at the Sunnybrook Rheumatology Clinic, and to determine whether the Clinic's current practices with methotrexate prescribing are in agreement with American College of Rheumatology (ACR) recommendations.

**Methods:** This is an ongoing retrospective chart audit study to determine whether baseline LFTs are performed in patients prior to initiating MTX therapy, how often LFTs are subsequently performed for monitoring purposes, and how LFT values are used to adjust MTX dosing. Rheumatology patients (>18 years of age and > 1 year of MTX therapy) had all available LFT values recorded from their blood work records. LFT values of importance included aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), albumin, creatinine and C-reactive protein (CRP). The MTX dose of the patient concurrent to the date of blood work sampling was also recorded, along with any changes in MTX dosing and reasoning behind the dosing change.

**Results:** Of the 82 patients whose charts were audited, 22 (27%) had a note from the rheumatologist to hold or temporarily discontinue MTX. MTX was discontinued in 4 (5%) patients due to elevated transaminases because of suspected hepatotoxicity. All 4 patients had elevated AST and ALT values, while ALP remained within reference ranges. On average, methotrexate was discontinued when blood work showed an AST value 1.7 times above the upper reference value, and ALT was 1.9 times above the upper reference value. 3 of 4 patients were restarted on MTX an average of 2.8 months after temporary discontinuation due to elevated transaminases.

**Conclusion:** MTX-induced hepatotoxicity may progress to irreversible hepatic injury but is mitigated by diligent monitoring and safe prescribing practices. At the Sunnybrook clinic, an interdisciplinary pharmacist-rheumatologist team approach to the care of rheumatology patients allows for a larger patient "safety net". This is especially critical when prescribing effective drugs that may cause significant side effects such as methotrexate.

### **Unilateral Small Vessel Vasculitis of the Leg – Possible Complication of Intra-Articular Steroid Injection?**

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**Case Report:** Objective: We report a case of biopsy-proven, unilateral small vessel vasculitis (SVV) of the leg post intra-articular steroid injection. We aim to discuss the clinical differential diagnosis and potential etiologies of this rare presentation of vasculitis. Method: The English medical literature was reviewed for unusual presentations of cutaneous small vessel vasculitis with an emphasis on reports of a unilateral presentation. Any reported association between intra-articular steroid injection and vasculitis was particularly sought. Results: A 79-year-old Vietnamese woman presented with a purpuric and pustular left thigh and leg eruption. The clinical differential diagnosis included vasculitis and herpes zoster infection. A skin biopsy confirmed a leukocytoclastic vasculitis (LCV), and no viral cytopathic change was reported. Unilateral LCV is rare. There is one reported case of unilateral LCV post-steroid injection for a cutaneous neuroma. This case also presented with a purpuric and pustular eruption suggestive of herpes zoster infection. Other reported causes of unilateral purpuric eruptions include idiopathic purpura in a rheumatoid arthritis patient, an area overlying a deep infection in an HIV positive patient, and capillaritis (Schamburg's disease). Possible other etiologies for this presentation in our patient include underlying connective tissue disease given her positive serology (ANA and ENA with positive SCL-70) and clinical features of scleroderma (sclerodactyly of hand digits bilaterally and digital ulcers), and vasculitis secondary to her hepatitis C-associated cryoglobulinemia. Conclusion: There is a paucity of literature regarding a unilateral presentation of small vessel vasculitis. The temporal relationship with an intra-articular injection is fascinating but causation cannot be confirmed. The eruption in its early stages can mimic a hemorrhagic herpes zoster infection and awareness of the possibility of a unilateral presentation of vasculitis can help secure a correct diagnosis.

### **A Case of Multiple Myeloma Presenting as Polyarthritis and Cutaneous Vasculitis**

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**Case Report:** Background: Multiple myeloma (MM) is a plasma cell neoplasm that can present with cutaneous or musculoskeletal manifestations. The arthropathy in MM is due to AL amyloid deposition in joints, leading to a symmetrical polyarthritis which can mimic rheumatoid arthritis (RA). Cutaneous vasculitis in MM is histologically similar to vasculitis due to other causes, and thought to be immune mediated. Individually, each manifestation is rare; here we present a case of MM presenting with both symmetric polyarthritis and cutaneous vasculitis. Case: A 57-year old female presented to a community rheumatology clinic with acute onset of symmetrical polyarthritis and a purpuric lower extremity rash. Over the preceding three months, she had significant fatigue and lost 20 pounds. Her past medical history included chronic myofascial back pain and hypothyroidism. Investigations revealed negative rheumatoid factor, anti-cyclic citrullinated peptide and antinuclear antibody. She was diagnosed with seronegative RA and prednisone and methotrexate were initiated. Serum protein electrophoresis was also performed which revealed an IgG M-protein with kappa light chain specificity. Ancillary investigations including hemoglobin, calcium, creatinine, and skeletal survey were normal, thus leading to a diagnosis of

smoldering myeloma. Despite methotrexate and prednisone she continued to have symptoms and was admitted to hospital for further work-up. Admission examination revealed 12 swollen joints, and joint ultrasound revealed small effusions at bilateral proximal interphalangeal and metatarsophalangeal joints, with no active synovitis or erosions. Synovial fluid analysis from the knee was non-inflammatory with no crystals and negative culture. A skin biopsy confirmed leukocytoclastic vasculitis. Investigations for alternative causes of vasculitis including hepatitis B and C, cryoglobulins, antineutrophil cytoplasmic antibodies, were negative. The diagnosis was thus unchanged from seronegative RA with concurrent cutaneous vasculitis, and the patient's prednisone was increased and plaquenil and leflunomide were initiated. One month later, despite good adherence to medical therapy, the patient returned to hospital with progression of cutaneous vasculitis with development of very painful leg ulcerations. Investigations revealed new hypercalcemia (calcium = 3.4 mmol/L), which prompted revision of her diagnosis from smoldering myeloma to MM. She was transferred to the regional cancer centre and started on chemotherapy, after which her symptoms improved. Conclusion: This case demonstrates a presentation of symmetric polyarthritis and cutaneous vasculitis as a result of smoldering myeloma with subsequent transformation to MM. It is important to keep a broad differential when considering the etiology of such symptoms, especially when standard therapies appear to be ineffective.

### 38

#### **Schnitzler's Syndrome Treated with Anakinra: Report of Effect on Two Refractory Cases**

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**Case Report:** Objective: Schnitzler's syndrome is a rare acquired auto-inflammatory syndrome characterized by chronic urticarial rash and monoclonal gammopathy. Other frequent clinical manifestations include: fever, lymphadenopathy, arthralgias/arthritis, bone pain with abnormal bone remodeling, leukocytosis, elevated ESR/CRP, and a neutrophilic dermal infiltrate on skin biopsy. This syndrome was described initially by Dr. Schintzler in 1972 and since then there has only been 196 reported cases. The diagnosis relies on clinical and biological features specified in the Strasbourg criteria and the exclusion of diseases with similar characteristics. There is an increased risk of lymphoproliferative disorders associated with this disease, and the patient's quality of life can be severely impaired. Treatment with anti-histamines is ineffective, and there is variable efficacy of DMARDs. Patients are usually corticoid-dependent. The inflammatory cytokine interleukin-1 seems to play a central role in the pathogenesis of this disease. Recently, complete resolution of these symptoms has been described in patients treated with biologic agents blocking IL-1 such as anakinra and canakinumab. Methods: The clinical features and response to treatment with anakinra in two patients with severe and refractory Schnitzler's syndrome, is reported. Results: Two females, aged 53 (Patient A) and 46 (Patient B) years old, presented with treatment-resistant urticarial rash and monoclonal IgM gammopathy. A diagnosis of Schnitzler's syndrome was made; both cases fulfilled the Strasbourg criteria. Their disease duration prior to diagnosis was 1.2 and 5 years, respectively. Both patients were corticoid-dependent. Each had failed treatment with: colchicine, certirzine, cyclosporine, as well as, dapsone and cimetidine (Patient A) and hydroxyzine and montelukast (Patient B). Both patients attained prompt and near complete resolution of their symptoms with anakinra; one patient required an increase in dose of anakinra after a relapse. This response to treatment was associated with a reduction in leukocyte count and ESR/CRP. Conclusion: Schnitzler's syndrome is a disabling disorder with a long term risk of AA amyloidosis and overt lymphoproliferation. Increased recognition of this rare syndrome is crucial, as treatment with anakinra can lead to dramatic responses with improved quality of life. The long term efficacy and safety of anakinra, with respect to treatment of Schnitzler's syndrome has yet to be assessed.

### **Assessing Treatment Durability of Infliximab in the Management of Psoriatic Arthritis and Rheumatoid Arthritis Patients in a Canadian Setting**

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**Objective:** The efficacy of anti-TNF in the management of psoriatic arthritis (PsA) and rheumatoid arthritis (RA) has been demonstrated in numerous controlled clinical trials. The objective of this analysis was to assess in Canadian routine clinical practice the durability of treatment with infliximab (IFX) in PsA and RA and the determinants associated with sustainability of IFX.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. Patients with PsA or RA treated with IFX who were enrolled between 2002 (2005 for PsA patients) and 2012 were included in this analysis. Dose optimization was defined as an increase in the frequency and/or dosing of IFX. Kaplan Meier (KM) estimates and Cox proportional models were used in the analysis.

**Results:** A total of 92 PsA and 830 RA patients were included in the analysis. Mean (SD) age of the PsA and RA patient cohorts was 48.7 (9.9) and 55.8 (13.4) years, respectively, and mean (SD) duration since diagnosis was 6.8 (9.1) and 10.2 (10.1) years, respectively. Twenty seven (29.3%) PsA patients and 407 (49.0%) RA patients had discontinued treatment. Overall KM-based mean (SE) duration of treatment was 41.4 (3.6) months and 61.3 (2.2) months for PsA and RA patients, respectively. Longer treatment duration was associated with significantly greater improvements in pain (parameter estimate PsA: -0.21,  $P=0.020$ ; RA: -0.27,  $P<0.001$ ), patient global (PsA: -0.35,  $P<0.001$ ; RA: -0.28,  $P<0.001$ ) and HAQ-DI (PsA: -0.01,  $P<0.001$ ; RA: -0.01,  $P<0.001$ ). Significant associations with duration of treatment in PsA patients were observed for disease duration (HR=1.04), previous biologic (HR=2.10), baseline TJC28 (HR=1.10), baseline PASI (HR=0.86) and concomitant use of traditional DMARD(s) (HR=0.16) or NSAID(s) (HR=0.38). For RA patients, IFX dose optimization (HR=0.72) and concomitant use of steroids (HR=1.78) were identified as significant predictors of treatment durability.

**Conclusion:** The results of this observational study have shown a high durability of treatment with IFX for patients with PsA or RA in a real-world setting. Concomitant medication use significantly impacts treatment durability. Furthermore, longer disease duration, higher TJC, less severe skin disease at initiation and previous biologic use in PsA, and absence of IFX dose optimization in RA, may be associated with reduced treatment durability.

### **What is the Real World Relationship between Patient-Reported Pain or Patient Global Assessment and Disease Activity Indices in Rheumatoid Arthritis? An Analysis from the Prospective,**



### **Observational Registry, BioTRAC**

Regan Arendse (Saskatoon); Michael Starr (McGill University, Montreal); Proton Rahman (Memorial University of Newfoundland, St. John's); John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Division of Rheumatology, University of British Columbia, Vancouver); Milton Baker (University of Victoria, Victoria); William Bensen (St Josephs Hospital and McMaster University, Hamilton); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Philip Baer (Scarborough); Denis Choquette (Institut de Rhumatologie de Montréal, Montreal); Isabelle Fortin (Centre de santé et de services sociaux de Rimousk, Rimouski); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Susan Ottawa (Janssen Inc., Toronto); May Shawi (Janssen Inc., Toronto); Francois Nantel (Janssen, Toronto); Allen Lehman (Janssen Inc., Toronto)

**Objective:** Patient-reported outcomes such as pain and patient global assessment of disease activity (PtGA) have been critiqued for not accurately assessing rheumatoid arthritis (RA) disease activity as they may reflect aspects not directly related to the disease (e.g., fibromyalgia, low back pain, depression) or related to non-RA conditions. The aims of this analysis are to: 1) describe the relationship between patient-reported pain and disease activity, as measured with DAS28-ESR, CDAI, and SDAI, in a real-world, routine clinical care setting and 2) assess the occurrence of non-remission driven solely by pain using PtGA as a proxy for pain.

**Methods:** BioTRAC is an ongoing, Canadian prospective registry of rheumatology patients initiating treatment with infliximab or golimumab. Data were used from RA patients treated with infliximab between January 2002 and June 2011. Correlation of pain (VASmm) with DAS28-ESR, CDAI and SDAI in a continuous or binary (low disease activity: yes vs. no; remission: yes vs. no) scale was assessed with linear regression and logistic regression, respectively. For the assessment of non-remission due to PtGA, DAS28-ESR, CDAI, and SDAI remission rates were compared to “non-PtGA” remission rates, calculated by subtracting the relative contribution of PtGA to the index.

**Results:** The analysis included 838 RA patients who had 4,582 assessments. A significant ( $P < 0.001$ ) positive linear relationship was found between pain and DAS28-ESR (standardized coefficient ( $\beta$ )=0.662), CDAI ( $\beta$ =0.660), and SDAI ( $\beta$ =0.659). Increased pain was associated with reduced odds of achieving remission or low disease activity as defined by DAS28-ESR, CDAI, and SDAI. Correlation analysis showed that a strong positive linear correlation existed between pain and PtGA ( $r=0.914$ ), supporting the use of PtGA as a proxy for pain. Cross-tabulation of remission achievement with “non-PtGA” remission achievement revealed that omission of PtGA from the DAS28-ESR, CDAI, and SDAI indices would result in the re-classification of an additional 2.0%, 9.3%, and 9.6% of the cases as remission.

**Conclusion:** The results of this analysis indicate increased pain is associated with higher disease activity as measured by the DAS28-ESR, CDAI and SDAI, which may be due to the strong correlation of pain with PtGA. Omission of PtGA from these disease activity indices resulted in the classification of additional cases as remission cases to an extent that paralleled the strictness of the remission criteria (i.e., from the less “strict” DAS28-ESR index to the more “strict” SDAI). Therefore, the CDAI and SDAI might be more sensitive to pain not directly related to RA.

## **41**

### **Coexistence of Rheumatoid Arthritis and Gout: Clinical Characteristics and Trend (2004-2013)**

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**Objective:** The coexistence of gout and Rheumatoid arthritis (RA) has been speculated for years. Despite

sporadic case reports of such co-existence, the general belief has been that these two diseases do not occur in the same patient. Since 1964 to 2013 there have been approximately 40 cases of concomitant RA and gout reported in the literature. There have been, however, more cases reported recently. This indicates a possible increase in the incidence of this coexistence. This study aims to describe the clinical characteristics of patients with coexisting rheumatoid arthritis and gout.

**Methods:** A retrospective rheumatology review of patients from the University of Alberta database was performed (2004-2013). 1987 ARA Revised Classification Criteria for RA or 2010 ACR criteria for RA were used for the diagnosis of rheumatoid arthritis, and 1977 ARA Classification Criteria for gout or positive monosodium urate crystals on synovial fluid analysis or synovial/node biopsy were used for the diagnosis of gout. Medical records were reviewed retrospectively. The data were analyzed using descriptive statistics.

**Results:** We identified 10 patients with both RA and gout (7 men and 3 women) fulfilling both existing criteria for RA and gout used in clinical practice. The mean age was 70.6 +/- 7.09 (years +/- SD). Mean age at the onset of first disease in our study population was 54 +/- 6.4 (years +/- SD). The mean age at onset of their second diagnosis was 65.3 +/- 5.4 (years +/- SD). Six patients were anti-CCP positive, 3 patients were anti-CCP negative and 1 patient did not have anti-CCP checked. Nine of 10 patients were RF positive and 1 patient was RF negative. Six of 10 patients were hyperuricemic; 3 patients were on uric acid lowering therapy at the time of identification for study. The X-ray findings on the patients with these conditions had usual characteristic findings of either RA or gout in the joints affected by the each disease respectively. Overall it was noted that particularly in joints affected by both diseases the gout findings may predominate and the RA changes may be milder.

**Conclusion:** Despite the general belief and the scarce case reports in the literature, RA and gout can co-exist in the same patient. Dual energy CT of the affected joints (CT-gout protocol), may be a useful tool in diagnosing difficult cases, especially in differentiating rheumatoid nodulosis from tophaceous gout. There may be that gout findings predominate and RA findings are milder in joints affected by both conditions.

## 42

### **Prognosis of Seronegative Patients in a Large Prospective Cohort of Patients with Early Inflammatory Arthritis**

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**Objective:** Rheumatoid Factor (RF) and anti-Cyclic Citrullinated Peptide (anti-CCP) are believed to be associated with more severe clinical outcomes; however, studies in Early Inflammatory Arthritis (EIA) have yielded conflicting results. The objective of this study is to determine the prognosis of baseline anti-CCP and RF-negative patients at 12 months follow-up in the Canadian Early Rheumatoid Arthritis cohort (CATCH).

**Methods:** Data were collected on patients enrolled in CATCH, a multicentre, observational, prospective inception cohort of patients with Early Inflammatory Arthritis (EIA). Treatment was based on physician discretion. IgM RF was measured and depending on the site, two different anti-CCP2 IgG (CCP) kits were used (Euroimmune™ and Inova™). Disease activity was determined using the Disease Activity Score-28 (DAS28) and remission was defined as a DAS28 < 2.6. Presence of erosions was determined using plain radiographs of the hands and feet. Follow-up was 12 months. Multiple logistic regression was used to

account for confounders.

**Results:** 216/841 (26%) of patients were negative for both RF and anti-CCP2. These patients were older (57 years old) and more likely male (31%) compared to seropositive patients (51 years old and 23% male),  $p < 0.001$ . Seronegative patients were less likely to meet 1987 ACR and 2010 ACR/EULAR criteria for RA, however, at baseline they had higher swollen joint counts (SJC) (9 vs 6), more erosive disease (32% vs. 23%) and higher DAS28 scores (5.00 vs. 4.75),  $p < 0.05$ . Seronegative patients had shorter duration of symptoms (166 days vs. 192,  $p = 0.007$ ). The initiation of DMARDs, biologics and steroids was similar between the two groups. Seronegative patients had greater reductions compared to seropositive patients in SJC (7 vs.4) and similar DAS28 scores (2.97 vs. 2.83) at 12 months follow-up;  $p = 0.0017$  and  $p = 0.3$ , respectively. Accounting for confounders, seronegative patients were as likely to achieve DAS28 remission as seropositive patients (OR 1.18; 95%CI: 0.70-1.99), however, they were less likely to have erosive disease at follow-up (OR 0.43; 95%CI: 0.19-0.95,  $p < 0.04$ ).

**Conclusion:** Although seronegative EIA patients have higher disease activity at baseline compared to seropositive patients, they have a good response to treatment and are less likely to have erosive disease at follow-up.

### 43

#### **Work Limitations and Disability in a Canadian Population with Systemic Vasculitis**

Ali Bateman (London); Sherry Rohekar (University of Western Ontario, London); Lillian Barra (London)

**Objective:** Despite recent advances in the treatment of systemic vasculitis (SV), long-term sequelae from damage, such as chronic dyspnea, kidney impairment, neuropathic or arthritic pain, vision or hearing loss and cognitive impairment can significantly impact function. The objective of this study is to assess work limitations and disability in SV.

**Methods:** Participants are enrolled in an ongoing single centre prospective cohort of SV. Inclusion criteria are diagnosis of SV by a Rheumatologist, age  $> 18$  and  $< 65$  years. Participants completed the Work Limitations Questionnaire (WLQ), which consists of 25 questions and categorizes limitations to work performance into physical, mental, interpersonal, time-management, and output demands. Other work-related measures were self-reported via a questionnaire. The Birmingham Vasculitis Activity Score (BVAS), Vasculitis Damage Index (VDI) and Health Assessment Questionnaire (HAQ) were obtained at the time the WLQ was completed. Pain was measured using a visual analogue scale of 0 to 10. Work-disabled was defined as not working, early retirement or reduced hours at work due to SV.

**Results:** 28 subjects met inclusion criteria: mean age 50 years (range 18-62), 70% female and disease duration 4 years (range 0.4-18). The majority of patients had ANCA-associated vasculitis (64%), 22% had other primary SV, 7% had secondary SV and 7% had large vessel vasculitis. Mean BVAS was  $2.44 \pm 1.47$ , VDI was  $2.96 \pm 2.03$  and pain score was  $3.11 \pm 2.93$ . 29% were work-disabled. After receiving a diagnosis of SV, 46% of participants reported a decline in income due to work limitation (mean decline was 22%). Loss of work productivity by the WLQ score was 17%. For work-disabled subjects, HAQ and pain VAS were significantly higher compared to those working ( $p = 0.044$  and  $p = 0.031$ , respectively) and the WLQ score significantly correlated with HAQ and pain VAS (Pearson coefficients of 0.34 and 0.49, respectively).

**Conclusion:** Work disability and loss of work productivity are frequent in patients with systemic vasculitis and are associated with higher HAQ and pain scores.

### 44

#### **Consumer Informing Research: A Survey of Canadians' Views and Research Priorities in Chronic Inflammatory Diseases**

Cheryl Koehn (Arthritis Consumer Experts, Vancouver); Gail Attara (Gastrointestinal Society, Vancouver); Allan Stordy (Canadian Skin Patient Alliance, Calgary); Pam Montie (Vancouver); John Esdaile (Arthritis Research Center of Canada and Division of Rheumatology, University of British Columbia, Richmond); Linda Li (University of British Columbia, Richmond)

**Objective:** Incorporating consumers' views in grant proposal development is a crucial step that ensures research aligns with consumers' needs. This study aims to assess the public's views and priorities in chronic inflammatory disease research.

**Methods:** This study was led by consumer leaders from three inflammatory disease groups: arthritis (C. Koehn, P. Montie), gastrointestinal disease (G. Attara) and skin disease (A. Stordy). A cross-sectional online public survey was developed to address two areas: 1) individuals' views about research on medication and treatment adherence, and 2) priorities in research related to physical activity. The survey invitation was sent to members of the participating consumer organizations. In addition, our survey recruitment was promoted by the news media, Vancouver Sun, as an example of consumer engagement in arthritis research.

**Results:** Between July and August 2013, 636 individuals completed the survey. 509 (80.0%) were women, with 396 (62.3%) between the age 54 and 73 years. 453 (71.2%) respondents were from British Columbia. Approximately 33% had RA, 16% had psoriasis, 11% had lupus, 11% had psoriatic arthritis, 9% had ankylosing spondylitis, 7% had Crohn's disease, 6% had ulcerative colitis and 6% had gout. 114 (17.9%) respondents were diagnosed < 3 years ago. 555 (97.5%) believed it was important to invest in research on medications for decreasing heart attacks, leg clots or premature death, all of which are consequences of chronic inflammatory diseases. Although medication adherence is an issue in chronic disease management, nearly 58% of respondents were not interested in ways to help them remember taking medications as prescribed and on time. 456 (81.7%) respondents indicated a desire to increase physical activity. The top research questions related to physical activity include: 1) how to be active while having inflammation, 2) how much activity is good for people with multiple chronic inflammatory diseases, and 3) how to motivate people to stay physically active.

**Conclusion:** By engaging leaders in consumer communities early in the research process, we were able to identify consumers' research priorities within a short period. Our results indicated a strong support for research on medications to prevent consequences of inflammation, although there was less enthusiasm for research to improve medication adherence. Consumers also identified research priorities in physical activity participation.

## 45

### **A Proof-of-Concept Study of ANSWER, A Web-Based Methotrexate Decision Aid for Patients with Rheumatoid Arthritis**

Linda Li (University of British Columbia, Richmond); Paul Adam (Mary Pack Arthritis Program, Vancouver); Catherine Backman (Arthritis Research Center of Canada, and Occupational Science and Occupational Therapy University of British Columbia, Vancouver); Sydney Brooks (The Arthritis Society - Ontario Division, Toronto); Allyson Jones (Edmonton); Diane Lacaille (Arthritis Research Centre of Canada, Richmond); Peter Tugwell (Institute of Population Health, University of Ottawa, and the Division of Rheumatology, Department of Medicine, University of Ottawa, Ottawa); Elaine Yacyshyn (University of Alberta, Edmonton); Charlene Yousefi (Richmond); Dawn Stacey (University of Ottawa, Ottawa)

**Objective:** Patient decision aids are designed to present the potential benefits and harm of treatment options, clarify individuals' preferences, and provide a structure for discussion at a clinic visit. We applied the concept of edutainment (a form of entertainment that is designed to educate and to amuse) to develop a web-based decision aid called the ANSWER. Designed for patients with rheumatoid arthritis (RA),

ANSWER presents information on methotrexate (MTX) in print, voice recording, and animated stories created with Adobe Photoshop. This study aims to assess the extent to which ANSWER reduces patient's decisional conflict, improves their medication knowledge and their skills of being 'effective healthcare consumers'.

**Methods:** We used a pre-post study design. Eligible participants had a diagnosis of RA, had been prescribed methotrexate but were unsure about starting it, and had access to the internet. Outcome measures included: 1) Decisional Conflict Scale (DCS), 2) Methotrexate in RA Knowledge Test (MiRAK), and 3) Effective Consumer Scale (EC-17). Paired t-tests were used to assess changes before and after the intervention.

**Results:** Of the 30 participants, 23 were women (76.7%) with a mean age of 54.90 years (SD=14.91). The median disease duration was 1 year (IRQ=0.3; 5.0). The mean DCS was 49.50 (SD=23.17) pre-intervention and 21.83 (SD=24.12) post-intervention (difference= -27.67, 95% CI= -15.44, -39.89;  $p < 0.001$ ). Before using the ANSWER, 13.3% of participants scored  $< 25$ , compared to 70% after the intervention. Similar results were observed in the MiRAK (pre: 30.62, SD=9.26; post: 41.67, SD=6.81; difference: 11.03, 95% CI=6.73, 15.34;  $p < 0.001$ ), but not the EC-17 (pre: 68.24, SD=12.46; post: 72.94, SD=12.74; difference: 4.71; 95% CI= -1.81, 11.22;  $p=0.15$ ). After using the ANSWER, 20 participants (66.6%) were able to make a decision (14 would take MTX, 6 would decline MTX and talk to their doctor about other treatment options). 10 participants (33.3%) remained unsure about their preferred choice.

**Conclusion:** Patients' decision quality and MTX knowledge improved after using the ANSWER. However, caution should be taken when interpreting the results due to the lack of a control group. The lack of a statistically significant change in the EC-17 might reflect the fact that it takes time to develop effective consumer attributes, such as how to find resources or set priorities. Supported by a CIORA grant.

## 46

### Ovarian Involvement in Eosinophilic Granulomatosis with Polyangiitis

Maia von Maltzahn (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Mary Kinloch (Saskatoon); Margaret Truchan (University of Saskatchewan, Saskatoon)

**Case Report:** We report a rare case of histologically confirmed eosinophilic granulomatosis with polyangiitis involving the ovary and adnexa in an 81-year old woman. This patient presented to the general internal medicine hospital service with recurrent abdominal pain, nausea, diarrhea and new left foot drop. Her past medical history was significant for asthma, diverticulosis, hypertension, and a long-standing (8+ years) diagnosis of sensorimotor axonal neuropathy of unknown etiology. During radiographic evaluation of her abdominal pain, a cystic ovarian mass was observed, leading subsequently to her undergoing an oophorectomy. Investigative findings during the course of her admission included: an elevated blood eosinophil count of  $4.54 (0.00-0.60 \times 10^9/L)$ , negative ANCA serology, paranasal mucosal thickening compatible with chronic sinusitis was observed on CT scan of the head. Nerve conduction studies confirmed an asymmetric motor and sensory neuropathy consistent with mononeuritis multiplex. Sural nerve biopsy demonstrated evidence of vasculitis with axonal loss within large myelinated axons. A bone marrow biopsy revealed hypercellularity with eosinophilia. Subsequent review of histopathology from the patient's oophorectomy, confirmed vasculitis of the medium-sized arteries within the ovaries and fallopian tubes. The collective findings established a diagnosis of multisystemic involvement of Eosinophilic Granulomatosis with Polyangiitis (EGPA). This patient was initiated on appropriate corticosteroid/ immunosuppressive therapy with a gratifying response. This case is the first to report histologically established ovarian involvement in EGPA.

### **Effect of Biologic Disease Modifiers (BDMARDs) on Cardiovascular Risk of Patients with Rheumatoid Arthritis (RA)-2 Years Prospective Cohort Study**

Majed Khraishi (St. John's); Rana Aslanov (Memorial University of Newfoundland, St. John's); Katie Doyle (St. John's)

**Objective:** To assess the effect of BDMARDs on a 10-year CVD risk and the incidence of CV events in patients with RA after 24 months of observation.

**Methods:** 220 patients with RA on biologics were prospectively followed-up. The Framingham Risk Score (FRS) was used for the assessment of 10-year CVD risk. The presence of CV risk factors was ascertained at the baseline and at 24 months. Analyses of the relationships between lipids and inflammatory indices before and after treatment with biologics were performed. Treatment changes were also analyzed. Paired t-test and Multivariate Regression analyses were performed.

**Results:** 220 patients (73% females) with the mean (SD) age of 56.2 (11.6) years were prospectively followed up to 24 months. Nine patients with MI and 5 patients with TIA/Stroke had their CV events prior to the study. Two patients had MI during the study. 19.1% patients smoked at the baseline (one quit during the study). Sixty-five patients were on Lipid-lowering treatment. TC did not change after 1 year but was reduced after 2 years of observation ( $3.0 \pm 2.8$  vs.  $2.0 \pm 2.5$ ,  $p < 0.001$ ). HDL increased at 12-month and reduced at 24-month period ( $0.7 \pm 0.7$  vs.  $0.8 \pm 0.7$ ,  $p = 0.042$  and  $0.7 \pm 0.7$  vs.  $0.6 \pm 0.7$ ,  $p = 0.025$ , respectively). LDL means at 12 and 24-month periods showed improvement from  $1.8 \pm 1.6$  to  $1.3 \pm 1.5$ ,  $p < 0.001$ . The AI was significantly reduced during the two follow-up periods. The correlation between Adalimumab and TC/LDL lipids was significant ( $r = 0.161$ ,  $p = 0.017$  and  $r = 0.150$ ,  $p = 0.026$ ) as well as between Golimumab and HDL/LDL levels ( $r = 0.143$ ,  $p = 0.034$  and  $r = 0.145$ ,  $p = 0.033$ ). The overall CVD risk reduced in 12 months ( $12.5 \pm 9.3$  vs.  $12.1 \pm 9.0$ ;  $p = 0.019$ ) and in 24 months ( $12.5 \pm 9.3$  vs.  $11.9 \pm 8.9$ ;  $p < 0.001$ ). The analysis of the impact of individual BDMARD on 10-year CV event risk showed improvement in Tocilizumab ( $14.3 \pm 9.1$  vs.  $12.9 \pm 8.5$ ;  $p = 0.002$ ) and Abatacept ( $14.0 \pm 10.0$  vs.  $13.4 \pm 10.0$ ;  $p = 0.042$ ) groups.

**Conclusion:** Two counts of CV event were observed during the study period. Our results showed a trend in reducing a 10-year CV event risk over 24-month period in patients with RA. This improvement was influenced by many factors such as lipid-lowering treatment (29.5% of patients), proper control of blood pressure and plasma glucose level. The study results demonstrated a favorable effect of BDMARDs on the serum levels of atheroprotective HDL-C and their AI. Good control of the inflammation by BDMARDs effectively decreased it and possibly played a pivotal role in reducing the risk for cardiovascular event.

### **Multicenter Validation of the Lupus Activity Scoring Tool (LAST) as Compared to the SELENA SLEDAI (SS) Modification**

Majed Khraishi (St. John's); Rana Aslanov (Memorial University of Newfoundland, St. John's); Sanjay Dixit (McMaster University, Hamilton); Krista Fudge (Western Memorial Hospital, Corner Brook); Vandana Ahluwalia (Brampton); Sarah Khraishi (Nexus Clinical Research, St. John's)

**Objective:** To validate the LAST in multiple clinical settings using its correlation to the SELENA SLEDAI modification. To test the usability and the accuracy of an electronic application of the same tool.

**Methods:** This multicenter study was initiated in four Canadian clinics: two in Newfoundland and two in Ontario. The LAST included patient global assessment of disease activity (PGA), physician global assessment of disease activity (PHGA), C3, C4 and Anti-ds Anti-DNA titer abnormalities, and a formula incorporating the current immunomodulating medication used as an indication of SLE activity. Patients who met the SLE ACR 1997 criteria update were recruited and evaluated in the study centres using LAST. Some of the patients were prospectively followed and evaluated by the same tool at each visit. The SS was

also calculated for each visit. Descriptive statistics and correlation bivariate were conducted. The LAST scores of the disease activity of patients with multiple assessments were compared to the SS scores.

**Results:** Thirty one patients (90.3% females) with 68 assessments from four study centers were included in this analysis. The mean (SD) age was 45.9 (14.7) years and the mean (SD) of disease duration was 14.2 (6.0) years. Scores from the LAST were obtained at each visit in addition to the SLEDAI scores. The mean (SD) SLEDAI score was 6.6 (3.5). The mean (SD) LAST (with C3, C4 and Anti-ds Anti-DNA) score was 34.5 (17.8). The SLEDAI scores were consistent and strongly correlated ( $r=0.791$ ;  $p<0.001$ ) with the LAST scores at the baseline and follow-up visits: SS scores 0-4 corresponded to the LAST scores of 0-30 while SS scores of 8 or higher corresponded to 50 and higher, respectively. The electronic applications of the LAST were easy to use and no errors were found with their results as compared to the manually obtained scores.

**Conclusion:** The Lupus Activity Scoring Tool (LAST) is a new disease activity index that correlates well with the SELANA SLEDAI modification. The use of simple clinical variables as a measure of SLE activity seems to be valid under different clinical settings with different assessors. The development of easy to use electronic apps will make the use of these activity tracking tools simpler and can possibly be utilized in non-specialist settings.

## 49

### **Impact of Psoriatic Arthritis (PsA) on Health Care Utilization (HCU) and Quality of Life (QoL)**

Majed Khraishi (St. John's); Rana Aslanov (Memorial University of Newfoundland, St. John's); Heather Zurel (St. John's); Sarah Khraishi (Nexus Clinical Research, St. John's)

**Objective:** To assess and compare utilization of healthcare services by patients with Early (EPsA) and Established (EstPsA) PsA. To assess the Quality of Life of PsA patients over 12 months

**Methods:** 151 patients with PsA were followed prospectively for a 12-month period, 58 patients with EPsA and 93 with EstPsA (defined as  $<2$  and  $\geq 2$  years from onset of arthritis symptoms). The HCU was examined using "Health Care Utilization Resource Use" form. The QoL was evaluated using EUROQOL-5D and SF36 tools. The association of disease severity and treatment with patients' utilization of health care services and their QoL analyzed and compared between two cohorts.

**Results:** At baseline, patients with EPsA utilized more health care services than those with EstPsA. By 12 months, 60% ( $p=0.009$ ) patients with EPsA and 63% ( $p=0.104$ ) with EstPsA were treated by MTX vs. 35% and 52% at the baseline. Average DAS28 score at baseline was higher in patients with EPsA (3.9 vs. 3.3; 95%CI 0.05-0.88;  $p=0.028$ ). DAS28 score improved over 12 months in both cohorts: EPsA 3.9 (1.2) vs. 2.7 (1.1),  $p<0.001$ ; EstPsA 3.3 vs. (1.2) to 2.6 (1.3),  $p<0.001$ . HCU by EPsA patients did not change from baseline (0.82 vs. 0.91,  $p=0.604$ ); while EstPsA patients reduced the utilization of the health care services (0.33 vs. 0.14,  $p=0.001$ ). DAS28 and HCU were strongly associated in both cohorts. DAS28 and HAQ associated with QoL in EPsA cohort ( $r=-0.74$ ,  $p<0.001$ ;  $r=-0.66$ ,  $p<0.001$ ; and  $r=-0.44$ ,  $p=0.001$ ;  $r=-0.42$ ,  $p=0.001$ ). By 12 months, EPsA patients slightly improved their Physical Health, while EstPsA patients showed significant improvement in both Physical (48.3 vs. 56.4,  $p<0.001$ ) and Mental (60.9 vs. 68.2,  $p=0.002$ ) components of SF36; EQ-5D also showed improvement for EstPsA patients from 56.7 to 70.7,  $p<0.001$ . Treatment of EstPsA patients with MTX was strongly correlated with their improvements in QoL.

**Conclusion:** PsA causes considerable disability and affects the QoL of patients even at early stages of the disease. Our findings showed that patients with EPsA seem to utilize more health care services. Early initiation of treatment with DMARDs may reduce the burden of PsA on the health care system, improve patients' well-being and quality of life.

## 50

### **Long-Term Efficacy and Safety of Tocilizumab (TCZ) Monotherapy in Patients (PTS) with Rheumatoid Arthritis (RA) Previously Methotrexate (MTX) Naïve or MTX Free for 6 Months Prior to Study Start**

Majed Khraishi (NL Research Technologies (NLRT), St. John's); Anthony Sebba (University of South Florida, Tampa); Andrew Anisfeld (Genentech, South San Francisco); Jenny Devenport (Genentech, South San Francisco); Corrado Bernasconi (Roche, Basel); Devi Smart (Roche, Basel); Daniel Galindez (Roche, Welwyn); Chiedo Mporu (Roche, Basel); Juan Gomez-Reino (Hosp Clin U, Santiago de Compostela); Graeme Jones (University of Tasmania, Hobart)

**Objective:** In this post hoc exploratory analysis, efficacy and safety were evaluated in pts from AMBITION who remained on TCZ monotherapy in the long-term extension (LTE) study up to 240 wks.

**Methods:** Pts randomized to TCZ 8 mg/kg monotherapy in AMBITION (n=286) who entered the LTE (n=243) were included. During the LTE, MTX/other disease-modifying anti-rheumatic drugs (DMARDs) could be added for pts who did not achieve a 50% reduction in number of tender and swollen joints from baseline of the core study. The rate, timing and nature of added DMARDs were characterized. Efficacy and adverse events (AEs) were assessed up to 240 wks.

**Results:** Of 243 pts who entered the LTE, 57.2% (n=139) remained on monotherapy until withdrawal or data cut, 9.9% (n=24) added a DMARD before LTE entry and 32.9% (n=80) added a DMARD after LTE entry (18.5% [n=45]  $\leq 3$  wks post-entry; 14.4% [n=35]  $> 3$  wks post-entry). DMARDs included MTX (93% [97/104]), hydroxychloroquine (3% [3/104]), leflunomide (2% [2/104]) and parenteral gold (2% [2/104]). Of the 139 pts who remained on TCZ monotherapy, 102 (73%) reached 240 wks of treatment and 37 (27%) withdrew. During the first 24 wks, sharp decreases were shown in SJC (19.0/4.8), TJC (32.5/10.5) and DAS28 (data not shown – missing data were handled using last-observation-carried-forward. For physician and pt global assessments of disease activity, no imputation of missing baseline values was performed); and continued to decrease or were maintained thereafter. Similar trends in improved disease state were observed; 40.1% and 16.7% of pts achieved DAS28  $< 2.6$  and clinical disease activity index (CDAI) remission, respectively, by wk 24; rates increased or were maintained thereafter; absolute numbers achieving these endpoints increased to wks 192 and 120. Absolute numbers achieving DAS28  $\leq 3.2$  and CDAI low disease activity increased to wks 120 and 96, respectively. AEs for all pts in this analysis (n=243) were consistent with TCZ's known safety profile.

**Conclusion:** For pts who stayed on monotherapy during the trial, TCZ treatment provided durable efficacy over time, as demonstrated by increasing proportions and/or numbers achieving low disease activity and remission thresholds. AEs reported were consistent with TCZ's known safety profile; no new safety signals were detected.

## 51

### **The Influence of Age at Disease Onset on Disease Activity in Rheumatoid Arthritis: Results from Ontario Best Practices Initiative**

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**Objective:** The population of elderly individuals with rheumatoid arthritis (RA) is increasing. The aim of this study was to assess whether age at disease onset affects disease activity in RA patients.

**Methods:** All patients enrolled in the Ontario Best Practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care, were included in the study (N= 2177). Patients were recruited at



any stage of RA disease with  $\geq 1$  swollen joints. Patients were categorized as late onset rheumatoid arthritis (LORA) if their disease onset was  $\geq 60$  years of age (N=519) and as young onset rheumatoid arthritis (YORA) if disease onset occurred before 60 years (N=1658). Differences in baseline characteristics between groups were compared using chi-square and t-tests. The main outcome of interest was mean Disease Activity Score [DAS28] at entry into the registry. Linear regression models, adjusted for age, gender, disease duration, seropositivity, use of DMARDs and/or biologics were performed to assess the effect of age at disease onset on DAS28. P-values  $< 0.05$  were considered statistically significant.

**Results:** The mean (SD) age of patients was 57.4 (12.9) years. At cohort entry, mean DAS28 score was modestly higher in LORA group compared to YORA group (4.6 vs 4.5,  $p = 0.025$ ). LORA patients were significantly less likely to be female (68.2% vs 80.3%) and had shorter disease duration (2.8 vs 10.3) compared to YORA. LORA patients were less likely to be seropositive and had higher acute phase reactants at baseline. Tender and swollen joint counts did not significantly differ between the two groups. LORA patients had higher prevalence of co-morbidities, including cardiovascular, neurologic and renal disease, diabetes, osteoarthritis and cancer. LORA patients were more frequently treated with DMARDs (80.9% vs 66.5%,  $p < 0.001$ ) or steroids (33.8% vs 27.7%,  $p = 0.009$ ), but received less biologic therapy (11.5% vs 25.3%,  $p < 0.001$ ) compared to YORA patients. In multivariate models, age of disease onset was consistently associated with higher disease activity.

**Conclusion:** Despite differences in baseline characteristics, LORA patients had a slightly higher DAS28 scores compared to YORA patients at entry into the registry. After adjusting for confounding variables, age of disease onset was associated with worse disease activity in RA patients.

## 52

### **Efficacy of Steroid Injections to Treat Dactylitis in PsA Patients**

Marianne Stroz (Kingston); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Vinod Chandran (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

**Objective:** Dactylitis is a clinical hallmark of psoriatic arthritis (PsA) affecting up to 48% of PsA patients. Currently, dactylitis is treated empirically with NSAIDs, DMARDs, anti-TNF agents, or steroid injections, depending on the severity of the dactylitis and associated disease. A previous study by our group clearly demonstrated the efficacy of DMARDs and anti-TNF agents in treating acute dactylitis, especially anti-TNFs. However, there is little evidence for response of dactylitis to steroid injections. Our objective was to compare the resolution of acute dactylitis in patients treated with DMARDs or anti-TNF agents to patients treated with steroid injections in a longitudinal PsA cohort.

**Methods:** Patients are followed prospectively according to a standard protocol. Acute dactylitis was defined as acute and painful swelling of an entire digit. Charts of patients presenting with dactylitis between 1978 and 2013 were reviewed to document the treatment change at the time of presentation with the first episode of acute dactylitis. Treatment change included the addition of a new DMARD or anti-TNF agent to therapy (systemic) or a steroid injection (local). Response was evaluated at the patient's follow up visit 1-12 months later (median, 4.67 months). Response was defined as either complete resolution of all digits for systemic treatment or resolution of the injected digit for local treatment.

**Results:** Of the 381 patient charts reviewed, 275 had data available for analysis. Of these patients', 64.4% were male and the average age was 41.7 years. Upon presentation of dactylitis, 141 patients underwent treatment changes at the clinic: 32 patients received steroid injections alone, 5 patients received steroid injections and were started on a new DMARD and 104 patients were started on a new DMARD or anti-TNF therapy. 75.0% of patients responded to steroid injections alone compared to 70.6% of patients who responded when started on a new DMARD or anti-TNF. No significance was found between the effects of local vs. systemic treatment ( $p = 0.82$ ). Additionally, only 56.7% of patients who had no treatment change

achieved resolution which was significantly lower than patients who received a change in treatment ( $p=0.04$ ).

**Conclusion:** Patients with dactylitis who receive local steroid injects receive no additional benefit than if started on a new systemic therapy. However, a treatment change was more beneficial than doing nothing. A randomized control trial comparing the effects of steroid injections, DMARDs and anti-TNF agents seems warranted to determine the best approach to treating patients with acute dactylitis.

## 53

### **Health-Related Quality of Life (HRQoL) across Systemic Autoimmune Rheumatic Diseases (SARDs)**

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**Objective:** SARDs are multisystem diseases associated with impaired HRQoL. The objectives of this study were twofold: firstly, to demonstrate our capacity to use a harmonized dataset derived from four existing SARD cohorts to pursue cross-disease research; and, secondly, to compare the magnitude of impairment in HRQoL in four SARDs and determine whether SARD type has an independent effect on HRQoL.

**Methods:** We included incident subjects enrolled in four longitudinal SARD cohorts, namely the Canadian Scleroderma Research Group (SSc), the McGill Systemic Lupus Erythematosus Cohort (SLE), patients enrolled in one site (Jewish General Hospital) of the Canadian Early Arthritis Cohort Study (RA) and the Canadian Inflammatory Myopathy Study (myositis), and whose data were entered in a harmonized database. The outcomes of interest were the Medical Outcomes Trust Health Survey (SF-36v1 for SLE, SF-36v2 for CSRG and CIMS, or SF-12 for CATCH), which can be summarized using Physical Component Summary (PCS) and Mental Component Summary (MCS) scores. Multivariate analysis was conducted to determine whether SARD type had an independent effect on HRQoL, after adjusting for sociodemographic variables (age, sex, race/ethnicity and education) and disease duration.

**Results:** The study included 333 SSc subjects (82% women, mean age 54 years, 51% limited, 46% diffuse), 112 SLE subjects (94% women, mean age 36 years), 54 RA subjects (63% women, mean age 58 years) and 13 myositis subjects (69% women, mean age 51 years). Mean PCS scores were  $37.1 \pm 11.4$  in SSc,  $40.9 \pm 10.2$  in SLE,  $36.4 \pm 11.3$  in RA and  $33.6 \pm 11.6$  in myositis. Mean MCS scores were  $47.5 \pm 12.3$  in SSc,  $40.6 \pm 14.1$  in SLE,  $47.2 \pm 12.1$  in RA and  $41.5 \pm 12.0$  in myositis. Disease was an independent predictor of HRQoL: SLE patients had significantly lower MCS scores compared to SSc patients ( $\beta -4.26$ , CI 95% -7.80; -0.72,  $p=0.0184$ ), and a trend to have worse MCS scores compared to RA patients ( $\beta -4.66$ , CI 95% -9.56; 0.23,  $p=0.0619$ ). In addition, there was a trend towards worse physical HRQoL in myositis patients compared to SSc ( $\beta -6.09$ , CI 95% -12.58; 0.40,  $p=0.0658$ ).

**Conclusion:** Cross-SARD research provides a novel approach to gain greater understanding of the commonalities and differences across rheumatic diseases. A limitation of our study was the different versions of our outcome measure. The differences in HRQoL which were suggested provide impetus to pursue more comprehensive HRQoL studies, including trajectories over time.

### **Systemic Autoimmune Rheumatic Disease and PM2.5 Air Pollution Levels in Alberta**

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**Objective:** To estimate whether a diagnosis of systemic autoimmune rheumatic disease (SARD) is associated with air pollution in a population-based sample.

**Methods:** We evaluated population-based data from Alberta, 1993-2007. The case definition for SARDs was based on three algorithms: >2 physician billing claims with the International Classification of Diseases (ICD)-9 code 710 (within 2 years but at >2 months apart), or >1 such billing code by a rheumatologist, or >1 hospitalization with an ICD10 diagnostic code corresponding to a SARD diagnosis (M32.1, M32.8-32.9, M33-M34, M35.0, M35.8-35.9, M36.0). These codes include systemic lupus erythematosus, Sjogren's Syndrome, scleroderma, polymyositis, and dermatomyositis. Yearly average residential exposures to ambient fine particulate matter (PM2.5) were assigned using satellite-derived data associated with the dissemination area for each Alberta resident. The dissemination area used to assign PM2.5 exposure levels was derived from the postal code that was recorded most proximal to the date of the first ICD code for a SARD. Bayesian hierarchical latent class regression models were used to estimate the probability that any given resident of Alberta was a SARD case, given data on our three algorithms. The individual level probabilities were applied to estimate the total number of cases according to groups characterized by age, sex, urban-versus-rural residence, and PM2.5 levels. This information was used in the hierarchical model to generate odds ratio (OR) estimates for a resident of Alberta being a SARD case, based on personal characteristics (age, sex, urban-versus-rural residence) and PM2.5 levels of all the dissemination areas across Alberta. The hierarchical model accounted concurrently for these characteristics, as well as an interaction term between age and sex.

**Results:** In our hierarchical model, which accounted concurrently for age and sex (and an interaction term between them), the probability of being a SARD case was distinctly higher among females versus males (OR 7.00, 95% credible interval, CrI, 5.24-9.02) and for residents aged >45 versus those younger (OR 5.97, 95% CrI 4.50-7.85), with evidence for effect modification, such that the OR for older females was 28.49 (95% CrI 20.7-36.9). We also estimated an increased probability for being a SARD case among residents who lived in urban versus rural locations (OR 1.16, 95% 1.05, 1.27). Independent of these effects, the odds of being a SARDs case increased with PM2.5 levels (OR 1.08 per ug/m3, 95%CI 1.04-1.11).

**Conclusion:** After adjusting for age, sex and urban/rural status, exposure to PM2.5 was associated with an increased risk of SARDs.

### **Guidelines for Classification and Diagnosis of Fibromyalgia Spanning Three Continents**

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**Objective:** Fibromyalgia (FM) has emerged as a cluster of symptoms and co-morbidities, characterized by subjective complaints without physical or biomarker abnormality. Areas of debate include classification, value of diagnostic label, tender point examination, and best clinical care setting. Recommendations in recent guidelines addressing these issues were examined for consistencies and differences.

**Methods:** Systematic searches from January 2008 to February 2013 of the US-American National Guideline Clearing House, the Scottish Intercollegiate Guidelines Network, Guidelines International Network and Medline for evidence-based guidelines for the management of FM were conducted. Inclusion criteria required that the guideline was commissioned by a scientific organisation, guideline group was interdisciplinary, systematic search strategy was outlined, criteria for classification of evidence and recommendations were stated and the process for establishing recommendations was outlined.

**Results:** The literature search yielded 24 citations (19 excluded for duplication, 1 without criteria for assigning evidence, 1 not scientific society commissioned) with three guidelines independently developed in Canada, Germany and Israel included. Recommendations concerning definition, classification, clinical diagnosis and general principles of care were based predominantly on expert consensus, with limited literature evidence. All three countries justified the need for guidelines based on high FM prevalence, controversies surrounding diagnosis/management, reduced health-related quality of life and high health care costs with unanimity for the following parameters: FM was defined by the 1990 ACR classification criteria; FM is clinically diagnosed by a typical cluster of symptoms, following a composite history, physical examination, and selected laboratory tests; diagnosis confirmation with 2010 ACR diagnostic criteria if desired; importance of assigning a diagnostic label; education focussed towards a biopsychosocial model, planned treatment strategy and expected outcome; recognition that FM is a continuum disorder or can coexist with other medical or mental conditions. Differences between guidelines were reflected in the concept of FM as representing a clinical construct of pain and other symptoms, a functional somatic syndrome, or a central hypersensitivity syndrome identified by each, tender point examination replaced by examination for soft tissue tenderness by 2, care in the primary care setting by 2, and 1 discouraging focus on a triggering event.

**Conclusion:** Guidelines from three continents showed remarkable consistency regarding the clinical concept of FM, acknowledging the need to provide confidence in a clinical diagnosis, importance of assigning a diagnostic label, and acceptance that FM is neither a distinct rheumatic nor mental disorder, but a cluster of symptoms spanning a broad range of medical disciplines.

## 56

### **A Paradigm Change for Treatment Strategies for Fibromyalgia Syndrome Reflected by Recommendations of Recent Evidence-Based Interdisciplinary Guidelines Developed Independently in Three Countries**

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**Objective:** Although the ideal treatment for fibromyalgia (FM) remains elusive, the medical community requires direction in the care of these patients. The literature however abounds with copious reports of various treatments that drive health-care costs, but provide ever increasing confusion for patients and physicians. We have compared treatment recommendations for FM provided by recent evidence-based guidelines.

**Methods:** Systematic searches from January 2008 to February 2013 of the US-American National Guideline Clearing House, the Scottish Intercollegiate Guidelines Network, Guidelines International Network and Medline for evidence-based interdisciplinary guidelines on the management of FM were conducted. Inclusion criteria required that the guideline was commissioned by a scientific organisation, the guideline group was interdisciplinary, the systematic search strategy was outlined, criteria and process for classification of evidence and recommendations were stated.

**Results:** Three evidence-based interdisciplinary guidelines for the treatment of FM in Canada, Germany

and Israel fulfilled inclusion criteria. All three guidelines emphasized a patient-tailored approach according to key symptoms. Non-pharmacologic strategies were the major positive first choice recommendation for all with emphasis on aerobic exercise, cognitive behavioural therapy and multicomponent therapy (exercise and psychological). Acupuncture, hypnosis/guided imagery and Tai Chi were recommended by the German and Israeli guideline, whereas the Canadian guidelines indicated only short term benefits for acupuncture, and categorized hypnosis/guided imagery and Tai Chi as psychological and exercise interventions respectively with some evidence for effect, but none were specifically recommended. Pharmacologic treatments were less enthusiastically recommended by all three groups. With the qualifier that drugs provide only modest effect, the Canadian and Israeli guidelines gave strong recommendation for the anticonvulsants (gabapentin and pregabalin) and serotonin noradrenaline reuptake inhibitors, whereas these drug categories received only weak recommendation by the German guideline. All groups cautioned about the side effects of drugs manifesting as symptoms of FM. Use of strong opioids was discouraged by all, with the Israeli and German guideline providing specific negative recommendation for many other drug categories including non-steroidal agents, systemic steroids, benzodiazepines, thyroid hormone replacement, amongst others. Although not providing specific negative treatment recommendations, the Canadian guidelines cited lack of evidence to support many treatments which would therefore constitute “off-label” use.

**Conclusion:** Recent evidence-based interdisciplinary guidelines concur on the importance of treatments tailored to the individual patient and further emphasize the necessity of self-management strategies which include exercise and psychological techniques. Contrary to popular perception, drug treatments were recommended with reservation regarding both efficacy and side effect profile.

## 57

### **Rheumatologists Lack Confidence in Knowledge of Cannabinoids in the Management of Rheumatic Conditions: A Needs Assessment of Canadian Rheumatologists**

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**Objective:** Pharmacologic treatment of rheumatic pain is sub-optimal, leading patients to seek alternate treatments. Although herbal cannabis (marihuana) has had medicinal use for centuries, scientific study of cannabinoid effects is recent. With patient advocacy for access to cannabinoids, regulatory bodies worldwide are considering the merits of legalizing medical cannabis. As arthritis is cited as a common reason for medical cannabis use, rheumatologists should be better informed to advise patients. We have assessed rheumatologists’ self-reported confidence in their knowledge of cannabinoids and their perceived competence in providing prescriptions.

**Methods:** Using a 19-question needs assessment survey, sent via email to the entire Canadian Rheumatology Association membership, we have examined rheumatologists’ confidence in 1) knowledge of cannabinoids in general, including phyto-, syntheto- and endocannabinoids, and 2) perceived competence and ability to advise patients regarding indications, use and precautions for cannabinoids in general, and herbal cannabis specifically

**Results:** 128 (25%) of all 510 members responded. Over three quarters were not confident in their knowledge of cannabinoid molecules, with two thirds reporting poor knowledge of the physiology of the endocannabinoid system. While 45 % of respondents stated no current role for any cannabinoid

preparations for rheumatology patients, 70% believe this applies specifically to medical cannabis. Only 16 (13%) had ever previously recommended a trial of medical marihuana. Over 90% were not confident in writing a prescription for medical cannabis when required to indicate dosing, frequency and method of administration. When respondents were grouped as “Confident” in knowledge of cannabinoid molecules (n=33) vs. “Not-Confident” (n=95), the following were reported respectively: Current role for medical cannabis 48% vs. 23%; Previous prescription of pharmacological cannabinoid 33% v.12%; Previous recommendation for medical cannabis 27% vs.7%; No previous recommendation for either 39% vs. 81%; Would not recommend any cannabinoid in future 33% vs. 67%. Only 33% of knowledge confident respondents reported competence in prescribing medical cannabis. Concerns about risks of marihuana use were in line with current literature.

**Conclusion:** The overwhelming majority of rheumatologists reported lack of confidence in their knowledge of cannabinoids, and uncertainty about their competence to prescribe cannabinoid treatments and herbal cannabis in particular. This survey highlights a major disconnect between patients’ advocacy, policy makers and physician need to provide competent patient care within the bounds of medical ethics and deontology. Guidance is required to inform rheumatologists on the prevailing evidence for the safe and effective use of cannabinoids in rheumatic conditions.

## 58

### **Disability in Fibromyalgia is Associated with Greater Self Reported Symptoms and Functional Impairment**

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**Objective:** It is intuitive that disablement due to illness should be reflected in illness severity. When illness measurement is based on subjective report only, the reliability of symptom report is crucial. Societal costs for fibromyalgia (FM) are high with disability rates of 30% reported in the developed world. We have examined clinical characteristics of FM patients currently employed or receiving disability payments

**Methods:** Of 246 participants in a cohort study of FM, 90 were employed, 77 receiving disability payments. Demographic and disease severity measures included: pain VAS, patient global assessment (PGA), Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire (HAQ), McGill Pain Questionnaire (MPQ), Pain Disability Index (PDI), Pain Catastrophizing Scale (PCS), anxiety and depression by Arthritis Impact Measurement Scale (AIMS). Between-group differences in discrete and continuous variables were assessed for statistical significance with the Chi-Square test and one-way analysis of variance, respectively. Linear regression was used to assess between-group differences in disease activity while adjusting for potential confounders.

**Results:** The prevalence of disablement was 30.8%. Disabled patients were significantly older (49.1 vs. 45.9;  $P=0.020$ ), more likely to smoke cigarettes (33.8% vs. 15.6%;  $P=0.006$ ) or marijuana (13.0% vs. 3.3%;  $P=0.020$ ). No significant differences were observed in pain duration (10.7 years) and gender (female: 91.0%). Prior/current occupation type differed significantly between groups: disabled patients were more likely previously employed in manual professions or service industry, with employed patients occupied in education/clerical/health fields ( $P=0.001$ ). Significant between-group differences were observed for management strategies: disabled patients used a greater count of medications ( $P=0.001$ ), more opioids ( $P=0.001$ ), antidepressants ( $P=0.032$ ), tranquilizers ( $P<0.001$ ), and cannabinoids ( $P=0.053$ ), and participated less in exercise activity ( $P=0.009$ ). Those disabled demonstrated more allodynia ( $P=0.027$ ) and

pain related behaviour ( $P=0.002$ ). Except for depression and anxiety, all other parameters were significantly higher in the disabled group: pain VAS ( $P<0.001$ ), PGA ( $P<0.001$ ), FIQ ( $P<0.001$ ), HAQ ( $P<0.001$ ), MPQ ( $P<0.0001$ ), PCS ( $P=0.005$ ) and PDI ( $P<0.001$ ). All associations remained significant except for HAQ, MPQ, and PCS when adjusted for age and education.

**Conclusion:** A significant proportion of FM patients are unemployed due to disability. The subjective report of symptom severity for those disabled may be explained by true disease severity, negative impact of medications, or patient perception of illness and suffering. Alternately, justification for ongoing disablement may be the driver for augmentation of subjective illness report. As all measurements in FM are subjective, disabled patients may be an important confounder for understanding outcome in FM.

## 59

### **Abatacept and Anti-Tumor Necrosis Factor Monoclonal Antibodies: Efficacy and Safety Comparisons**

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**Objective:** A paucity of clinical trial data exists comparing the efficacy and safety of biologic therapies for RA. This study evaluated remission rates and safety for patients treated with subcutaneous (SC) or intravenous (IV) abatacept compared with the anti-TNF monoclonal antibodies, adalimumab and infliximab, in a post hoc, cross-trial comparison.

**Methods:** In the head-to-head AMPLE study,<sup>1</sup> patients were randomized (1:1) to SC abatacept (125 mg weekly) or SC adalimumab (40 mg bi-weekly), plus background MTX. In the double-blind, double-dummy ATTEST study,<sup>2</sup> patients were randomized (3:3:2) to IV abatacept (~10 mg/kg every 4 weeks), infliximab (3 mg/kg every 8 weeks), or placebo, plus background MTX. In both trials, patients were biologic naïve and had active RA despite prior MTX. Remission according to Disease Activity Score (DAS)28 (C-reactive protein; CRP) and Simplified Disease Activity Score (SDAI) was evaluated over 12 months for all treated patients with data available. Safety was evaluated for patients who received  $\geq 1$  dose of study drug.

**Results:** In AMPLE, 318 and 328 patients received SC abatacept and adalimumab, respectively; in ATTEST, 156 patients received IV abatacept and 165 received infliximab. Baseline DAS28 (CRP) scores (mean $\pm$ SD) were  $5.5\pm 1.1$  in AMPLE and  $6.4\pm 0.9$  in ATTEST. Disease duration was  $1.9\pm 1.4$  and  $1.7\pm 1.4$  years for abatacept and adalimumab in AMPLE, and  $7.9\pm 8.5$  and  $7.3\pm 6.2$  years for abatacept and infliximab in ATTEST. Remission rates at 12 months were similar for treatment groups in each trial (DAS28 [CRP] remission: AMPLE, 43.3% abatacept vs 41.9% adalimumab; ATTEST, 29.9% abatacept vs 21.4% infliximab; SDAI remission: AMPLE, 23.3% vs 24.8%; ATTEST, 13.1% vs 11.4%). Over 12 months, 3.5% vs 6.1% of abatacept- vs adalimumab-treated patients, and 2.6% vs 7.3% of abatacept- vs infliximab-treated patients discontinued due to adverse events (AEs); 10.1% vs 9.1% and 9.6% vs 18.2% experienced SAEs; 1.6% vs 1.2% and 0.6% vs 1.2% had malignancy; 3.1% vs 1.2% and 1.3% vs 0.6% experienced autoimmune events; serious infections occurred in 2.2% vs 2.7% and 1.9% vs 8.5%.

**Conclusion:** Greater proportions of patients in the AMPLE trial achieved remission vs ATTEST; however, patients in AMPLE had shorter disease duration and lower baseline disease activity. Both SC and IV abatacept demonstrated similar remission rates to anti-TNF therapies, regardless of disease duration. Safety outcomes were mostly balanced, with more SAEs and serious infections with infliximab versus abatacept, and more discontinuations due to AEs or serious infections with anti-TNF agents versus abatacept. References: 1. Weinblatt ME. Arthritis Rheum 2013;65:28–38. 2. Schiff M. Ann Rheum Dis

60

**Two-Year Results from the AMPLE Trial: Low Disease Activity and Association Between Remission and Changes in Physical Function and Radiographic Outcomes with Subcutaneous Abatacept or Adalimumab**

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**Objective:** Remission and low disease activity (LDA) are now achievable goals in RA. Year 1 data from the head-to-head AMPLE study showed comparable rates of remission and LDA for patients treated with subcutaneous (SC) abatacept or adalimumab, with background MTX.<sup>1</sup> To assess whether these responses are maintained over time, and to evaluate the relationship with functional and radiographic outcomes, we report Year 2 data from AMPLE.

**Methods:** AMPLE was a 2-year, Phase IIIb, randomized, investigator-blinded study. Biologic-naïve patients with RA despite prior MTX were randomized to 125 mg SC abatacept weekly or 40 mg SC adalimumab bi-weekly, with background MTX.<sup>1</sup> The proportions of patients achieving remission (Disease Activity Score [DAS]28 [C-reactive protein; CRP] < 2.6, Clinical Disease Activity Index [CDAI] ≤ 2.8, Simplified Disease Activity Index [SDAI] ≤ 3.3, Routine Assessment of Patient Index Data [RAPID]3 < 3, Boolean score ≤ 1) or LDA (DAS28 [CRP] ≤ 3.2, CDAI ≤ 10, SDAI ≤ 11, RAPID3 ≤ 6) are presented. Physical function (assessed with the Health Assessment Questionnaire-Disability Index [HAQ-DI]; responders defined as an improvement of ≥ 0.3) and radiographic non-progression (defined as change in modified total Sharp score of ≤ smallest detectable change) were analyzed in patients achieving remission at 2 years.

**Results:** A total of 646 patients were treated (abatacept, n=318; adalimumab, n=328). Baseline clinical characteristics were balanced between treatments. The proportions of patients in remission or LDA at Year 2 were comparable for both treatments, and were higher than at Year 1.<sup>1,2</sup> More patients achieved DAS28 (CRP) remission (50.6% abatacept vs 53.3% adalimumab) compared with CDAI (32.0% vs 30.3%), SDAI (31.2% vs 32.5%), and RAPID3 (31.0% vs 26.5%) remission, with the smallest proportion achieving Boolean remission (20.7% vs 20.5%). Depending on the criteria used, 65.9–80.2% of adalimumab patients and 72.7–81.2% of abatacept patients who were in remission at Year 1 were also in remission at Year 2. Across criteria, >70% of patients in remission at Year 2 were HAQ-DI responders and >85% were radiographic non-progressors at Year 2. Improvement in HAQ-DI and radiographic outcomes at Year 2 were consistent between treatments.

**Conclusion:** Over 2 years of the AMPLE study, rates of remission and LDA increased over time across all criteria and remained comparable for SC abatacept and adalimumab. All remission criteria demonstrated high correlation with physical function and radiographic outcomes, with similar improvements in each treatment group at Year 2. References: 1. Weinblatt M, et al. *Arthritis Rheum* 2013;65:28–38.2. Fleischmann R, et al. *Ann Rheum Dis* 2013;72(Suppl. 3):626.

61

**2-Year Results from the AMPLE (Abatacept versus Adalimumab Comparison in Biologic-Naïve RA Patients with Background Methotrexate) Trial: Changes in Patient-Reported Outcomes in Response to Subcutaneous Abatacept or Adalimumab in Rheumatoid Arthritis**



Roy Fleischmann (University of Texas Southwest Medical Center, Dallas); Michael Weinblatt (Brigham & Women's Hospital, Boston); Michael Schiff (University of Colorado, Denver); Dinesh Khanna (University of Michigan, Ann Arbor); Michael Maldonado (Bristol-Myers Squibb, Princeton); Anagha Nadkarni (Bristol-Myers Squibb, Princeton); Daniel Furst (University of California at Los Angeles, Los Angeles)

**Objective:** RA is a debilitating disease that can impact health-related quality of life (HRQoL) through activity impairment, loss of independence and reduced work productivity. Year 1 data from the 2-year head-to-head AMPLE study showed comparable improvements in HRQoL and similar onset of response with subcutaneous abatacept and adalimumab on background MTX for multiple patient-reported outcomes (PROs).<sup>1</sup> Longer term data are important to assess maintenance of response over time. Here, we present PRO data from 2 years of the AMPLE study.

**Methods:** AMPLE is a Phase IIIb, randomized, investigator-blinded study. Biologic-naïve patients with RA despite prior MTX were randomized to 125 mg abatacept weekly or 40 mg adalimumab bi-weekly, plus MTX. Patient global assessment (PtGA) was measured by 100 mm visual analogue scale. Physical function was evaluated using the Health Assessment Questionnaire-Disability Index (HAQ-DI). HRQoL was assessed using the Short Form-36 (SF-36; including Physical and Mental Component Summary subscores [PCS and MCS]). The Activity Limitation Questionnaire (ALQ) measured the number of days that patients were unable to perform usual activities during the previous 30 days. Psychosocial independence was assessed using the ALQ and subscale items from the SF-36 survey. Physical independence was evaluated using items from the HAQ-DI. The Work Productivity and Activity Impairment questionnaire assessed work productivity. Data are mean (SE) improvements from baseline, unless stated otherwise.

**Results:** 646 patients were treated (abatacept, n=318; adalimumab, n=328). A similar proportion of abatacept- and adalimumab-treated patients (54.1% and 48.8%, respectively) achieved a HAQ-DI response (improvement of  $\geq 0.3$  units from baseline) at 2 years. Improvements (% [SD]) in PtGA at 2 years were 43.5 (3.7) vs 40.6 (3.6)% for abatacept and adalimumab, respectively. Improvements in all domains of the SF-36 observed at 1 year were maintained at 2 years (PCS: 9.3 [0.6] vs 8.6 [0.6]%; MCS: 4.1 [0.6] vs 3.3 [0.6]%, abatacept vs adalimumab at Year 2). At Year 2, comparable improvements in activity limitation, and psychosocial and physical independence were observed for abatacept and adalimumab (-6.4 vs -5.6 days, 0.8 vs 0.7, 0.9 vs 0.9, respectively). Improvements in overall work impairment at Year 2 were -25.4% for abatacept and -20.5% for adalimumab.

**Conclusion:** Year 2 data from this head-to-head study show that the improvements in PROs with both subcutaneous abatacept plus MTX and adalimumab plus MTX observed at Year 1 are maintained up to Year 2, with similar onset and durability of response. Reference: 1. Fleischmann R, et al. Arthritis Rheum 2012;64(Suppl 10):S577.

## 62

### **Head-To-Head Comparison of Subcutaneous Abatacept Versus Adalimumab on Background Methotrexate in RA: Blinded Two-Year Results from the AMPLE (Abatacept Versus Adalimumab Comparison in Biologic-Naïve RA Subjects with Background Methotrexate) Study**

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**Objective:** AMPLE is the first 2-year, head-to-head study in patients with RA, comparing biologic agents on background MTX. At Year 1, subcutaneous abatacept and adalimumab demonstrated comparable

efficacy, including radiographic outcomes, with similar safety.<sup>1</sup> Here we report 2-year results.

**Methods:** AMPLE was a 2-year, Phase IIb, randomized, investigator-blinded study with a primary efficacy endpoint (ACR20 response) at Day 365. Biologic-naïve patients with active RA despite prior MTX were randomized (1:1) to 125 mg abatacept weekly (without an IV load) or 40 mg adalimumab bi-weekly, with background MTX.<sup>1</sup> All efficacy analyses were done using the intent-to-treat population, with non-responder imputation where appropriate. Radiographs were assessed using the van der Heijde modified total Sharp score and were read through to Year 2, including re-reading Year 1 images, by readers blinded to treatment allocation and sequence.

**Results:** Baseline characteristics of the 646 treated patients were similar between groups;<sup>1</sup> 79.2% (252/318) of abatacept patients and 74.7% (245/328) of adalimumab patients completed Year 2. At Year 1, 64.8% of abatacept and 63.4% of adalimumab patients were ACR20 responders. Consistent with Year 1, clinical efficacy measures and inhibition of radiographic progression were comparable between abatacept and adalimumab at Year 2 (ACR20 response: 59.7% vs 60.1%; mean change in DAS28 (CRP): -2.4 vs -2.3; HAQ-DI response (change of  $\geq 0.3$ ): 54.1% vs 48.8%; radiographic non-progression (smallest detectable change  $\leq 2.2$ ): 84.8% vs 83.8%). Similar rates of AEs, SAEs (13.8% vs 16.5%), and malignancies (2.2% vs 2.1%) were observed for abatacept and adalimumab. More autoimmune AEs occurred with abatacept (3.8% abatacept vs 1.8% adalimumab); none were SAEs. Fewer infections (3.8% vs 5.8%) and opportunistic infections (3 vs 5 patients) occurred with abatacept than adalimumab, including two cases of tuberculosis in the adalimumab arm that led to discontinuation. There were fewer discontinuations due to AEs (3.8% vs 9.5%), SAEs (1.6% vs 4.9%), or serious infections (0/12 vs 9/19 patients) with abatacept than adalimumab. Injection-site reactions (ISRs) occurred less frequently with abatacept than with adalimumab (4.1% vs 10.4%).

**Conclusion:** In this first active comparator study between biologic agents in patients with RA with an inadequate response to MTX, subcutaneous abatacept and adalimumab were equally efficacious in clinical, functional, and radiographic outcomes over 2 years. The frequency of AEs was similar in both groups, but with fewer discontinuations due to AEs, SAEs, or serious infections, and fewer local ISRs in patients treated with SC abatacept. Reference: 1. Weinblatt M, et al. Arthritis Rheum 2013;65:28–38.

## 63

### Arthritis Disability in Three On-Reserve First Nations Communities on Vancouver Island: Results of a Population-Based Survey

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**Objective:** Increased prevalence and severity of arthritis have been reported among Aboriginal peoples. The aim of our study was to assess the prevalence of arthritis in three on-reserve First Nations communities served by the Kwakiutl District Council (KDC) on Vancouver Island.

**Methods:** An interviewer-administered household survey of all adults living in three on-reserve communities was performed to identify people who reported having received a diagnosis of arthritis by a

health professional, or, who reported chronic pain in the neck, back, or joints, with functional limitations. All adults identified as such, completed a second interview about their symptoms to classify the type of arthritis reported. Validated algorithms to classify spondyloarthritis (SpA), rheumatoid arthritis (RA), and osteoarthritis (OA) using self-report data on symptoms were used to identify the most likely diagnosis.

**Results:** Of the 536 residents, 447 (83%) participated in the household survey [mean (SD) age = 46 (16) years, 52% females]. Of these, 190 (43.5%) reported chronic joint, neck or back pain with functional limitation, and 138 (31.6%) reported having been diagnosed by a health professional with arthritis or rheumatism, excluding fibromyalgia. This is higher than reported in non-Aboriginal populations (non-age adjusted prevalence of 16% in national surveys using the same question). Of the 212 participants who reported chronic pain or an arthritis diagnosis, 201 (95%) completed the second interview [mean (SD) age = 54 (14) years, 57% females]. Of the 447 household survey participants, 7.1% reported having received a diagnosis of RA, 7.1% hip OA 8.7% knee OA, 8.0% hand OA, and 0.9% ankylosing spondylitis (AS). When applying classification criteria to self-report data, depending on the level of stringency used for the algorithms, 0.5% to 8% of participants fulfilled the SpA criteria, 3.4% to 17% the RA criteria, and 11.9% to 22% the OA criteria. Limitations of our study include lack of laboratory and radiological data, and reliance on self-reported symptoms to classify diagnosis, which can lead to misclassification and underreporting of cases with inactive or treated disease due to symptom control.

**Conclusion:** Overall, the prevalence of arthritis was high among the First Nations communities evaluated. The prevalence of reporting an arthritis diagnosis exceeded that reported in national surveys for non-Aboriginal peoples. The estimated prevalence of OA was similar, but the prevalence of RA and SpA were higher, in the KDC communities than reported in non-Aboriginal populations. Our findings for RA and SpA were congruent with reported prevalence in other First Nations populations.

## 64

### **Reliability and Responsiveness of the Standardized Universal Pain Evaluations for Rheumatology Providers for Children and Youth (SUPER-KIDZ)**

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**Objective:** Pain is the most common symptom in children and youth with juvenile idiopathic arthritis (JIA), however, currently there is no comprehensive validated pain measure for this population. The Standardized Universal Pain Evaluations for Rheumatology Providers for Children and Youth (SUPER-KIDZ) is a new multi-dimensional online pain tool, developed to fill this gap in clinical care. The objective of this study was to determine the test-retest reliability and responsiveness of the computerized 20-item version of the SUPER-KIDZ pain tool in children with JIA.

**Methods:** A single center prospective cohort study of JIA patients aged 8-18 years was performed. The SUPER-KIDZ questionnaire was administered to children expected to have stable pain for test-retest reliability analysis of each item using intra-class correlation coefficients (ICC) and weighted Cohen's kappa. Responsiveness of each SUPER-KIDZ item to change in pain was evaluated in patients undergoing intra-articular steroid injection(s) who are expected to have improvement in pain. Measures of responsiveness included standardized response mean (SRM), Wilcoxon signed rank test, linear mixed model regression, and receiver operating characteristic (ROC) curve analysis. Internal consistency of the three SUPER-KIDZ subscales (sensory, interference, emotional) was measured using ordinal reliability

alpha and item-total correlation.

**Results:** Fifty-one children were included, of which 40 (78%) were female, and had a median of 3 active joints (1-5) and median physician global assessment of 2.5 cm (1.5-4) on 10 cm visual analog scale. Internal consistency was acceptable (ordinal  $\alpha=0.73-0.92$ ) for the sensory, interference and emotional SUPER-KIDZ subscales. Good test-retest reliability (ICC or weighted kappa  $\geq 0.80$ ) was found for 15 SUPER-KIDZ items in at least one analysis. Reliability was strongest for the items on pain intensity, pain frequency, pain duration and physical function, and weakest for questions related to sleep, having fun, catastrophizing, and feeling angry. At 2 weeks post-injection, 16 items were responsive to change in pain (SRM=0.66-0.82, significant Wilcoxon signed rank and/or linear mixed model regression). ROC curve analysis of 9 items gave an area under the curve of  $\geq 0.70$ , adequately distinguishing between improved and unimproved subjects. The questions less responsive to change in pain were those related to fatigue frequency and emotional function (feeling angry, cheerful, worried).

**Conclusion:** The majority of items of the new online SUPER-KIDZ tool have excellent test-retest reliability and responsiveness properties. The questions regarding fatigue and emotional function are less responsive to change after a joint injection procedure and could be tested after a cognitive intervention. If validity is demonstrated, this measure could be implemented as a standardized comprehensive pain tool for JIA patients, thereby fulfilling a longstanding gap in the care of patients with JIA.

## 65

### **SUMMACTA: A Randomized, Double-Blind, Parallel Group Study of the Safety and Efficacy of Tocilizumab SC versus Tocilizumab IV, in Combination with Traditional DMARDs in Patients with Moderate to Severe RA**

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**Objective:** The objective of SUMMACTA study was to compare the efficacy and safety of TCZ SC and TCZ IV regimens in pts with adult RA who had an inadequate response to DMARDs (up to 20% may have failed one or more anti-TNF agents).

**Methods:** SUMMACTA is a 2-year, Phase 3 trial, which is a randomized, active controlled, parallel group study that includes a 24-week double-blind (DB) period, followed by a 72-week open-label phase. During the DB period, pts received TCZ SC 162 mg qw + placebo IV q4w or TCZ IV 8mg/kg q4w + placebo SC qw, in combination with traditional DMARDs. The primary endpoint was the proportion of patients achieving an ACR20 response at Week 24. The hypothesis of non-inferiority of TCZ SC with respect to TCZ IV regarding ACR20 response was tested by means of the 95% confidence interval (CI) and with a 12% non-inferiority margin (NIM). Additional clinical efficacy, immunogenicity and safety assessments were evaluated as secondary outcomes. Pts were stratified at baseline by body weight and region.

**Results:** A total of 1262 pts were enrolled globally. All patients' baseline characteristics were well balanced between TCZ SC and TCZ IV groups, including age, RA disease duration and DAS 28-ESR. At Week 24, 69.4% (95% CI: 65.5, 73.2) of TCZ SC-treated pts achieved an ACR20 response versus 73.4% (95% CI: 69.6, 77.1) of TCZ IV-treated pts. The weighted difference between groups was -4.0% [95% CI:

-9.2, 1.2]) and a 12% NIM was met. ACR50/70 responses, disease activity and physical function improvements were also comparable between the TCZ SC and TCZ IV groups. Up to Week 24, the proportions of pts with at least one adverse event (AE) or serious AE were 76.2% and 4.6%, respectively, in the TCZ SC group compared with 77.0% and 5.2%, respectively, in the TCZ IV group. The most common AE in both groups was infection. Injection site reactions occurred more frequently in the TCZ SC group than the TCZ IV group (10.1% vs 2.4%, respectively); but none required dose interruption or study withdrawal. No anaphylaxis was reported over the 24-week period.

**Conclusion:** TCZ SC 162mg qw demonstrated efficacy and safety profile comparable to TCZ IV 8mg/kg q4w. The TCZ-SC formulation could provide an additional, more convenient administration option and opportunity for home injection for patients with RA.

66

### **The First Reported Results of Lumbar Puncture, CT and MRI in a Case of Quinacrine Induced Psychosis Involving a Patient with Cutaneous Lupus Erythematosus**

Noura Al Osaimi (U Ottawa, Ottawa); Carole Richford (UBC, Vancouver); John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Division of Rheumatology, University of British Columbia, Vancouver)

**Case Report:** Objective: Presentation of the first reported results of lumbar puncture, CT and MRI in a case of quinacrine induced psychosis involving a patient with a diagnosis of cutaneous lupus erythematosus. Review of quinacrine induced psychosis. Methods and Result: We report here a case of a 22-year-old woman with SCLE who presented with an acute and serious psychiatric/CNS disease ultimately attributed to quinacrine who had an extensive and modern medical workup. The English medical literature was reviewed for quinacrine history, therapeutic uses and Psychiatric side effects. Since the second world war very few instances of psychiatric/CNS complications of quinacrine have been reported. Only one involved a patient with connective tissue disease (discoid lupus). None have included a full description of a modern workup for acute onset of psychiatric/CNS illness with: CT scan, MRI, lumbar puncture and EEG. Conclusions: It is important for clinicians to be aware of rare but potentially serious complications of agents that they prescribed. A knowledge of investigative results found by others in this setting may be of potential benefit.

67

### **Can People with Rheumatoid Arthritis Self Monitor their Disease Activity?**

Noura Al Osaimi (U Ottawa, Ottawa); Erin Carruthers (Arthritis Research Centre of Canada, Richmond); Charles Goldsmith (Arthritis Research Centre of Canada, Richmond); Paul Adam (Mary Pack Arthritis Program, Vancouver); Diane Lacaille (Arthritis Research Centre, University of British Columbia, Vancouver)

**Objective:** Background: In rheumatoid arthritis (RA) the target for treatment is clinical remission or minimal disease activity. Active involvement of patients in monitoring their own disease activity could enhance treatment by providing an early warning when targets are not met, indicating the need for a visit to evaluate treatment. Objective: To determine if patients can self-monitor their RA disease activity and accurately identify whether they have reached the target of low disease activity or remission.

**Methods:** RA disease activity states from patient self-reported data and rheumatologist evaluation were compared. All consecutive RA patients presenting for follow-up to seven participating rheumatologists were invited to participate. Consenting patients filled out a questionnaire and performed a self-report joint count. Rheumatologist joint count and lab values (CRP) were obtained from rheumatologists' charts. RA disease activity indices (CDAI, SDAI and RAPID-4) were used to calculate disease activity. In patient

versions of the CDAI and SDAI, physician global scores were replaced with patient global scores. Scores were categorized into four categories: remission, low, moderate or high disease activity. Because change in treatment is recommended with moderate or high disease activity, we also created two categories: remission or low vs. moderate or high. Patient-derived and rheumatologist-derived activity states were compared using percent perfect agreement, as well as Cohen's kappa for two-category comparisons and weighted kappa for four-category comparisons.

**Results:** We recruited forty-nine RA patients [mean(SD) RA duration: 9.9(12.3) years; mean(SD) age: 57.7(15.4) years; 76% female]. When comparing patient and rheumatologist assessment of disease activity state using two categories, Cohen's Kappa values (95% CI) were 0.51 (0.27;0.75); 0.59 (0.36;0.82); 0.59 (0.36;0.82); and 0.59 (0.36;0.82), and percent perfect agreement was 76%; 80%; 80%; and 80% for patient vs. rheumatologist CDAI, patient vs. rheumatologist SDAI, patient RAPID-4 vs. rheumatologist CDAI, and patient RAPID-4 vs. rheumatologist SDAI, respectively. When comparing patient and rheumatologist assessment of disease activity state using four categories, weighted Kappa values (95% CI) were 0.66 (0.51;0.81); 0.75 (0.64;0.87); 0.69 (0.56;0.81); and 0.69 (0.56;0.82), and percent perfect agreement was 51%; 61%; 47%; and 49%, for patient vs. rheumatologist CDAI, patient vs. rheumatologist SDAI, patient RAPID-4 vs. rheumatologist CDAI and patient RAPID-4 vs. rheumatologist SDAI, respectively.

**Conclusion:** There is moderate to good agreement between patient self-assessment and rheumatologist assessment of disease activity, with little difference between instruments used. These results suggest that patients are able to assess their own disease activity, which may be helpful in guiding the need for physician visit and medication adjustments. Supported by a CIORA grant.

## 68

### **How Low is Low Disease Activity? An Analysis from the Prospective, Observational Registry, BioTRAC**

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**Objective:** Composite measures of disease activity can facilitate clinical decision-making to achieve treatment goals, and treating-to-target has been shown to improve outcomes. Both CRA and ACR/EULAR recommend that treatment target should be remission or, when not possible, low disease activity (LDA). Low levels of acute phase reactants, patient-reported disease activity (PtGA), or tender joints included in such measures may result in meeting LDA criteria while having significant residual disease activity. This analysis examined the levels of individual components of composite measures in RA patients with LDA.

**Methods:** BioTRAC is an ongoing, prospective registry of RA, AS, or PsA patients initiating treatment with infliximab or golimumab as first biologics or after having been treated with a biologic for < 6 months. In this analysis, data from RA patients treated with infliximab for 6-18 months who were enrolled between 2002-2012 were used. LDA was defined using the DAS28-ESR (2.6-3.2), CDAI (2.8-10.0), and SDAI (3.3-11.0) criteria.

**Results:** 321 RA patients with mean age of 57.1 years and mean duration since diagnosis of 10.5 years

were included, providing information from 488 instances of LDA. Among patients with DAS28 LDA, mean (min,max) TJC28 was 1.3 (0,9), SJC28 was 1.2 (0,7), PtGA was 2.1 (0.0,10.0), and ESR was 21.0 (1.0,75.0). Similarly, disease parameters in patients with CDAI and SDAI LDA were, respectively: TJC28 [1.4 (0,6); 1.5 (0,8)], SJC28 [1.1 (0,7); 1.0 (0,6)], PtGA [2.3 (0.0,8.5); 2.3 (0.0,9.6)], MDGA [1.7 (0.0,9.0); 1.6 (0.0,9.0)], and CRP [6.7 (0.0, 68.0)]. More than two swollen joints were present in 18.2%/14.1%/14.5% of DAS28 / CDAI / SDAI instances, respectively, and MDGA was >2 in 24.0% / 18.6% / 18.2% of instances. With respect to HAQ-DI, patients with DAS28, CDAI and SDAI LDA had a mean (min,max) score of 0.96 (0.00,2.88), 1.00 (0.00,2.88), and 0.96 (0.00,2.88), respectively; with 8.5%, 11.3%, and 9.8% of cases having HAQ-DI $\geq$ 2.0 indicating severe to very severe disability.

**Conclusion:** Despite meeting the LDA criteria, significant residual disease may exist as indicated by the number of swollen joints and MDGA. Furthermore, a significant proportion of patients in LDA may have severe to very severe disability, although this may be due to long disease duration and irreversible damage. Altogether, although targeting LDA results in improved outcomes, it may not be an appropriate target for a significant portion of patients. Furthermore, treatment decisions should not be based solely on composite measures, but also take into consideration the global patient picture.

## 69

### **Does Low Disease Activity at Six Months Predict Remission at 12 Months in Rheumatoid Arthritis Patients Treated with Biologics in a Real-World Setting?**

Philip Baer (Scarborough); William Bensen (St Josephs Hospital and McMaster University, Hamilton); Andrew Chow (Credit Valley Rheumatology, University of Toronto, McMaster University, Mississauga); Rafat Faraawi (K-W Musculoskeletal Research Inc., Kitchener); Denis Choquette (Institut de Rhumatologie de Montréal, Montreal); Isabelle Fortin (Centre de santé et de services sociaux de Rimousk, Rimouski); John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Division of Rheumatology, University of British Columbia, Vancouver); Dalton Sholter (124 Street Medical Group, Edmonton); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Francois Nantel (Janssen, Toronto); May Shawi (Janssen Inc., Toronto); Allen Lehman (Janssen Inc., Toronto); Susan Ottawa (Janssen Inc., Toronto)

**Objective:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. Patients with RA treated with infliximab or golimumab who were enrolled between 2002 and 2012 and had 12 months of follow-up were included in this analysis.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA) with infliximab or golimumab as first biologics or after having been treated with a biologic for less than six months. Patients with RA treated with infliximab or golimumab who were enrolled between 2002 and 2012 and had 12 months of follow-up were included in this analysis.

**Results:** A total of 436 patients with a mean (SD) age of 56.1 (13.1) years and disease duration of 10.4 (9.9) years were included in the analyses. Mean (SD) DAS-ESR, DAS-CRP, CDAI, and SDAI at baseline were 5.7 (1.5), 5.3 (1.3), 34.3 (16.0), and 36.9 (16.7), respectively. At 12 months 25.3%, 32.5%, 15.9% and 16.5% had DAS-ESR, DAS-CRP, CDAI and SDAI remission, respectively. Significant predictors of DAS-ESR remission at 12 months were LDA at 6 months (OR = 7.9), change in SJC (OR = 1.1) and DAS-ESR (OR = 0.8) at 6 months. For DAS-CRP remission at 12 months, significant predictors were LDA at 6 months (OR = 8.0) and change in DAS-CRP (OR = 0.7) at 6 months. For CDAI remission at 12 months, significant predictor was LDA at 6 months (OR = 9.4). For SDAI remission at 12 months, significant

predictor was LDA at 6 months (OR = 9.9). Changes in CDAI, SDAI, TJC and SJC from baseline to 6 months were not associated with CDAI and SDAI remission at 12 months.

**Conclusion:** The results of this Canadian longitudinal observational study have shown that LDA at six months is a significant predictor of remission at 12 months. For patients achieving a low disease activity state at 6 months, there is a 7.9 to 9.9 odds ratio of achieving remission at 12 months. Data from this real-world registry suggest that a significant proportion of patients with LDA who had not achieved a therapeutic target of remission at 6 months do so at 12 months while maintained on the same biologic treatment.

## 70

### **Assessment of Rheumatoid Arthritis Disease Activity by Patients and Physicians: Do Physicians Detect Improvement Before the Patient Does?**

William Bensen (St Josephs Hospital and McMaster University, Hamilton); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Philip Baer (Scarborough); Andrew Chow (Credit Valley Rheumatology, University of Toronto, McMaster University, Mississauga); Regan Arendse (Saskatoon); Isabelle Fortin (Centre de santé et de services sociaux de Rimousk, Rimouski); Milton Baker (University of Victoria, Victoria); Boulos Haraoui (Université de Montréal, Montréal); Algis Jovaisas (Ottawa); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Allen Lehman (Janssen Inc., Toronto); Francois Nantel (Janssen, Toronto); May Shawi (Janssen Inc., Toronto); Susan Otawa (Janssen Inc., Toronto)

**Objective:** Patient (PtGA) and physician (MDGA) global assessment of disease activity measure the same construct from two different perspectives. This study assessed the agreement between these two measures over time as ascertained in Canadian routine clinical practice in RA patients treated with infliximab or golimumab.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or golimumab as first biologics or after having been treated with a biologic for

**Results:** A total of 675 patients assessed over 4193 visits during a mean follow up time of 20mons were included. The overall mean (SD) PtGA and MDGA was 3.73 (2.89) and 3.38 (2.67), respectively ( $P < 0.001$ ). At baseline the mean difference between the MDGA and PtGA was +0.41 ( $P < 0.001$ ). However, during all the follow-up assessments, this was reversed, with PtGA being significantly higher (worse) when compared to MDGA. The mean difference changed by -0.012 per month ( $P < 0.001$ ) indicating progressively higher scores by patients over time compared to physicians. The overall ICC and CA were 0.767 and 0.770, respectively, indicating moderate agreement. Both ICC and CA decreased over time. The mean difference between MDGA and PtGA assessments was non-significantly higher for females (-0.37) when compared to males (-0.29) and significantly higher for patients with history of MTX use (-0.43 vs. -0.18;  $P = 0.002$ ). TJC, SJC, CDAI and SDAI had positive and significant ( $P < 0.001$ ) associations with increased difference between MDGA and PtGA. Slope analysis showed that MD assessments declined by -0.265 / month and patient assessments declined by -0.189 / month ( $P < 0.001$ ).

**Conclusion:** The results of this longitudinal observational registry have shown that there is poor agreement between physician-based and patient-based assessments of disease activity. In addition, the rate of reduction in disease activity over time is considerably higher when rated by physicians when compared to patients. In this chronic condition, physicians should be aware of this increasing discordance between the patient and physician global when making treatment decisions and managing patient expectations over time.



### **Variability in the Classification of Remission Among Disease Activity Indices and their Correlation: An Analysis from a Prospective, Observational Registry**

William Bensen (St Josephs Hospital and McMaster University, Hamilton); Algis Jovaisas (Ottawa); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Philip Baer (Scarborough); Majed Khraishi (St-John's); Sanjay Dixit (McMaster University, Hamilton); Denis Choquette (Université de Montréal, Montréal); Michael Starr (McGill University, Montreal); Isabelle Fortin (Centre de santé et de services sociaux de Rimousk, Rimouski); Dalton Sholter (124 Street Medical Group, Edmonton); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); John Sampalis (JSS Medical Research & McGill University, St-Laurent); Allen Lehman (Janssen Inc., Toronto); Francois Nantel (Janssen, Toronto); May Shawi (Janssen Inc., Toronto); Susan Ottawa (Janssen Inc., Toronto)

**Objective:** In recent years, disease remission in rheumatoid arthritis (RA) has been assessed using various disease activity indices such as the DAS28, SDAI, CDAI, ACR/EULAR-recommended Boolean definition and the Patient Activity Scale (PAS). The aim of this analysis is to describe the agreement between these five indices in classifying remission as well as to assess their correlation in a routine clinical care setting.

**Methods:** BioTRAC is an ongoing, prospective Canadian registry of rheumatology patients initiating treatment with infliximab or golimumab. In this analysis, data from RA patients who were treated with infliximab between January 2002 and June 2011 and had available information in all indices were used. The definitions for remission were as follows: DAS28-ESR  $< 2.6$ ; SDAI  $\leq 3.3$ , CDAI  $\leq 2.8$ ; PAS  $\leq 1.0$ . Factor analysis was used to assess the variability due to each of the indices while inter-item correlation was measured with the Pearson correlation coefficient.

**Results:** Seven hundred twenty five RA patients who had 2,897 complete assessments were included in the analysis. Non-remission was classified by all indices in 68.8% of the cases, while 31.2% achieved remission in one (12.4%), two (3.5%), three (3.4%), four (4.2%) and all five types (7.7%) of indices. Factor analysis showed that PAS accounted for 71.5% of the matrix variance, followed by DAS28-ESR (12.4%), SDAI (9.2%), CDAI (5.2%), and Boolean remission (1.6%), suggesting that PAS may reflect different aspects than the clinical indices. PAS remission revealed the lowest correlation with remission classified by the remaining indices (DAS28-ESR 0.413; SDAI 0.522; CDAI 0.521; Boolean 0.567) and removal of any index, except PAS, would result in a lower overall Cronbach's alpha.

**Conclusion:** The results of this analysis show that variability exists in the classification of remission by various disease activity indices. This variability was found to be predominantly due to the Patient Activity Scale, a patient-driven composite tool, suggesting that the patient perception of disease activity may differ from that captured by clinical outcome measures.

### **Participant and Educator Feedback Informs Delivery of an Inflammatory Arthritis Education Program using Telemedicine in Rural Communities**

Carol Kennedy (St. Michael's Hospital, Toronto); Kelly Warmington (The Hospital for Sick Children, Toronto); Carol Flewelling (Toronto); Rachel Shupak (St Michael's Hospital, Toronto); Papachristos Angelo (Toronto); Caroline Jones (St. Michael's Hospital, Toronto); Dorcas Beaton (St. Michael's Hospital, Toronto); Sydney Lineker (The Arthritis Society, Toronto); Denise Linton (Toronto)

**Objective:** Telemedicine-based approaches to healthcare service delivery improve access to care. It was recognised that people with inflammatory arthritis living in rural areas had limited access to patient education and could benefit from the Prescription for Education (RxEd) program (format: one-day, audience: adults with inflammatory conditions, facilitators: specialized arthritis care providers). The

program was adapted to be delivered via interactive videoconferencing through two workshops for local and rural facilitators: Telemedicine Best Practices/Adult Education Principles; Improved Public Speaking. Objectives: To explore the feasibility of and participant satisfaction with the use of telemedicine delivery of the RxEd program in rural communities.

**Methods:** Participants included adults with inflammatory arthritis attending the RxEd program locally or at one of six rural sites. Participants completed course evaluations post-program. Educators completed post-program reflective logs (qualitative perceptions of videoconferencing technology, site interaction, small group learning). A debriefing meeting (RxEd educators, telemedicine coordinators, researchers) was held to discuss data and identify actionable delivery modifications.

**Results:** One hundred and seven persons (23 local; 84 rural, across 6 sites) attended one of two RxEd Telemedicine sessions. Eighty-eight completed the post-program evaluation (20 local; 68 rural). Rural participants were satisfied with the quality of the videoconference (% agree/strongly agree): could hear presenter (94%), could see slides (94%), could see who was speaking at rural sites (85%), adequate facilitation of interaction between sites (92%), could hear discussion between sites (77%). Many concerns identified by educators (1<sup>st</sup> session: n=9; 2<sup>nd</sup> n=10) in reflection logs were consistent with participant feedback. Suggested improvements included: use of two screens (speaker, slides) where possible; direct frontal camera angles; equality of interaction with rural sites; slide modifications to improve readability on screen and in handouts; and minor changes in program delivery.

**Conclusion:** Findings from this pilot confirm the feasibility of delivering RxEd to rural communities using telemedicine. Suggested improvements will be addressed where possible. Future evaluations will assess the effectiveness of telemedicine delivery of RxEd through comparisons of health-related outcomes in remote versus local participants. Supported by a CIORA grant.

### 73

#### **Effectiveness of Tocilizumab in a Community Practice Setting in Patients with Rheumatoid Arthritis**

Rafat Faraawi (K-W Musculoskeletal Research Inc., Kitchener); Sameeka Malik (K-W Musculoskeletal Research Inc., Kitchener); Kelly Roth (K-W Musculoskeletal Research Inc., Kitchener); Sabeeha Ahmed (K-W Musculoskeletal Research Inc., Kitchener); Louis Coupal (Montreal); Janice Meisner (Montreal)

**Objective:** This study assesses the effectiveness of TCZ in a real-world setting in patients with rheumatoid arthritis.

**Methods:** Patients were attending the infusion centre and receiving TCZ infusions for the treatment of rheumatoid arthritis during the study period from August 2010 until March 2013. Baseline patient characteristics and clinical data were collected by a retrospective chart review. Patients were then followed prospectively.

**Results:** Of the 41 patients analyzed, 85% were women with a mean age of 49 yrs ( $\pm 12.8$ ) and mean disease duration of 6 yrs ( $\pm 7.5$ ) at the time of treatment initiation. Of these patients, 58% were biologic-naïve, at least 88% had received prior DMARDs other than MTX and 63% had received steroids at some point. Seventy-eight percent were receiving MTX at the time of initiation of TCZ. Average swollen joint count was 5.9 ( $\pm 5.7$ ) and average tender joint count was 10.8 ( $\pm 8.7$ ) at baseline. Effectiveness of TCZ: The mean ( $\pm$ SD) DAS28 at baseline, 3, 6 and 12 mos was 4.78 (1.28), 2.79 (1.50), 2.57 (1.37), and 1.68 (1.28) and the mean change from baseline (95% CI) in DAS28 at 3, 6 and 12 mos was -1.72 [-2.28 to -1.16;  $P < .0001$ ], -2.12 [-2.61 to -1.63;  $P < .0001$ ] and -2.74 [-3.53 to -1.94;  $P < .0001$ ]. At baseline, the proportion of patients in DAS28 disease categories of remission ( $\text{DAS28} \leq 2.6$ ), low ( $\text{DAS28} \leq 3.2$ ), moderate ( $\text{DAS28} > 3.2 - \leq 5.1$ ) and high ( $\text{DAS28} > 5.1$ ) was 5%, 0%, 52% and 43%, respectively. The proportion of patients in DAS28 disease categories: remission, low, moderate and high was 50%, 17%, 25% and 8%, respectively at 3 mos, 55%, 14%, 23% and 9%, respectively, at 6 mos and 77%, 15%, 8%

and 0% at one year. Of the 643 infusions administered during the study period, a total of 15 mild infusion reactions were documented. With respect to serious adverse events (SAE), there were 7 events documented and none were anaphylaxis.

**Conclusion:** In conclusion, TCZ is effective for the treatment of rheumatoid arthritis in a real-world setting based on clinical evaluation with the DAS28 and the HAQ. We also conclude that TCZ is safe in a community setting as the infusions were well tolerated and SAEs were minimal. Of note is the rapidity of effectiveness with the proportion of patients achieving remission or low disease activity increasing from 5% to 67% of patients in the first 3 months after initiating treatment.

## 74

### **Amyloid (SAA) Arthropathy in Chronic Rheumatoid Arthritis: A Case Report**

Rajanjot Gill (University of Ottawa, Ottawa); Jacob Karsh (University of Ottawa, Ottawa); Susan Humphrey-Murto (University of Ottawa, Ottawa)

**Case Report:** Objective: We present a case of amyloid arthropathy in a patient with seropositive rheumatoid arthritis (RA) with two unique features; arthropathy as the only manifestation of systemic SAA amyloidosis, and excellent response to rituximab. Methods: A 66-year old woman presented with a large shoulder effusion in the setting of a flare of peripheral joints (SJC 11). Her past history was significant for seropositive RA for 20 years, and non-Hodgkin's lymphoma treated with autologous stem cell transplantation (SCT) in remission for 12 years. Her RA had been in remission for 10 years post SCT on hydroxychloroquine monotherapy, but gradually became more active for 1 year prior to the shoulder effusion. She was treated with additive combination therapy including Prednisone 10 mg daily, hydroxychloroquine, leflunomide and sulfasalazine. Results: Physical examination revealed a boggy moderate sized right shoulder effusion. She also had effusions in the wrists and multiple PIP and MCP joints (SJC 11). Lab investigations showed normal CBC, ESR, CRP, Cr, and liver enzymes. She was both RF (235 KIU/L) and anti-CCP (> 200 RU/ml) positive. Her shoulder was aspirated for 65 cc of synovial fluid (SF), and injected with steroids. Initial SF analysis was non-inflammatory (WBC count of  $156 \times 10^6/L$ ) and negative for crystals. Rapid reaccumulation led to further aspirations. In the SF amorphous material showed negative reaction with Congo red but strong reactivity for amyloid SAA, suggestive of local amyloid deposits. There was no evidence of amyloidosis on multiple gut biopsies (stomach, duodenum, colon, rectum), and no evidence of proteinuria. The patient was started on Rituximab with complete resolution of the shoulder effusion and improvement in peripheral joints (SJC 2) after one course. She remains well 4 months post treatment. Conclusion: Amyloid arthropathy is rare. Most case reports describe amyloid arthropathy secondary to AL amyloidosis in patients with plasma cell dyscrasias and secondary to beta2 microglobulin amyloidosis in patients on chronic hemodialysis. SAA amyloidosis seen in association with chronic inflammatory disorders such as RA, JIA, IBD or infectious diseases usually present with amyloid deposition in specific organs, with kidneys and gut being the primary sites. To date, amyloid arthropathy secondary to SAA amyloidosis has not been reported in the literature. This is an important observation and may serve as an important differential diagnosis to consider in RA patients with worsening joint pain. The excellent clinical response to rituximab has not previously been shown, and warrants further study.

## 75

### **Staphylococcus Aureus Infection following Facet Joint Injection Masquerading as Acute Polyarthrititis and Polymyalgia Rheumatica**

Raman Rai (McMaster University, Hamilton); Suneet Sekhon (McMaster University, Hamilton); Nader Khalidi (McMaster University, Hamilton)

**Case Report:** Background Spinal facet joint injection (FJI) for relief of mechanical back pain is generally considered to be a safe procedure with a low risk of infection. We present two cases of FJI-related *Staphylococcus Aureus* (SA) infection and review the literature on this rare complication. **Cases** Case one: A 58 year old female with a history of chronic degenerative low back pain had a lumbar FJI two weeks prior. She presented with worsening low back pain over one week without red -flag symptoms. She was discharged from the ER on two occasions with no systemic features of infection. She then developed an acute onset of polyarthrititis involving her feet, ankles, knees, wrist and hands in an asymmetric distribution. She was prescribed prednisone and NSAIDs by her family physician for presumed inflammatory arthritis and referred to a rheumatologist. Her condition worsened with new fevers, chills and fatigue. A wrist aspirate revealed purulent synovial fluid positive for SA. Subsequent blood cultures were also positive and MRI of the spine revealed lumbar facet septic arthritis and paraspinal abscesses. Treatment with antibiotics and surgical debridement led to an improvement in symptoms. Case two: A 59 year old male with a history of severe cervical spine osteoarthritis had a cervical FJI five months prior. He presented with a subacute worsening of neck pain over three weeks following an identifiable trigger (yard work). He was discharged from the ER on three occasions with analgesics. His ESR was found to be elevated (55 mm/hr) by his family physician and he was referred to rheumatology for query polymyalgia rheumatica. He was prescribed 15mg of prednisone with initial improvement then worsening requiring admission. Blood cultures were positive for SA and an MRI revealed cervical facet septic arthritis and several intramuscular abscesses. He improved with antibiotic therapy. Our literature review found 12 articles describing 13 patients with infectious complications following FJI. SA was isolated in 9/13 cases. The majority presented with worsening back pain within one week of injection, but one case had an insidious onset over seven weeks. MRI was used for diagnosis in all cases with epidural abscess being the most common complication. Surgical intervention was required in four cases. One patient died from sepsis, two were left with residual neurologic deficits; there was complete recovery in all others. **Conclusion** These cases and review demonstrate that although infections following FJI are rare, they may present atypically; this can make diagnosis challenging.

## 76

### **New Onset Dermatomyositis in Pregnancy: A Case Report and Review of the Literature**

Raman Rai (McMaster University, Hamilton); Suneet Sekhon (McMaster University, Hamilton); Mark Matsos (McMaster University, Hamilton)

**Case Report:** Background Dermatomyositis (DM) is an inflammatory condition typically characterized by proximal muscle weakness and skin changes. There is a relative paucity of literature describing outcomes of pregnancies in patients with dermatomyositis and most of these reports involve patients with a diagnosis prior to pregnancy. Here we present a case of DM that onset during pregnancy and review the literature around this rare initial presentation of DM. Case A 28 year old G5T2A2L2 female with a past history of obesity and PCOS presented with acute onset proximal muscle weakness and rash during her seventh week of gestation. The rash comprised of extensor surface erythema over the extremities, gottron's sign, periungal erythema and heliotrope rash. Muscle weakness was most prominent at the hip flexors (grade 1/5 by MRC scale) and shoulder abductors (grade 3/5). Investigations revealed an elevated CK (5314 U/L), negative ANA and normal TSH. An EMG was consistent with myopathy. It was not possible to perform a needle muscle biopsy because of body habitus and the risk of infection from an open muscle biopsy was felt to be high. She was started on prednisone 60mg/day with an initial improvement in strength. Two weeks later she experienced a flare with worsening rash, proximal muscle weakness and CK > 16,000 U/L necessitating readmission. She was treated with pulse steroids and IVIG (2g/kg total) with improvement in

her strength, rash and normalization of CK. Her pregnancy continued to progress normally. A literature search found 20 articles dating back to 1973 describing 22 patients with new onset DM in pregnancy. Eleven of these cases had onset in the first trimester with six occurring in the third trimester. Methods of diagnosis included clinical findings, EMG, skin and muscle biopsy. Treatments used included glucocorticoids (40-160 mg/day +/- pulse of prednisolone), IVIG in three cases and post-partum methotrexate in three cases. Maternal outcomes were largely positive with improvement intra-partum and normalization of skin and muscle findings at post-partum follow-up in most. There was one maternal death related to complications from eclampsia. Fetal outcomes were less favourable, with 10 fetal deaths in utero, nine cases requiring induction of labour (four of which were pre-term) and two normal term deliveries. Conclusion This case illustrates successful treatment of new onset DM in pregnancy using glucocorticoids and IVIG. Our review of the literature reveals that with treatment there are usually good maternal outcomes; however fetal outcomes tend to be poor.

77

### **New Online Resource for Promotion and Dissemination of Collaborative Research Results to the Public**

Sydney Lineker (Toronto); Raquel Sweezie (Toronto); Deanna Bowlby (Toronto); Jennifer Boyle (The Arthritis Society, Toronto); Lynn Moore (The Arthritis Society, Toronto); Johnathan Riley (Toronto); Penny Tantakis (Toronto); Ed Ziesmann (Toronto)

**Objective:** We are part of a Canadian disease-specific health charity that often collaborates with researchers on arthritis-focused projects funded by other organizations. Often results of this research do not reach people with arthritis, other arthritis stakeholders or the general public. To address this issue, a new section of our organization's website was developed to promote these partnerships and disseminate the research results.

**Methods:** The work included website design, development of English content, translation into French, and marketing and evaluation of the site. Content was provided by our research partners using an online template and included a lay language summary of each project, 'take home' messages for the public, links to partner websites, publications and any online educational materials developed in each project. People living with arthritis critiqued the summaries for clarity. Reading level was assessed using the Flesch-Kincaid Grade Level. For each summary, English and French, an online poll was developed to give the public an opportunity to provide feedback on usefulness and ease of understanding.

**Results:** This section of the website, titled "What's New in Research?", is now a centralized repository of peer-reviewed studies done with our research partners. To date, eight summaries representing research done in two provinces have been uploaded and are available at <https://www.arthritis.ca/research/summary/home> (http://www.arthrite.ca/page.aspx?pid=6807). Five people living with arthritis acted as reviewers. The reading level was set at Grade 12 or lower for each summary. "What's New in Research" has been marketed through the organization's multimedia channels including a peer mentor newsletter, a member's newsletter and social media (Facebook and Twitter). Across all summaries, a total of 38 online polls were completed in English and another 7 in French. In the majority of completed polls, respondents indicated that the summaries were useful (English, 70%; French, 88%), easy to understand (English, 97%; French, 100%), and worth recommending to friends and family (English, 66%; French, 63%). Feedback from our research partners is being sought to help improve the processes involved.

**Conclusion:** This project has enabled dissemination of research results for improving musculoskeletal health by 1) consolidating and summarizing the results of peer-reviewed research 2) promoting research partnerships and 3) communicating the importance of this research to the public. It allowed us to make the

results of research available to an audience that can utilize the information to better manage their arthritis.

78

### **Radiographs and MRI are Inaccurate in Assessment of Ulnar Deviation in Rheumatoid Arthritis Patients**

Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Allison Mitchell (Saskatoon); David Leswick (Saskatoon); Haron Obaid (Saskatoon); Samuel Stewart (Saskatoon); Michelle Street (Saskatoon)

**Objective:** To compare clinical goniometric measurements of ulnar deviation (UD) in rheumatoid arthritis (RA) patients to measures from standardized radiograph views and from MRI hand studies.

**Methods:** 15 RA patients with clinically apparent UD and 11 RA patients without UD on rheumatologic examination participated in this study. Each patient underwent a rheumatologic examination prior to recruitment. Subsequently goniometric measurements for UD at the metacarpal phalangeal (MCP) joint were performed by an occupational therapist (OT). Imaging studies included posterior-anterior hand radiographs using standard positioning, and MRI studies of dominant hands using Siemens Skyra 3T MRI scanner with dedicated Siemens 16 channel hand/wrist coil. Angulation measurements for radiographs and MRI were performed independently by two radiologists experienced in musculoskeletal radiology and blinded to rheumatologist, occupational therapist, and each other's assessments.

**Results:** Inter-observer agreement for radiographic and MRI measurements was high with correlations  $>0.97$  for both. Correlation between OT goniometric measurements and the imaging based measurements was limited at 0.496 for radiographs and 0.317 for MRI. Correlation between imaging modalities was 0.513. Compared to OT measurements, radiographic and MRI study measurements under-estimate the angulation in RA patients with UD.

**Conclusion:** Radiographs and MRI both under-estimate resting ulnar deviation angulation at the MCP joints in rheumatoid arthritis.

79

### **Actigraphic Evaluation of Periodic Limb Movements in RA Patients with and without Symptoms of Restless Legs Syndrome**

John Gjevre (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Bindu Nair (University of Saskatchewan, Saskatoon)

**Objective:** Patients with rheumatoid arthritis (RA) have a higher frequency of restless legs syndrome (RLS) than the general population. RLS is a disorder with generally both sensory symptoms and periodic limb movement motor manifestations. An estimated 25% of RA patients meet questionnaire criteria for RLS. As these criteria are subjective, concern has been raised that rheumatoid peripheral arthritis symptoms may mimic RLS symptoms, falsely elevating the RLS prevalence estimates in this population. In this study we compare objective, actigraphically measured periodic limb movements between RA patients meeting RLS subjective criteria and those who do not.

**Methods:** 64 patients with RA participated in this study. All patients completed a questionnaire which included RLS essential criteria, visual analogue scales (VAS) for pain, fatigue, global function, modified health assessment questionnaire (mHAQ), rheumatoid arthritis disease activity index (RADAI), Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale (ESS), Berlin instrument for OSA risk, depression and stress measures. All patients were instructed in use of the PAM-RL actigraphic device and sleep diary. Each patient wore the ankle actigraphic device for two consecutive nights. Data was subsequently downloaded utilizing PAM-RL software.

**Results:** Of the 64 RA patients the mean age was 54.4(14.9), mean BMI was 28.74(7.11). Twenty-six

participants met the four essential criteria for RLS. Comparison between the RLS and non-RLS groups did not reveal any significant differences in age, BMI, VAS pain, VAS global function, depression, stress, RADA1, ESS, or high risk categorization for OSA. There were significant differences observed for fatigue: RLS group 5.88(2.06) cm, compared to the non-RLS group at 4.44(2.91) cm ( $p = 0.044$ ), for mHAQ: 13.15(5.28), compared to 10.45(3.09) ( $p=0.028$ ), and for the PSQI, where the RLS group scored 9.76(3.46) compared to 6.03(3.29) ( $p < 0.001$ ). Examination of the actigraphic data did not demonstrate any difference in duration of sleep time. Periodic limb movements were higher in the RLS group at a mean of 20.04(21.76) compared to 10.62(12.35) ( $p= 0.015$ ) for night one, at 19.22(23.40) and 11.59(13.05) ( $p = 0.88$ ) for night two, with an average over the observation period of 19.63(22.13) for the RLS group and 11.13(12.10) for the non-RLS group ( $p = 0.033$ ).

**Conclusion:** Despite concern that peripheral arthritis may create a ‘RLS mimic’, we did observe a higher frequency of periodic limb movements in those meeting RLS criteria. This data supports the earlier reports of higher frequency of RLS in RA populations. Further we observed that patients meeting RLS criteria had higher fatigue and poorer sleep quality scores.

## 80

### **Caerebrovascular and Peripheral Vascular Involvement in Kimura's Disease**

Ripneet Puar (University of Manitoba, Winnipeg); Navjot Dhindsa (University of Manitoba, Winnipeg)

**Case Report:** Kimura’s disease (KD) is a chronic inflammatory condition characterized by painless subcutaneous masses that uniformly involve regional lymph nodes and often salivary glands. KD has predilection for the head and neck region and predominantly affects young Asian men. It is characteristically associated with eosinophilia and elevated serum IgE levels. Etiology is not known. Infections, allergic reaction and immune mechanisms are postulated. Renal disease is a recognized systemic manifestation. Raynaud’s phenomenon has been reported with KD. Case reports of thromboangiitis obliterans and stroke with internal carotid occlusion have been reported in patients with KD. We describe a case of established Kimura’s disease who presented with left sided facial droop and limb weakness. He was also noted to have absent left upper extremity distal pulses. Investigations revealed multivessel cerebral occlusion as well occluded left radial and ulnar arteries. This is the first reported case of intracerebral and peripheral vascular involvement with Kimura’s disease. Literature review and association of vasculitis versus vasculopathy in Kimura’s disease and therapeutic decision dilemmas in this poorly understood condition is presented.

## 81

### **Utilization of an Informational Needs Assessment to Develop an Education Program for Patients with Ankylosing Spondylitis (AS) and Related Axial Spondyloarthritis (SpA)**

Rita Kang (University Health Network- Toronto Western Hospital, Toronto); Rebecca Morton (Toronto); Christopher Hawke (University Health Network, Toronto); Laura Passalent (Toronto Western Hospital, Toronto); Robert Inman (University of Toronto, Toronto); Dinny Wallis (Toronto); Joan Blair (Toronto); Alison Lake (Toronto); Heather Sloman (Toronto); Debra MacGarvie (Toronto); Marc Doucet (Toronto); King Wong (Toronto)

**Objective:** The effectiveness of education programs for patients with arthritis has been well documented. Despite this, there has been minimal investigation into patient education specifically for ankylosing spondylitis (AS) and axial spondyloarthritis (SpA). The current evidence suggests that only 40% of patients with AS are being referred for education. AS patient education programs have demonstrated positive effects with respect to mobility, function, self-efficacy, and depression, however many of these effects are not sustained over the long term. Effective patient education programs are built on carefully

executed needs assessments. The objective of this study was to identify what patients with AS and SpA feel their current informational needs are. This information will be used to develop a comprehensive interprofessional evaluated patient education program for patients with AS and SpA attending the Toronto Western Hospital Spondylitis Clinic, Toronto, Ontario, Canada.

**Methods:** Patients with AS and SpA were emailed a link with an Informational Needs Assessment Survey. This included five multiple choice sections: 1. Demographics, 2. Disease, Diagnosis and Prognosis, 3. Management, 4. Relationships, 5. Emotions and an open ended question at the end of the survey. Descriptive statistics and bivariate analyses were used for data analysis. Qualitative statistical methods were utilized to address the open ended question section.

**Results:** The response rate was 32.1%, of which 66.1% were male. The sample group was primarily older adults, with 22.3% between the ages of 31 to 40, 23.2% between the ages of 41 to 60. The sample group was well educated, with 50.0% completing college or university and 24.1% completing graduate school. The average number of years since diagnosis was 11 years. Of those who completed the survey, 21 (19.4%) were newly diagnosed (diagnosed between 2010-2012) and 87 (80.6%) were diagnosed earlier than 2010. The Disease, Diagnosis and Prognosis and Management sections were found to be the most important informational needs. In addition: website, on-line audio/ video and E-learning were cited as the most useful ways to receive information in all five sections. Qualitative analysis indicated three major themes concerning patients including medication/pain, fatigue/activity/work and long term prognosis.

**Conclusion:** Based on the needs assessment, it was determined to develop an e-learning module for this patient population followed by self-management focused group education and exercise sessions. It is anticipated this unique education program for patients with AS and SpA will be a successful model using best practice in patient education. Supported by a CIORA grant.

## 82

### **Perceived Barriers to Health Care for RA Patients in Northern Saskatchewan**

Robyn Schuler (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Bindu Nair (University of Saskatchewan, Saskatoon)

**Objective:** Rheumatology subspecialists in Northern Saskatchewan are based in the urban centre of Saskatoon. However, more than half the population served live in smaller communities and rural areas. Some of which are quite isolated. There is geographic variation in physical access to specific health care services. 1. To assess the geographic residence distribution of RA patients followed in a university based outpatient clinic, 2. To assess outcomes of care for variation between patients based on residence, 3. To identify patient perceived barriers to health care access in Northern Saskatchewan

**Methods:** One hundred charts were reviewed from patients with established RA attending the Royal University Hospital Rheumatology based clinic. The data collection instrument was developed to assess and compare disease outcomes of RA patients within the Saskatoon Health Region (SHR) and outside SHR. Outcome measures included: joint replacement surgeries, duration of corticosteroids, narcotic utilization, frequency of immunomodulating therapy adjustments, acute phase markers, and employment. A pilot patient questionnaire was developed and 22 RA patients residing within the northern health regions, were interviewed to trial the questionnaire. Included were questions about the patients' understanding of geographic locations for health care services, distance they have to travel, difficulties this creates for them, including travel costs, lost work time, and demands on family members.

**Results:** The majority of RA patients attending this university based clinic resided outside the Saskatoon Health Region. Fourteen other health regions were represented. The trialed questionnaire results indicated that there were problems experienced by up to a third of patients in terms of access to primary care health services, pharmacy, laboratory or radiographic services. The majority of RA patients had been



unable to access PT/OT services in their health regions. Two thirds of patients felt that costs for travel represented a real barrier for them and over a third felt the location of their residence negatively impacted the health care they received. Comparison of chart extractions between RA patients residing in the SHR versus other health regions did not reveal significant differences in outcome measures examined. However, a trend was observed indicating patients residing in more rural and underserved areas may have a longer duration of continuous corticosteroid utilization and also may be less likely to undergo joint replacement surgery.

**Conclusion:** The majority of patients living outside SHR perceived existing barriers to access of health care services. A third felt these barriers negatively impacted their health care.

## 83

### **A “Giant” Peculiarity: Giant Cell Arteritis without an Elevated ESR or CRP**

Sandra Dumanski (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon); Jagoda Gorka (University of Saskatchewan, Saskatoon); Mark Hiken (Saskatoon)

**Case Report:** Although a positive arterial biopsy may be considered gold standard for diagnosing giant cell arteritis (GCA), an elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are considered hallmarks of the disease. These inflammatory markers remain an important element in the GCA classification criteria. We describe a case of biopsy-proven GCA in a patient presenting with normal ESR and CRP. A 68 year old Caucasian male was referred by his family physician for evaluation of possible GCA. He presented with symptoms of headache and bitemporal tenderness. His symptoms had been present since he struck his head with his truck door one month earlier. The patient was initiated on prednisone 60 mg/day by his family physician. Laboratory evaluation was performed that day, prior to starting prednisone. ESR was measured at 3 mm/hour and CRP at 1.2 mg/L. A request for TAB was made to the surgical service and a clinic evaluation in rheumatology clinic was arranged later that week. On evaluation in rheumatology clinic he persisted in reporting no symptoms of visual disturbance, jaw claudication, or B symptomatology. Examination revealed mild tenderness to palpation along the temporal/parietal portions of the scalp including along the temporal arteries. Arterial pulses were strong and there was no palpable nodularity. Despite four days of high dose prednisone, the patient did not feel he had experienced any reduction in his symptoms. No TAB was available for review as the surgical service upon evaluation of the patient declined to perform the biopsy. Considering the lack of clinical response to steroids, the negative inflammatory markers, and the onset of headache following an injury. A diagnosis of GCA was deemed unlikely. The patient was advised to discontinue his glucocorticoid therapy, to see his family doctor for re-evaluation of his headache, but also requested to have his CRP reassessed in one week's time. Interestingly, the repeat CRP was significantly elevated. Without delay the prednisone was re-initiated and an urgent TAB obtained. The pathologic review was characteristic of and diagnostic for GCA. Although elevated ESR and CRP remain hallmarks in the diagnosis of GCA, a number of case reports have observed 'ESR/CRP negative' GCA. Although elevated ESR/CRP often support the diagnosis of GCA, normal levels should not exclude the consideration particularly when clinical suspicion is strong. In this case, despite normal laboratory parameters, poor initial symptomatic response to corticosteroids and a distracting head trauma, our patient was proven to have GCA.

## 84

### **Use of an Online Questionnaire to Disseminate CRA Guidelines for RA Management**

Sankalp Bhavsar (Burlington); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program,

Newmarket); Orit Schieir (University of Toronto, Toronto); Vivian Bykerk (Toronto); Claire Bombardier (University of Toronto, Toronto); Sanjay Dixit (McMaster University, Hamilton)

**Objective:** There is a need for effective guideline dissemination strategies with the goal of reducing variability in medical practice and to improve the efficiency, effectiveness, and appropriateness of medical care. Studies have shown that the passive dissemination of guidelines is ineffective in changing performance or health outcomes. Instead, interactive medical education strategies and multifaceted interventions have been shown to be a consistently effective strategy. The Canadian Rheumatology Association (CRA) has developed 39 evidence-based recommendations for the management of rheumatoid arthritis (RA) which was published in 2 parts. The purpose of this study was to disseminate these guidelines through the use of an online questionnaire and assess potential persistent gaps between recommendations and clinical practice that may be targeted through focused implementation strategies.

**Methods:** We created a survey based on the CRA guidelines for RA management. We developed 24 multiple-choice questions which were distributed via email to rheumatologists registered with the CRA. This study provides the preliminary data for a series of articles being published in the CRA Journal where data will be presented addressing general treatment strategies in RA, pharmacologic treatment (glucocorticoids, DMARDs, biologics), and issues addressing perioperative care, latent tuberculosis infection, vaccination and malignancy.

**Results:** The survey was sent out to 432 members between April and May 2013, and 188 members (44%) responded. Overall, 77.8% of responses to questions were consistent with CRA guidelines. The greatest disparity between answers and recommendations related to general RA treatment strategies, particularly frequency of monitoring of disease activity and frequency of adjusting DMARD therapy. There was also a significant difference between current practice and guidelines with respect to the perioperative use of methotrexate, and there was a knowledge gap regarding the relationship between RA, RA therapy, and lymphoma.

**Conclusion:** Guideline dissemination strategies are essential to increase awareness and agreement surrounding the publication of evidence-based practice recommendations. The use of an online questionnaire with the subsequent publication of answers providing physician feedback on performance is an efficient and cost-effective strategy that can help increase physician knowledge and skills. In addition, identification of persistent gaps between evidence-based recommendations and practice can help guideline developers prioritize tailored guideline implementation strategies to improve overall health-care delivery for persons living with RA.

85

### **Anti-RNA Polymerase III Antibodies in the Diagnosis of Scleroderma Renal Crisis Sine Scleroderma**

Sankalp Bhavsar (Burlington); Raj Carmona (McMaster University, Hamilton)

**Case Report:** Introduction: Scleroderma renal crisis (SRC) occurs in approximately 10% of patients with systemic sclerosis, particularly in those with diffuse skin disease. SRC has rarely been described to occur in patients with systemic sclerosis without skin involvement (scleroderma sine scleroderma). SRC without skin disease represents a diagnostic challenge and can closely mimic the presentation of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS). Anti-RNA polymerase III antibody testing has been previously reported to be used in four patients to diagnose SRC in the absence of sclerotic skin disease. Methods: We report two patients with SRC both without skin disease at presentation with positive anti-RNA polymerase III antibodies. Results: The first patient, a previously healthy 32 year-old lady, initially presented with new onset of severe Raynaud's

phenomenon. A second patient, a 47 year-old previously healthy lady, initially presented with transient polyarthritis without Raynaud's. Neither patient had any evidence of skin thickening at presentation. The first patient had a positive ANA, but the second patient was repeatedly negative after initial low-titre positivity. Months later, both developed microangiopathic hemolytic anemia, thrombocytopenia, and renal failure. Kidney biopsies showed thrombotic microangiopathy. They were treated with plasma exchange (PLEX) for suspicion of TTP/HUS and had incomplete responses. They were subsequently treated with eculizumab for possible atypical HUS (aHUS). Both patients eventually developed diffuse skin thickening (6 weeks and 9 months after their respective renal presentations). Anti-RNA polymerase III antibodies were strongly positive suggesting that their renal presentations were secondary to SRC sine scleroderma. Both patients have been treated with ACE inhibitor therapy and are currently on dialysis. **Conclusions:** The diagnosis of SRC without skin disease is challenging. In patients presenting with a combination of microangiopathic hemolytic anemia, thrombocytopenia, and renal impairment, SRC should be considered in the differential diagnosis along with TTP/HUS, especially in patients who have any features of connective tissue disease. Anti-RNA polymerase III antibody testing is valuable to confirm the diagnosis along with close observation for the development of skin thickening. ACE inhibitor therapy and aggressive blood pressure control is the mainstay of treatment for SRC and should be instituted early with suspicion of SRC.

**86**

#### **Pulmonary Sarcoidosis, a Complication of Etanercept Treatment in Inflammatory Arthritis: A Report of Five Cases**

Liam Martin (University of Calgary, Calgary); Scott Rapske (Calgary); Weatherald Jason (Calgary); Szabo Lian (Calgary)

**Case Report:** **RATIONALE:** Sarcoid-like granulomatosis is an uncommon complication of anti-tumor necrosis factor (anti-TNF) therapy with only 48 cases previously described in the literature as of October, 2013. **METHODS:** We present 5 patients who developed sarcoid-like pulmonary disease while receiving etanercept therapy for inflammatory arthritis. Clinical, radiologic and histologic information were retrospectively reviewed. **RESULTS:** 5 patients [3 males; median age 49 (range 35-60)] were receiving etanercept for rheumatoid arthritis (3), psoriatic arthritis (1) and ankylosing spondylitis (1). The median time between etanercept introduction and diagnosis of sarcoidosis was 24 months (range 7-60 months). Bilateral hilar and mediastinal lymphadenopathy without interstitial abnormalities was present at diagnosis in 4 patients, with upper lobe ground glass and nodular opacities in the fifth patient. Histologic evidence of sterile, non-caseating granuloma was confirmed in 4 patients whereas 1 patient had consistent clinical symptoms with hilar and mediastinal lymphadenopathy on chest imaging that regressed upon etanercept discontinuation and prednisone treatment. Four patients had radiographic improvement while 1 patient had stable lymphadenopathy 2 years after discontinuation of etanercept. One patient remained on etanercept after the diagnosis of sarcoidosis and was asymptomatic despite radiographic progression to stage II sarcoidosis. However the interstitial reticulo-nodular opacities and mediastinal lymphadenopathy spontaneously regressed in this patient while still on etanercept treatment. **CONCLUSIONS:** Pulmonary sarcoid-like granulomatosis is an increasingly recognized complication related to tumor necrosis factor-alpha inhibitors. Awareness of this association is important for rheumatology and respiratory clinicians. The fifth case raises the question in regards to the role of etanercept in the development of sarcoidosis.

**87**

#### **Psoriatic Arthritis and Sweet's Syndrome: A Case Report and Review of the Literature**

Shannon Galway (University of British Columbia, Vancouver); Iman Hemmati (Department of Medicine, University of British Columbia, Vancouver); Alastair McLeod (University of British Columbia, Vancouver); Kenneth Blocka (The University of British Columbia, Vancouver)

**Case Report:** Objective: 1. To report an unusual case of psoriatic arthritis and Sweet's syndrome. 2. Review of literature on Sweet's syndrome and its association with psoriatic arthritis Method: A case of Sweet's syndrome is reported in a 36 year old gentleman with history of psoriatic arthritis. The English medical literature was reviewed for association of Sweet's syndrome and psoriatic arthritis. Results: Sweet's syndrome, also referred to as acute febrile neutrophilic dermatosis (AFND), is a rare condition with fever, neutrophilia, and tender erythematous skin lesions that typically show an upper dermal infiltrate of mature neutrophils. Sweet's syndrome can be idiopathic, but can also occur in the context of inflammatory diseases. Review of the literature revealed no reported case of Sweet's syndrome associated with psoriatic arthritis, although three cases of Sweet's syndrome associated with psoriasis have been described in the literature. Conclusion: We report the first case of Sweet's syndrome associated with psoriatic arthritis. Sweet's syndrome is known to be associated with autoimmune rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, and relapsing polychondritis. Psoriatic arthritis should be considered as a potential inflammatory disease associated with Sweet's syndrome.

88

### **Canadian Rheumatology Association Choosing Wisely**

CRA Choosing Wisely Committee Choosing Wisely (University of Toronto, Toronto)

**Objective:** Rheumatologists play a unique and vital role in guiding their patients toward the most effective rheumatology care, with an emphasis on both evidence-based investigation and treatment. To that end, the Canadian Rheumatology Association has joined the national Choosing Wisely Canada campaign to develop a list of 5 tests or treatments used in rheumatology that have evidence indicating that they may be unnecessary and not adding value, and thus should be questioned and discussed by physicians and patients.

**Methods:** A committee of 16 rheumatologists, consumers and allied health professionals from across Canada generated a list of things in rheumatology that may be unnecessary, outdated, non-specific or insensitive, using the Delphi method. Participants ranked items based on their agreement with content of the suggestion, prevalence of the item in their community, highest impact on costs and relevance of the item to their practice. Following this, the top items were presented to the entire CRA membership for their input. Finally, a targeted literature review is being completed of the final five items.

**Results:** Sixty-four unique items were proposed and after 3 Delphi rounds was narrowed down to 13 items. A total of 172 rheumatologists (36% of those contacted) participated in the member-wide survey. The respondent characteristics were similar to the membership at large in terms of gender and geographical distribution. Based on evidence existing, relevance to rheumatology practise and member survey results including agreement and impact ratings, 5 topics were chosen for literature review.

**Conclusion:** Rheumatologists have many opportunities to impact overutilization of care. Final completion of the literature review will identify explicit starting points for eliminating waste in rheumatology care.

89

### **Impact of a Rheumatology Consultation Service in Hospitalized Patients**

Shirley Chow (Toronto); Dafna Gladman (University of Toronto, Toronto); Heather McDonald-Blumer (Mount Sinai Hospital, Toronto)

**Objective:** 1) To describe the nature of the hospital rheumatology consultations service 10 years apart for educational merit 2) To compare two academic teaching hospitals in one centre 3) To determine whether a hospital rheumatology consultation service alters diagnostic accuracy, and changes or expedites treatment.

**Methods:** Consecutive patients seen on the consultation service at the University Health Network/ Mount Sinai Hospital (UHN/MSH) from July 1 to December 31 2010, and Sunnybrook Health Sciences Centre (SHSC) from July 1 2011- June 30 2012 were recorded in a logbook. Using a standardized case form, the charts were reviewed and the patients' demographic information, admitting diagnosis, reason for consultation, referring service, final rheumatologic diagnosis, duration of hospital stay, treatment implemented and outcome were recorded.

**Results:** At UHN/MSH 268 patients were recorded over this 6 month period. These included 163 females and 105 males with a mean age of 55 years (range 19 to 92 years). This is more than the 238 consults seen over a 10 month period in 1999 at UHN/MSH. At SHSC 238 patients were recorded over 12 months. These included 120 females and 118 males with a mean age of 68 years (range 18 to 96 years). The most common diagnoses seen at UHN/MSH were 62 connective tissue diseases, 59 crystal induced arthropathy; 25 vasculitis; and 22 polyarthritis. This is similar in breadth as 1999 at UHN/MSH. The most common diagnoses at SHSC were 66 crystal induced arthropathy; 26 vasculitis; 26 polyarthritis; and 23 regional syndromes. The consults were requested from different medical services, but most commonly internal medicine at 104 at UHN/MSH and 156 at SHSC. At UHN/MSH there were 82 emergency referrals (31%), 158 urgent referrals (59%), and 28 non-urgent referrals (10%). The rheumatology team helped establish the diagnosis in 177 patients, confirmed the diagnosis in 57 consults, and did not change the diagnosis in 34 patients. 74 of 80 patients with swollen joints had their joints aspirated or injected, and 94 patients had steroids or disease modifying therapy initiated or adjusted. This was similar at SHSC.

**Conclusion:** The rheumatology hospital consultation service provides consultation from various specialties for a variety of rheumatic diseases, thus providing an excellent educational experience. Most referrals were for emergent or urgent rheumatic diseases thus providing expert needed care. The service helped establish or confirm the diagnosis and helped initiate treatment. This study provides the groundwork for further research.

## 90

### **Impact of Male Sex on Survival in Systemic Sclerosis**

Haseena Hussein (Toronto Scleroderma Research Program, Mount Sinai Hospital, Toronto Western Hospital, University of Toronto, Toronto); Sindhu Johnson (Division of Rheumatology, Toronto Western Hospital, University Health Network Pulmonary Hypertension Programme, Toronto General Hospital, Mount Sinai Hospital and University of Toronto, Toronto)

**Objective:** Systemic sclerosis (SSc) has a female predominance with a female-to-male ratio of 3:1. Sex differences have been seen in many autoimmune diseases; however, little is understood about the effect of sex on SSc disease manifestations and survival. The objectives of this study were to evaluate differences in survival and disease manifestations between males and females with SSc.

**Methods:** We conducted a retrospective cohort study of patients from the Toronto Scleroderma Program who fulfilled the American College of Rheumatology (ACR) classification criteria for SSc and were >16 years of age. We evaluated differences in age of onset, disease manifestations, serology, and survival between males and females.

**Results:** 907 patients (745 females, 162 males) were included. Males more frequently had diffuse SSc than women (45% versus 31%,  $p = 0.007$ ). Men were more likely to have renal crisis (10% versus 7%),

abnormal nail fold capillaries (30% versus 25%), digital ulcers (35% versus 32%), esophageal dysmotility (89% versus 85%), telangiectasia (81% versus 77%), and interstitial lung disease (42% versus 32%). Females more frequently had anticentromere antibodies (19% versus 9%), pulmonary arterial hypertension (38% versus 33%), and Raynaud's phenomenon (96% versus 94%). There were 186 deaths (37 males, 149 females). Males had increased mortality compared to females (Hazard Ratio (HR) 1.56,  $p=0.02$ ). The median survival time was 17.3 years for males and 24.7 years for females. After adjusting for differences in SSc subtype, serology and presence of interstitial lung disease, men still had increased mortality compared to females (HR 1.64,  $p = 0.009$ ).

**Conclusion:** Males with SSc have an increased burden of disease and decreased survival compared to females with SSc.

## 91

### **Effects of Rituximab and Infliximab on Carboxypeptidase B and its Substrates in Rheumatoid Arthritis Synovium**

Stefan Edginton (University of Manitoba, Winnipeg); Hani El-Gabalawy (University of Manitoba, Winnipeg); Carol Hitchon (University of Manitoba, Winnipeg); Miranda Ma (Winnipeg)

**Objective:** Inflammation and coagulation play important roles in the pathogenesis of rheumatoid arthritis (RA). Carboxypeptidase b (CPB) promotes coagulation and may have an anti-inflammatory role in arthritis through its ability to cleave pro-inflammatory mediators osteopontin (OPN) and complement C5a. We evaluated synovial expression of CPB, C5a and OPN at baseline and 16 weeks after treatment with rituximab or infliximab and explored associations with clinical response.

**Methods:** RA patients receiving infliximab ( $n=10$ ) or rituximab ( $n=5$ ) had a synovial biopsy at baseline and 16 weeks post therapy. Expression of CPB, C5a, OPN, the macrophage marker CD68 and T-cell marker CD3 was assessed using immunohistochemistry and image analysis. Two blinded investigators (SE & MM) scored 3 separate areas from each sample. The average score (% area positive staining) at each time point, and the change in synovial expression from baseline were calculated. Clinical disease activity scores (DAS) were obtained at baseline, the second arthroscopy, and one year. Synovial expression and associations between biomarkers with clinical activity were evaluated using non-parametric tests.

**Results:** The patients receiving infliximab and rituximab were clinically similar with an average age 44( $\pm$ 14) years; 93% RF positive; and baseline DAS 5.43 (1.07). At 12 weeks, 1 patient had a good and 6 a moderate EULAR response. At 1 year, 3 had a good and 4 a moderate response EULAR response. CPB staining was most intense in the synovial lining layer, around blood vessels and in some lymphocytic infiltrates. OPN and C5a staining was more diffuse throughout the synovium. At baseline, the CPB expression correlated with CD68 ( $r=0.8$   $p=0.001$ ), and CD3 ( $r=0.7$

$p=0.006$ ). Compared to baseline, at 16 weeks post-treatment there was reduced expression of C5a (5.05 vs 0.98  $p=0.001$ ) and CD3 (5.9 vs 3.2  $p=0.031$ ) with a trend to reduced CD68 expression (2.96 vs 1.9  $p=0.053$ ). The expression of CPB and OPN at 16 weeks were correlated ( $r=0.6$   $p=0.011$ ).

Synovial expression did not correlate with baseline DAS. At 16 weeks C5a expression correlated with DAS ( $r=0.57$   $p=0.04$ ) and a trend with DAS 1 year post treatment, ( $r=0.54$   $p=0.06$ ). 16-week OPN levels were negatively correlated to 1-year DAS scores ( $r=-0.57$   $p=0.044$ ).

**Conclusion:** Carboxypeptidase b expression may be linked to macrophages and T-lymphocytes. Synovial C5a and osteopontin expression may provide insight into response to treatment and could potentially play a role in predicting future clinical response in rheumatoid arthritis.

## 92

## **Changes in ERAP1 Expression can Affect Autophagy and Could be Pathogenic in Ankylosing Spondylitis**

Zhenbo Zhang (Toronto Western Research Institute, Toronto); Nigil Haroon (Toronto)

**Objective:** Functional interaction of ERAP1 and HLA-B27 have been proposed to play a role in the pathogenesis of AS. We were the first group to demonstrate that ERAP1 variants can alter HLA-B27 expression in AS patients. Changes in B27 expression can trigger the unfolded protein response which in turn is a trigger for autophagy. We studied the effect of altered ERAP1 levels and AS associated ERAP1 variants on autophagy and downstream mediators.

**Methods:** C1R (B lymphoblastoid) cells have been stably transfected with HLA-B2705. The endogenous ERAP1 was silenced in these C1R-B27 cells with ERAP1-shRNA (C1R<sup>ERAP1sh</sup>). After confirming stable ERAP1 suppression, we transfected either the common variant ERAP1 (ERAP1<sup>WT</sup>) or one of the two AS-associated ERAP1 variants, K528R or Q730E into the C1R<sup>ERAP1sh</sup> cells. Scrambled sequence shRNA and Lentivirus expression vector alone were used as control. Western blot (WB) for ERAP1 suppression was done using ERAP1 antibody. Exogenous ERAP1 expression was assessed with anti-HA antibody. Stable cells expressing ERAP1<sup>WT</sup> or ERAP1-variants were selected by hygromycin. Stable cell lines were lysed and RNA extracted followed by generation of cDNA. The Human Autophagy RT<sup>2</sup> Profiler PCR Array was used to profile the expression of 84 key genes involved in autophagy in UPR-caused stable cells. Autophagy related genes identified to be differentially expressed in cells with different ERAP1 variants were confirmed by qRT-PCR. The expression of IL17A, IL23A, TNF $\alpha$  and NF $\kappa$ B1 were also studied.

**Results:** More than 80% suppression of ERAP1 was seen by western blot and more than 75% suppression by qRT-PCR in C1R<sup>ERAP1sh</sup>, compared to cells treated with scrambled-sequence shRNA. Using Anti-HA antibodies uniform strong expression of ERAP1<sup>WT</sup> and variant forms of ERAP1 were seen in the respective C1R cell lines. Autophagy PCR Array showed significant upregulation of autophagy related genes in the C1R cell lines after suppressing ERAP1. Similarly, the C1R cell with AS associated ERAP1 variants that are known to trigger higher FHC formation and UPR responses, had higher expression of autophagy related genes. The autophagy-specific genes that showed the most significant variation with ERAP1 were ATG5, ATG12, ATG16L1, LC3I and LC3II. The same cells with increased autophagy had greater expression of IL17A, IL23A, TNF $\alpha$  and NF $\kappa$ B1

**Conclusion:** ERAP1 suppression triggers autophagy and release of proinflammatory cytokines. AS-associated ERAP1-variants that are known to have decreased ERAP1 function leads to higher autophagy responses compared to the common variant of ERAP1. Autophagy may be an important player in the pathogenesis of ankylosing spondylitis.

## **93**

### **Electronic Web-Based Rheumatologic Assessment Tool to Improve Communication with Allied Health Professionals: A 12 Month Pilot Project.**

Anthony So (Queen's University, Kingston); Igal Raizman (Queen's University, Kingston); Henry Avern (Queen's University, Kingston)

**Objective:** A pilot project to determine the feasibility of a web-based assessment tool for use by Allied Health Professionals for the ongoing management of Rheumatoid Arthritis patients in an outpatient setting over the period of 12 months. The primary outcome assessed was identifying the need for therapeutic intervention.

**Methods:** A physiotherapist from the Canadian Arthritis Society communicated her patient assessments during her community visits using a webform. This webform had categorical, continuous, and visual data input (swollen joint count [SJC] homunculus) as well as free text input in

a comment section. The form contained JavaScript code that performed calculations for SDAI, CDAI, DAS28, as well as a novel Gestaltometer Score, which is currently being validated, that incorporates variables from well-known prognosticators of inflammatory joint diseases to determine whether a patient requires a therapeutic intervention. Patients who scored high on the Gestaltometer Score, SJC, or had worrisome comments in the free text input section were brought to clinic for an early follow-up. Patients who did not score high in any of the aforementioned sections were seen in a regular follow up visit by a rheumatologist. The visit to a rheumatologist was considered the gold standard to determine the validity of the form's assessment.

**Results:** A total of 42 forms were filled out by the physiotherapist for 20 patients. 2 patients and 2 forms were excluded because a physician filled out one form and the other was for another rheumatologist's patient. The form detected 22 of 22 patient encounters that eventually required an earlier intervention. The form detected 16 of 18 patient encounters for which no interventions were required. The two patients encounters that scored positive for requiring earlier intervention had just recently been started on DMARD agents and full efficacy had not been achieved yet.

**Conclusion:** The results suggest that this tool is an effective method for Allied Health Professionals to identify patients who need therapeutic interventions, and to efficiently communicate the relevant outcome data informing this decision. Globally, the webforms had a sensitivity of 100% for identifying patients who ultimately required earlier therapeutic interventions with 89% specificity. Version two of the webform will incorporate the homunculi for tender and damaged joints as visual inputs and will be used by more physiotherapists and nurse practitioners. We are also piloting the revised form for use by family doctors in remote settings.

## 94

### **The Effects of Tumor Necrosis Factor Inhibitors and Corticosteroids on Bone Mineral Density in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis: A Meta-Analysis of Randomized Controlled Trials**

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**Objective:** Inflammatory arthritis is a minor risk factor for osteoporosis and it may be that treating systemic inflammation can improve bone mineral density (BMD). The aim of this study was to examine if DMARDs, steroids, and biologics for rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (PSO), and ankylosing spondylitis (AS) affect BMD.

**Methods:** Medline, Embase, and Cochrane were searched from 1960 to present using English randomised controlled trials in adults. Review articles were excluded. Studies were grouped based on disease, treatment type, and site of BMD measurement (wrist, lumbar spine (LS), hip).

**Results:** 393 studies were identified; 13 were eligible (11 RA, 0 PsA, 0 PSO, 2 AS). For RA, significantly less wrist bone loss was seen with biologics ( $\Delta\text{BMD} = 0.27\text{SD}$ , 95% CI 0.07-0.47,  $P=0.009$ ,  $I^2=0\%$ ) and corticosteroids ( $\Delta\text{BMD} = 0.54\text{SD}$ , 95% CI 0.23-0.85,  $P=0<0.001$ ,  $I^2=0\%$ ). Biologics had no significant effect on LS and hip BMD. Corticosteroids had more bone loss compared to placebo on LS ( $\Delta\text{BMD} = -0.25\text{SD}$ , 95% CI -0.42 to -0.08,  $P=0.003$ ,  $I^2=52\%$ ) but no difference for hip. For AS, significant BMD increase was seen with biologics in both LS ( $\Delta\text{BMD} = 0.98\text{SD}$ , 95% CI 0.73-1.23,  $P<0.001$ ,  $I^2=16\%$ ) and hip ( $\Delta\text{BMD} = 0.38\text{SD}$ , 95% CI 0.14-0.63,  $P=0.002$ ,  $I^2=0\%$ ). There was insufficient data to meta-analyze other diseases.  $\Delta\text{BMD}$  were reported as standardized mean difference.



**Conclusion:** Based on our RA analysis, biologics and steroids yielded less wrist bone loss (where synovitis is often present) but had no effect on hip. Corticosteroids affected more bone loss in LS whereas biologics had no effect on LS. For AS, biologics yielded increase in both LS and hip BMD.

## 95

### **There is Still a Care Gap in Osteoporosis Management for Patients with Rheumatoid Arthritis**

Jennifer Watt (Western University, London); Andrew Thompson (University of Western Ontario, London); Nicole Le Riche (University of Western Ontario, London); Janet Pope (University of Western Ontario, London)

**Objective:** To assess compliance rates with the current Canadian osteoporosis guidelines and whether the Fracture Risk Assessment Tool (FRAX) score in patients with rheumatoid arthritis (RA) correlated with the likelihood of receiving osteoporosis treatment and having a bone mineral density test.

**Methods:** Charts of serial RA outpatients were reviewed to collect bone mineral density (BMD) test data and patients' use of calcium, vitamin D, and osteoporosis treatment. Odds ratios (OR) were calculated to determine if a higher FRAX score or particular patient characteristics increased the likelihood of osteoporosis treatment or having a BMD test.

**Results:** Using the FRAX tool, the 10-year risk of major osteoporotic fracture was high in 92 (12.5%), moderate in 216 (29.3%), and low in 429 (58.2%) patients. Compared to those at low risk, patients identified as high risk were more likely to receive OP treatment (OR 16.31, 95% CI 9.45-28.13,  $p < 0.0001$ ); calcium (OR 3.89, 95% CI 2.43-6.25,  $p < 0.0001$ ); vitamin D (OR 3.46, 95% CI 2.12-5.64,  $p < 0.0001$ ); and to have had a BMD (OR 10.22, 95% CI 5.50-18.96,  $p < 0.0001$ ). Among 124 patients currently taking prednisone, half (46.8%) were prescribed a bisphosphonate. BMD tests were performed in 415 patients (56.3%), but only 228 were recorded on the specialists' charts.

**Conclusion:** Although compliance with current OP guidelines remains low among all patients with RA, higher risk patients were more likely to have a BMD and receive treatment, as indicated by the clear dose response seen along the 10-year fracture risk from low to medium to high-risk groups.

## 96

### **Assessing Significant Flares in Rheumatoid Arthritis: Validity of the Outcome Measures in Rheumatology Preliminary Flare Questions in the Canadian Early Arthritis Cohort**

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**Objective:** Rheumatoid arthritis (RA) flares are common, poorly defined, and understudied. A tool is needed to measure significant RA flares that may signal need for evaluation for treatment change. Qualitative and quantitative research by the OMERACT RA Flare Group with patients and providers has identified an RA Flare Core Domain Set, ratified by OM 2012 attendees. Next, we identified preliminary flare questions (PFQs) to assess core domains. Here, we report evidence of discriminant validity of PFQs between patients who report flaring and those not in flare and convergent validity among PFQs and validated RA measures in a cohort of patients with early RA (ERA).

**Methods:** 1190 patients in the Canadian early Arthritis CoHort (CATCH) completed PFQs at visits from 11-2011 through 5-2013. Both patients and MDs independently rated if patient was in flare. Patients completed PFQs for pain, physical function (PF), fatigue, stiffness, participation and coping over 1 week prior to visit using 11-point scales, as well as HAQ, SF12, RADAI, WPAI and Patient Global. Wilcoxon rank sum and  $\chi^2$  were used to compare groups. Correlations (Spearman, polychoric, polyserial) were calculated between PFQs and relevant HAQ, SF12, WPAI, RADAI items and other scales.

**Results:** Participants were mostly female (74%), white (81%), and 55% had > high school education. Mean (SD) age was 53 (15) years and RA duration 6 (3) months. 33% of patients and 38% of MDs classified patient as being in flare; agreement for being in flare was 62% and not in flare 73% (kappa = .33; 95% CI .28-.39). Scores were significantly ( $p < .001$ ) higher across all domains in patients reporting flare. Correlations were strongest between PFQ pain and other pain scales ( $r$ 's=.84-.88). Moderate-strong correlations were evident among PFQ with other measures of PF ( $r$ 's= .63-.75), fatigue ( $r$ 's= .52-.85), stiffness ( $r$ =.66), participation ( $r$ 's=.60-.77) and coping ( $r$ 's=.30-.55).

**Conclusion:** In ERA patients who report being in flare, PFQ scores were significantly higher across all domains. There was substantial agreement among single item PFQs and other validated RA measures. Results provide evidence of the validity of OMERACT PFQs to assess flares in RA patients. Additional psychometric evaluation is needed to establish the reliability, validity, and responsiveness of items and relevant thresholds across a range of RA populations and settings prior to widespread use.

97

### **Illness Perception in Patients with Rheumatoid Arthritis**

Nam Le (McGill University, Montreal); Maria Bazan Bardales (McGill University, Montreal); Susan Bartlett (McGill, Montreal); Ines Villarroya (Barcelona); Ines Colmegna (McGill University, Montreal)

**Objective:** In accordance with Leventhal's Common Sense Model of Self-Regulation, rheumatoid arthritis (RA) patients' illness perceptions affect their behavioural reactions to RA symptoms. As cultural diversity asserts that people hold different beliefs depending on their background, RA patients from different cultures are bound to hold different illness perceptions. Accounting for these beliefs can enable clinicians to adjust their medical approach, and help them devise more patient-centered treatments. The objective of this study was to assess illness perceptions among English Canadian RA patients and to evaluate the impact that specific sociodemographic and disease related characteristics have on RA patients' beliefs.

**Methods:** Adult English speaking RA patients, followed at the Royal Victoria Hospital outpatient rheumatology clinic, were consented and requested to fill out the Revised Illness Perception Questionnaire (IPQ-R). Additional information was retrieved from electronic databases and patients' medical charts. Between-group comparisons were conducted to evaluate differences on 8 aspects (identity, cause, timeline acute/chronic, timeline cyclical, personal control, treatment control, consequences, emotional representation) of illness perception and patients' sociodemographic and disease related characteristics.

**Results:** The sample consisted in 18 RA patients, 66% females, 67% older than 50 years old, most of them with seropositive, established RA on disease modifying anti rheumatic therapy. Non-significant differences in illness perceptions were found based on sex, age or disease duration. Individuals who were in remission (16%) or had low disease activity (50%) reported higher perceptions of treatment control. RA patients mostly attributed RA to heredity (39 %), altered

immunity (11 %) and pollution (11 %).

**Conclusion:** Patients with longer disease duration seem to better understand their illness and tend to be less distressed about their condition. Moreover, patients whose disease is more severe have less confidence in their treatment. Lastly, consistent with previous, a significant proportion of RA patients consider heredity as the primary cause of RA.

98

### **Antibody-Mediated Inflammatory Brain Diseases in Children**

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**Objective:** Antibody (AB) -mediated inflammatory brain diseases (IBrainD) are increasingly recognized, devastating diseases affecting previously healthy children. In the past decade, significant progress has been made in the detection of specific antibodies. However, lack of early clinical recognition often leads to a delay in diagnosis and late initiation of treatment. Therefore, the objectives of this study were to: 1) To describe the presenting clinical spectrum and the distinct entities of AB-mediated IBrainD in children and 2) to review the current diagnostic investigations and evaluate the patient outcome.

**Methods:** A single center cohort study of consecutive patients age  $\leq 18$  years diagnosed with an AB-mediated IBrainD at the Hospital for Sick Children, Toronto between January 2005 and July 2013 was performed. The diagnosis of an AB-mediated IBrainD required 1) a newly acquired neurological and/or psychiatric deficit and 2) a confirmatory antibody detected in serum and/or cerebrospinal fluid. Children with a presumed AB-mediated IBrainD without confirmatory test were excluded. Standardized clinical data, laboratory test results and neuroimaging features at presentation were captured. Treatment regimens were collected. Outcome: PSOM (pediatric stroke outcome measure) at last clinical follow-up categorized into normal function/mild deficit or moderate to severe deficit.

**Results:** A total of 169 children were diagnosed with IBrainD in the study period; of whom 20 (12%) were found to have AB-mediated IBrainD including 14 females (70%). The median age at diagnosis was 12.1 years (range 3.1-17.1). Eight patients had neuromyelitis optica (NMO) and anti-NMDA-receptor encephalitis respectively, two Hashimoto's encephalitis, one glutamic acid decarboxylase (GAD) encephalitis and one AB mediated cerebellitis. Median time from symptom onset to diagnosis was 47 days (range 6-741). All children presented with focal neurological deficits, 11 (55%) had seizures including all anti-NMDAR, Hashimoto's encephalitis and GAD encephalitis patients. Upon presentation, six patients required ICU admission. All patients received B cell targeted therapy. After a median follow up time of 1.3 years (range 0.7-5.7) only 12 (67%) had a good neurological outcome, one child had died.

**Conclusion:** Children with antibody mediated IBrainD represent an important proportion amongst the IBrainD, NMO and anti-NMDAR encephalitis being the most frequent disease entities. Seizures at presentation together with focal neurological deficits are a hallmark of anti-NMDAR encephalitis. A significant amount of children (33%) had residual neurological deficits interfering with daily life activities.

99

### **Efficacy of Methotrexate Monotherapy Compared to Combination Therapy with**

## **Methotrexate and Hydroxychloroquine in the Treatment of Early Rheumatoid Arthritis after 12 Months of Treatment.**

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**Objective:** Early treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drug (DMARD) therapy leads to better clinical outcomes. Methotrexate (MTX) is the most commonly used DMARD in treating RA either as a monotherapy or in combination with other DMARDs. However, data on the short and long-term efficacy of MTX used at the current doses in treating early RA is lacking. The purpose of this study is to compare the short-term and long-term efficacy of high dose oral MTX (20–25mg/ week) alone and in combination with hydroxychloroquine (HCQ) 400mg daily in DMARD-naïve patients with early RA as determined by changes in Disease Activity Score 28 (DAS28) and Health Assessment Questionnaire (HAQ) scores.

**Methods:** Patients diagnosed with RA at our Early Inflammatory Arthritis Clinic from 01/2008 to 09/2010 were included in this study. Data collected prospectively on patients includes: age, gender, co-morbidities, medications, DAS28 and HAQ scores, rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) status. Patients were treated with MTX or MTX/HCQ based on participating physicians' practice. Patients in each group were offered a pulse of corticosteroids as acute treatment for their disease. Treatment responses were compared within and between groups after 3 and 12 months of treatment using pre- and post-treatment DAS 28 and HAQ scores.

**Results:** There were 35 patients in the MTX and 39 in the MTX/HCQ groups respectively. There were no statistical differences between the two groups for age, gender, medications, co morbidities or duration of symptoms. RF status, anti CCP status, baseline DAS28, baseline HAQ scores and the number who received pulse steroid therapy at diagnosis were similar between groups. DAS28 scores improved in both groups, but the improvement was statistically significant in MTX/HCQ group compared to MTX group at the 3-month (-2.24 vs -1.31,  $p=0.003$ ) and 12-month assessments (-2.95 vs -1.88,  $p=0.047$ ). The improvement in HAQ scores was not significant between the two groups at the 3-month (-0.66 vs -0.47,  $p=0.25$ ) and 12-month assessments (-0.580 vs -0.341,  $p=0.163$ ). Significant number of patients on MTX group had escalation of treatment with additional DMARDs compared to the MTX/HCQ group at the 12-month treatment period (17/31 MTX; 9/34 MTX/HCQ,  $p=0.0246$ ).

**Conclusion:** This study demonstrates that MTX/HCQ is more effective than MTX alone in the initial and long-term treatment of early RA using the objective measurement of effectiveness (DAS28). Dual therapy should therefore be considered as the initial therapy in patients with early RA.

100

## **Baseline C-Reactive Protein Levels in a North American Native Population: A Study of Preclinical Rheumatoid Arthritis**

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**Objective:** Serological abnormalities such as anti-CCP and RF can appear years before the onset of

symptoms in people with RA. Previous studies have been inconsistent in elucidating patterns of C-reactive protein (CRP) levels prior to clinical manifestations of the disease. In this study, we conducted serial measurements of CRP in preclinical RA patients from a North American Native (NAN) population that has among the highest prevalence of RA in the world.

**Methods:** First degree relatives (FDRs) of NAN RA patients were studied. Previously unaffected FDRs that developed RA (Transitioners n=9) were identified, and three unaffected FDR Controls (n=27) were stringently matched to each Transitioner. Control matching criteria was based on variables in the literature that have been demonstrated to influence baseline CRP levels, including age, gender, body mass index (BMI), smoking history, and diabetes mellitus (DM) status. Commercially available enzyme-linked immunosorbent assays were used to measure high-sensitivity CRP (hsCRP) serially in stored serum samples. Statistical significance was considered as  $p < 0.05$  using student's t tests.

**Results:** Transitioners had a mean (SD) age of 32.3 (15.0) years (vs 32.3 (13.7) for Controls), had 4.1 (1.8) preclinical samples analyzed for hsCRP over 56.7 (25.1) months of follow up (vs 4.4 (1.7) samples analyzed over 55.7 (17.5) months for Controls), had a BMI of 27.2 (8.7) (vs 27.9 (7.9) for Controls), and a smoking history of 8.4 (6.3) pack years (vs 7.9 (11.0) Controls). Both cohorts were 67% female. There were no statistically significant differences between the two cohorts in matching criteria except for DM status: three Transitioners, and no Controls reported DM at entry into the study. There were no significant differences in serial hsCRP levels between the cohorts. The mean (SD) of the first available hsCRP (mg/L) levels of Transitioners was 1.18 (1.03) vs Controls 1.43 (1.07) ( $p=0.546$ ). The mean of all serial hsCRP levels in Transitioners was 1.18 (0.89) vs Controls 1.57 (0.86) ( $p=0.625$ ). The lowest hsCRP level available was 0.82 (0.72) in Transitioners vs Controls 1.10 (0.95) ( $p=0.415$ ), and tended to be lower in SE negative subjects (0.37 (0.47) vs 1.2 (1.2)  $p=0.05$ ). As expected, hsCRP correlated with BMI (Spearman rho  $r=0.5$   $p=0.001$ ).

**Conclusion:** Despite previous reports that patterns of inflammatory markers may antedate RA in the preclinical period, we found no clear association between CRP levels in NANs prior to RA development compared to controls. However, the sample size may have precluded a demonstration of such an association.

## 101

### Academic Detailing to Optimize Care for RA by Family Physicians – Results of a Satisfaction Survey

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**Objective:** The message of paradigm shift in the treatment of Rheumatoid Arthritis (RA) has not yet reached all family physicians (FPs). We used academic detailing (AD) as a means to improve compliance with RA treatment guidelines by FPs. AD involves visits by trained health care professionals (frequently pharmacists) to physicians in their offices to provide unbiased, evidence-based information on a selected topic. This study presents the results of FPs' satisfaction with the AD intervention for RA.

**Methods:** AD was offered to all 419 FPs practicing in the intervention areas (including Burnaby, New Westminster, North Vancouver, Coquitlam, and Port Coquitlam), identified using the BC College of Physicians' list. FPs in full-time specialized practices, administrative roles or hospitalists were excluded. A pharmacist trained in AD techniques and in RA management visited FPs in their office, delivered a standardized presentation, offered opportunity for one-on-one discussion and provided a resource kit designed to help FPs implement the recommended practice changes. Two weeks after each AD visit, a brief survey was sent to participating FPs. The survey asked them to rate their satisfaction and the usefulness of the AD visit, including the material presented and the resource kit provided. Questions also compared AD with other CME methods for its educational value and convenience.

**Results:** AD was delivered to 99/419 FPs in the intervention area (24% participation rate). Of these, 62 completed the survey (62.6% response rate, 50% women, 53.2% aged > 50, 66.1% had previously received AD on other topics, 48.3% had  $\geq 10$  RA patients in their practice). Using a 10 point scale (1=not at all; 10=extremely), mean(SD), usefulness of the visit was rated at 8.35(1.38), usefulness of the written material was 8.35(1.24), usefulness of the tool kit was 8.43(1.07), relevance of the topic to their practice was rated at 7.93(1.82), educational value was 8.34(1.34), convenience compared with other CME methods was 9.21(1.33), improvement in confidence in prescribing DMARDs was 7.71(1.42); and 91.9% of FPs reported the AD intervention would change their practice at least a little.

**Conclusion:** AD was perceived by participating FPs as useful for managing patients with RA, providing high educational value, and convenience. It was generally well accepted by the FPs surveyed, who also reported improved confidence and expecting to change their practice. The effectiveness of the intervention at changing actual practice compared to a control group will be evaluated using prescription rates of DMARDs obtained from administrative data.

## 102

### **Effect of Certolizumab Pegol Over 48 Weeks in Patients with Axial Spondyloarthritis, including Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis**

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**Objective:** Previous reports of RAPID-axSpA have demonstrated the efficacy and safety of certolizumab pegol (CZP), in patients (pts) with axial spondyloarthritis (axSpA) including pts with ankylosing spondylitis (AS) and pts with no sacroiliitis on X-ray (nr-axSpA), to Week (Wk) 24.

We report clinical efficacy and safety of CZP in axSpA pts to Wk48

**Methods:** The RAPID-axSpA trial is double-blind and placebo (PBO) controlled to Wk24 and dose-blind to Wk48. 1 Pts fulfilled ASAS criteria and had active axSpA, including both AS pts and nr-axSpA pts. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W) continued on their assigned dose in dose-blind phase; PBO pts entering dose-blind phase were re-randomized to CZP loading dose followed by CZP 200mg Q2W or CZP 400mg Q4W after Wk24. We present efficacy data for all pts originally randomized to CZP and imaging outcomes for all pts. Endpoints included ASAS20 and ASAS40 responses, ASAS PR and ASDAS outcomes. Also included were BASDAI, BASFI, BASMI-linear, total spine pain, fatigue, ASQoL, SPARCC and ASspiMRI-a. Outcomes are presented at Wk24 and Wk48. Safety sets consists of all pts treated with CZP at any stage of the 48wk trial.

**Results:** 325 pts were randomized, of which 218 received CZP from Wk0. Of pts randomized to CZP at baseline (BL), 93% completed Wk24 and 88% Wk48. ASAS20, ASAS40 and ASAS PR were maintained from Wk24 to 48 and improvements from BL in BASDAI, BASFI, BASMI-linear, ASDAS and ASDAS-ID were also maintained to Wk48. Reductions in pain, fatigue and ASQoL were also observed between Wk24 and Wk48. In the MRI sub-study (CZP N=104), reduction of inflammation, as measured by SPARCC and ASspiMRI-a, was maintained to Wk48. Similar improvements were seen with both dosing regimens and in both AS and nr-axSpA subpopulations. In the safety set (N=315), adverse events (AEs) occurred in 248 pts (78.7%; event rate per 100 pt-yrs=419.5), serious AEs in 25 (7.9%). Serious infections occurred in 10 (3.2%) pts, including suspected tuberculosis in 3 (1.0%) of which 1 was confirmed (from Mexico). No deaths or malignancies were reported.

**Conclusion:** In the RAPID-axSpA trial, improvements observed over 24 wks in clinical efficacy, patient-reported and MRI outcomes were sustained over 48 wks in both CZP dosing regimens. Similar sustained improvements in clinical, patient-reported and MRI outcomes were observed in both AS and nr-axSpA subpopulations. The safety profile was in line with that observed for CZP in RA

## 103

### **Relationship between MRI and Clinical Remission in Patients with Non-Radiographic Axial Spondyloarthritis after Two Years of Adalimumab Therapy**

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**Objective:** The objectives of this analysis were to determine 1.) The efficacy of adalimumab in improving inflammation on MRI in patients with non-radiographic axial spondyloarthritis (nr-axSpA) and 2.) The relationship between MRI and clinical remission.

**Methods:** ABILITY-1 was a 12-week, phase 3, double-blind, randomized, placebo-controlled trial of adalimumab (40 mg every other week [eow]) in patients with nr-axSpA who had an inadequate response, intolerance, or contraindication to NSAIDs. Patients completing the double-blind period

could enroll in an open-label extension (adalimumab 40 mg eow) of up to 144 weeks. MRI of the sacroiliac joint (SIJ) and spine were performed at baseline, weeks 12, 52, and 104, and were read using the SPARCC scoring system (6 discovertebral unit method for the spine) by 2 independent readers blinded to time sequence. Mean reader scores were used. This post hoc analysis evaluated the efficacy of adalimumab in improving MRI inflammation at weeks 52 and 104 in the overall population and in patients with positive MRI [SPARCC score  $\geq 2$  for either the SIJ or spine] and/or an elevated CRP at baseline (MRI+ and/or CRP+ subpopulation). Clinical remission was defined by ASDAS inactive disease (ID, ASDAS < 1.3), and MRI remission was defined by SPARCC score < 2.

**Results:** 142 (69 adalimumab, 73 placebo) of the total efficacy population (N=185) were in the MRI+ and/or CRP+ subpopulation. MRI obtained at weeks 52 and 104 showed sustained mean improvements with long-term adalimumab therapy in SPARCC SIJ and spine scores for the overall (SIJ: -3.7 [n=149] and -3.8 [n=131] for weeks 52 and 104, respectively; spine: -1.2 [n=148] and -1.4 [n=130]) and MRI+ and/or CRP+ (SIJ: -4.6 [n=116] and -4.8 [n=102]; spine: -1.7 [n=115] and -2.0 [n=101]) populations. Of the patients in ASDAS ID at week 104, 68%, 68%, and 44% had MRI remission of the SIJ, spine, or both SIJ and spine, respectively. Furthermore, 58%, 63%, and 62% of patients in MRI remission at week 104 for the SIJ, spine, or both SIJ and spine were also in ASDAS ID.

**Conclusion:** In ABILITY-1, adalimumab therapy of up to 2 years in nr-axSpA patients resulted in reduction of inflammation on MRI. The majority of patients in clinical remission were noted to also have MRI remission. However, resolution or absence of inflammation on MRI did not always correspond to clinical remission.

## 104

### **Can Satisfactory Reliability of the 7-Joint Ultrasound Score be Attained by Inexperienced Readers in a Single Calibration Exercise? Results from the BIODAM Program**

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**Objective:** While ultrasound assessment of patients with RA using the 7-joint score (US7) demonstrates reliability in the hands of experienced readers it is unclear to what degree this has external validity, and whether satisfactory calibration can be attained over the course of a single calibration exercise conducted over one day at a single location. We aimed to assess the feasibility and impact on inter-reader reliability of a one-day structured program of training based on an eCRF designed to provide real-time feedback on reader reliability during the process of scanning.

**Methods:** Six patients with rheumatoid arthritis were examined by 12 sonologists from 6 countries and 12 centers in 6 rater pairs who performed the US7 score. The US7 score includes the clinically dominant wrist, the second and third metacarpophalangeal (MCP) and proximal interphalangeal joints, and the second and fifth metatarsophalangeal (MTP) joints, which were evaluated for synovitis (SYN), tenosynovitis/paratenonitis (TS), and erosions (ER) from the dorsal side and



palmar/plantar aspects by gray-scale (GS) and power Doppler (PD) ultrasound. Additional lateral scans were performed at the MCP2 and MTP5 joints. Scores were entered into an eCRF custom designed to provide immediate calculation of reliability data (eCaRe-US reliability). Training of readers focused on the most discrepant features observed in exercise 1. All reader pairs repeated the examination in different patient order. Mean (SD) weighted kappa values, mean (SD) per cent agreement rates, inter-observer intra-class correlation (ICC) for summed scores (SYN, TS, ER) were calculated.

**Results:** Improvement in reliability was mainly observed in assessment of SYN-GS and PD.

Primary regions of improvement in SYN-GS were dorso-median and ulnar wrist (k 0.31 to 0.54 and 0.17 to 0.34), PIP2 and 3 dorsal (k 0.03 to 1 and 0.13 to 1), MCP2 and 3 palmar (k 0.04 to 0.37 and 0.06 to 1.0), and MTP5 dorsal (k 0.06 to 1.0). Improvement in detection of SYN-PD was mainly observed in the wrist. Regions where reliability was not improved were MCP2 dorsal, PIP2 and 3 palmar, and MTP2 dorsal. Erosion assessment was lengthy and considered challenging for routine practice.

**Conclusion:** Substantial enhancement of reliability for detection of synovitis by ultrasound may be observed with limited calibration of inexperienced readers. We have identified specific regions that require more intensive calibration, specifically, MCP2 dorsal, PIP2 and 3 palmar, and MTP2 dorsal.

## 105

### **Evidence that Fat Metaplasia is a Key Intermediary in the Development of Sacroiliac Joint Ankylosis following Repair of Erosions in Patients with Spondyloarthritis**

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**Objective:** We hypothesized that ankylosis in the SIJ develops following repair of erosion and that fat metaplasia is a key intermediary step in this pathway.

**Methods:** We used the SPARCC SIJ Structural Score (SSS) method to assess fat metaplasia (FAT), erosion (ER), BF, and ankylosis (ANK). This score relies on the T1W sequence and assesses 5 consecutive coronal slices anteriorly through the cartilaginous portion of the joint from the transitional slice. Lesions are scored dichotomously (present/absent) in SIJ quadrants (fat, erosion) or halves (backfill, ankylosis). Scoring ranges are: FAT (0-40), ER (0-40), BF (0-20), ANK (0-20). Four readers independently assessed 45 pairs of MRI scans blinded to time point (baseline, 2 years) from 45 cases in a prospective cohort receiving either standard (n=22) or anti-TNF (n=23) therapies. In a second study, two readers independently assessed 147 pairs of scans blinded to time point (baseline, 2 years) from cases on standard (n=69) or anti-TNF (n=78) therapies. Univariate analyses and multivariate linear regression focused on identifying significant MRI predictors of change in BF and ANK scores, adjusted for age, sex, symptom duration, treatment, CRP (baseline and 2-year change), SPARCC SIJ inflammation score (baseline and 2-year change), and baseline SSS scores for FAT, ER, BF, and ANK.

**Results:** Using mean SSS scores for 4 readers in the 45 cases, resolution of ER was significantly associated with the development of BF ( $p = 0.0082$ ) and new ANK ( $p=0.045$ ) at 2 years. Using mean scores of two readers in the 147 cases, resolution of erosion was significantly associated with the development of BF ( $p < 0.0001$ ), fat metaplasia ( $p < 0.0001$ ) and new ANK ( $p=0.0001$ ) at 2 years. New ANK was also significantly associated with development of fat metaplasia ( $p=0.0005$ ). Associations were also significant in both treatment groups. A decrease in erosion

score was a significant predictor for development of new BF in the multivariate regression model (adjusted  $R^2 = 0.44$ , F ratio 14.6,  $p < 0.0001$ ) (change in SSS erosion:  $\beta = -0.74$ ,  $t = -4.1$ ,  $p = 0.0001$ ). 31 (21.1%) of patients developed new ANK and these had significantly more resolution of erosion than patients without new ANK ( $p = 0.014$ , Mann-Whitney). Significant independent predictors of new ANK in the multivariate model (adjusted  $R^2 = 0.24$ , F ratio = 10.0,  $p < 0.0001$ ) were baseline BF score, decreased erosion score and development of new fat metaplasia

**Conclusion:** Ankylosis in the SIJ develops following repair of erosion and fat metaplasia is a key intermediary step in this pathway.

## 106

### **12- and 24-Week Patient-Reported Outcomes from a Phase 2b Dose-Ranging Study of Baricitinib, an Oral Janus Kinase 1/ Janus Kinase 2 Inhibitor, in Combination with Traditional Disease-Modifying Antirheumatic Drugs in Patients with Rheumatoid Arthritis**

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**Objective:** Baricitinib (formerly, LY3009104/INCB028050) is a novel, oral inhibitor of the JAK1 and JAK2 in the JAK-STAT pathway known to be of importance in the pathobiology of rheumatoid arthritis (RA) and has previously been shown to improve the signs and symptoms of RA after 12 weeks of treatment.<sup>1</sup> This study evaluates the patient-reported outcomes (PROs) within a 24-week blinded phase 2b study for 1 mg, 2 mg, 4 mg, and 8 mg baricitinib once daily (QD) at 12 weeks, and 4 mg and 8 mg at 24 weeks.

**Methods:** Patients with active RA and on stable doses of methotrexate were randomized (2:1:1:1:1) to receive either placebo (PBO) or 1 of 4 QD baricitinib doses (1, 2, 4, or 8 mg) for 12 weeks. Patients assigned to placebo or 1 mg were reassigned to an exploratory 4 mg QD or 2 mg BID group between weeks 12 and 24 and were excluded from the primary 24-week analysis; patients initially assigned to 2 mg, 4 mg, or 8 mg remained on the same treatment. PROs included patient global assessment (PtGA) of disease activity (Visual Analog Scale [VAS]), pain (VAS), physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]), health-related quality of life (Medical Outcomes Study [MOS] Short Form 36 [SF-36]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F]), and duration of morning stiffness. Analyses were done using analysis of covariance (ANCOVA). Statistical comparisons of means were conducted for each active treatment group against the PBO group; p-values were not adjusted to correct for multiple comparisons.

**Results:** Of 301 randomized patients, those who received baricitinib experienced clinically meaningful improvements in most PROs as early as week 2 vs. PBO as well as at 12 weeks. These improvements were maintained or continued to improve through 24 weeks (e.g., change from baseline for 4 and 8 mg groups, respectively, FACIT-F: 5.32 [SEM: 1.31], 5.00 [SEM: 1.52]; SF-36 PCS: 7.32 [SEM: 0.97], 7.67 [SEM: 1.23]).

**Conclusion:** In this phase 2b study in patients with RA, those who received baricitinib reported clinically meaningful improvements as early as week 2 in most PROs relative to PBO as well as at 12 weeks. These improvements were maintained or continued to improve through 24 weeks.

## 107

### **Lupus Patients have a High Prevalence of Abnormalities on Resting ECG that are**

### **Associated with Increased Risk for Cardiovascular Events**

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**Objective:** To describe all abnormalities on resting ECG in a cohort of lupus patients and determine the prevalence of specific abnormalities associated with increased risk for CV events.

**Methods:** Resting ECG was performed on all consecutive patients attending The Lupus Clinic between October 2012-May 2013. Participants underwent a standard digitally recorded 12-lead ECG at supine rest. Coded ECGs were reviewed and interpreted by a cardiologist using the Minnesota code classification system. ECGs were grouped as normal and abnormal.

Abnormalities included: pathological Q waves, ST-segment and/or T-wave abnormalities, LVH, left or right bundle branch block, left-axis deviation, arrhythmia and atrial enlargement. We further determined the prevalence of at least one or more of the ECG findings that may be associated with subsequent CV events: ST-segment and/or T-wave abnormalities, LVH, left-axis deviation, or bundle branch block. We also determined the number of patients who had at least one or more of these variables.

**Results:** 274 patients were studied. 88.7% of the patients were female with mean age of 47.7 +/- 14.0 and lupus duration of 17.0 +/- 11.5 years. Of 274 resting ECGs 40.5% were abnormal. 21 patients had axis deviation of which 13 had left, 5 had right and 3 fulfilled criteria for left anterior fascicular block. 7 patients had atrial enlargement (3 right and 4 left). 32 patients with arrhythmia were identified (3 1st degree atrioventricular block, 10 sinus bradycardia, 4 sinus tachycardia, 3 ectopic atrial rhythm, 3 long QTc, 2 isolated premature atrial and 1 isolated premature ventricular contractions, 2 ventricular bigeminy, and 2 short PR interval). ST-segment abnormalities and/or T-wave abnormalities in 54 (19.7%) LVH in 27 (9.9%), left-axis deviation in 16 (5.8%) and bundle branch block in 13 (4.7%). LBBB were present in 1 patient (0.4%) and in RBBB 12 (4.4%). 17 (6.2%) patients had pathological Q waves (which may indicate previous infarct). 115 (41.9%) patients had at least one of the 4 ECG findings that may be associated with subsequent CV events. 23 (8.4%) patients had 2 more ECG abnormalities and 6 (2.2%) were observed to have at least 3 ECG abnormalities.

**Conclusion:** 41% of the ECG had abnormal findings. All of the abnormal ECGs demonstrated at least one ECG finding associated with an increased risk for subsequent CV events. Further studies will determine whether ECG can serve as risk stratification factor for CVD in SLE patients.

108

### **Empirical Treatment of Dermatomyositis with Intravenous Immunoglobulin in Pregnant Patient**

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**Case Report:** Objective Describe the peri-partum course of a patient with dermatomyositis (DM) treated with intravenous immunoglobulin (IVIG). Method Case study verified by healthcare team. Results A 34-year-old nulligravida teacher (TF) with DM presented for pre-conception counseling. She was diagnosed two years ago based on an initial presentation of heliotrope rash, muscle weakness, elevated CK, ESR, and CRP, confirmed by muscle biopsy. TF was initially treated with azathioprine, but could not tolerate it due to GI side-effects. Methotrexate, hydroxychloroquine, and prednisone successfully controlled her symptoms and had been

continued since. Past medical history was otherwise unremarkable. As disease was not active for at least six months, TF was given the go-ahead for family planning. She was advised to discontinue methotrexate for three months before conception. Two months later, she developed an extensive DM rash, leading her rheumatologist to consider IVIG infusions. After three infusions of IVIG, TF became pregnant. As IVIG was considered to be non-harmful to fetus, she was advised to continue IVIG infusions, hydroxychloroquine and prednisone throughout pregnancy. At 29 weeks gestation, TF developed placental insufficiency and was delivered via urgent Caesarean section. Her son's birthweight was 2 lbs, 14 oz and was later diagnosed with hypospadias. TF had a significant flare four months post-partum, developing muscle weakness and mechanics' hands. IVIG was continued, with methotrexate and an increased dosage of prednisone added to induce remission. Conclusions IVIG has been largely reserved for refractory DM but is now undergoing resurgence for management in the peri-natal period due to its limited side-effect profile and presumably safe fetal exposure (as opposed to the conventional treatment of high-dose steroids or immunosuppressive agents). This case deviates in both outcome and complications from cases reported in literature, which detail largely positive results using the IVIG/prednisone regimen with successful term births and no maternal/fetal complications or post-partum flares. However, TF had more aggressive disease than the pregnancy-associated DM patients described in literature, with subclinical disease indicated by persistently elevated inflammatory markers. In addition, TF developed placental insufficiency abruptly despite remaining on monthly infusions of IVIG and lacking risk factors for placental insufficiency. Moreover, she had a significant post-partum flare. For this reason, TF is comparable to the "refractory DM group" that has 37-71% improvement with IVIG. To our knowledge, this case is the sole presentation of DM in pregnancy that was not fully clinically controlled with IVIG. Hence, this case underlines both the potential and limitations for IVIG during the peri-natal period for rheumatologic conditions.

## 109

### **Do Sustained Clinical Remission and Sustained Low Disease Activity Equally Predict Functional Status in Early Rheumatoid Arthritis?**

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**Objective:** Sustained clinical remission (REM) is the therapeutic goal in rheumatoid arthritis (RA) but low disease activity (LDA) is often considered an acceptable substitute. Little is known whether sustained LDA is "as good" as sustained REM for reducing disability in early rheumatoid arthritis (ERA). Our objectives were to: (1) compare the prevalence of sustained REM and sustained LDA in ERA patients and describe any differences in core variables among the groups and; (2) determine if sustained REM/LDA are independently associated with function, measured by the health assessment questionnaire disability index (HAQ-DI).

**Methods:** ERA patients with at least 2 years of follow-up in the Canadian early Arthritis CoHort (CATCH) (N=833) were included in the analysis. REM/LDA was classified according to

the clinical disease activity index (CDAI;  $\leq 2.8$  vs. 2.9-10) and simplified disease activity index (SDAI;  $\leq 3.3$  vs. 3.4-11). REM/LDA was defined as sustained if present for  $\geq 2$  consecutive visits or  $\geq 6$  months during the first 18 months. Linear regression models were performed with HAQ-DI score at 2 years as the outcome, and each REM/LDA definition as the independent variable, adjusted for baseline confounders.

**Results:** Seventy-seven (9%) patients achieved sustained REM by each the CDAI and SDAI definitions over the first 18 months. 426 (51%) were in sustained CDAI LDA and 333 (40%) were in sustained SDAI LDA. At baseline, there were no significant differences in demographic, clinical, or laboratory variables between patients in REM vs. LDA by either index. At follow-up, mean HAQ-DI scores showed mild-to-moderate disability but scores were significantly lower for those achieving sustained REM compared to sustained LDA. Joint counts, pain, fatigue and global assessment of health were also significantly lower in the REM groups compared to the LDA groups at year 2. Multivariable regression analyses showed that sustained CDAI REM and sustained SDAI REM were both independently associated with lower HAQ-DI than sustained LDA ( $p < 0.001$ ).

**Conclusion:** HAQ-DI scores at year 2 are significantly lower among patients who achieve sustained REM vs. sustained LDA. This difference is greater than the minimal clinically important difference for HAQ of 0.22, suggesting that reaching LDA alone may not sufficiently prevent disability. Future research exploring which other clinical variables and/or treatment strategies may explain this difference is needed.

## 110

### **Risk Factors for Symptomatic Avascular Necrosis in Childhood-Onset Systemic Lupus Erythematosus**

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**Objective:** Childhood-onset systemic lupus erythematosus (cSLE) has a more severe clinical course with higher disease activity and involvement of major organs compared to adult-onset SLE. Avascular necrosis (AVN) is a significant morbidity causing pain and disability. Our objective was to examine the frequency and risk factors for symptomatic AVN in cSLE.

**Methods:** A single center matched case-control design was used. 617 patients with cSLE followed at SickKids Lupus Clinic between July 1982 and June 2013 were included in the study. The AVN cohort consisted of 37 patients identified with clinical findings of symptomatic AVN and diagnosis confirmed by one or more imaging modalities. Three controls were matched to each AVN patient by date and age at diagnosis ( $\pm 1$  year). Baseline clinical, laboratory and treatment characteristics were compared between the patients with AVN and the controls by univariate analyses and if statistically significant, were included in a multivariable logistic regression model.

**Results:** A total of 37/617 (6%) patients developed symptomatic AVN during follow-up at SickKids. The majority was female (30/37, 81%) and of Asian descent (20/37, 54%). The mean age at diagnosis was 16.1 years ( $\pm 2.1$ ), with median time to AVN of 1.52 years. Only 2/37 (5%) of patients developed AVN prior to the onset of puberty. The hip was the most commonly involved joint (26/37, 70%) with bilateral involvement

in 49% (18/37) of patients. Compared to the matched non-AVN cohort, patients with AVN had higher incidence of CNS disease ( $p=0.003$ ), nephritis ( $p<0.001$ ), acute or chronic renal failure ( $p=0.029$ ), but less frequent photosensitivity ( $p=0.006$ ). Patients with AVN also required greater cumulative prednisone from cSLE diagnosis to AVN ( $364\pm53$  vs.  $232\pm36$  mg/kg,  $p<0.001$ ), higher prednisone dose at time of AVN diagnosis ( $\pm 3$  months,  $0.30\pm0.25$  vs.  $0.19\pm0.24$  mg/kg,  $p=0.012$ ), maximal daily prednisone dose ( $1.25\pm0.36$  vs.  $0.71\pm0.53$  mg/kg,  $p<0.001$ ) and more frequent use of pulse methylprednisolone therapy (39% vs. 10%,  $p<0.001$ ). The median prednisone dose at time of AVN was 0.27 vs. 0.09 mg/kg. Multivariable regression analysis confirmed nephritis, CNS disease, maximal daily prednisone dose and use of pulse methylprednisolone as significant predictors of symptomatic AVN development. Overall disease activity from SLE diagnosis to AVN diagnosis as measured by adjusted mean SLEDAI was not significantly different ( $6310\pm976$  vs.  $4994\pm440$ ,  $p=0.165$ ). **Conclusion:** cSLE patients with severe organ involvement including nephritis and CNS disease, higher maximal daily dose of prednisone, and more frequent use of pulse methylprednisolone are more likely to develop symptomatic AVN.

## 111

### **Body Mass Index is a Predictor of Joint Effusion in Knee Osteoarthritis**

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**Objective:** Risk factors for knee effusion in osteoarthritis (OA) are poorly understood. Because obesity is a state of chronic inflammation and inflammation is involved in effusion, we evaluated the association of obesity with progressive and incident knee effusion in a longitudinal cohort study.

**Methods:** A population-based cohort with knee pain, aged 40-79, was assessed at baseline and at 3 years ( $N=163$ ). Baseline body mass index (bBMI) and past BMI at age 25 (pBMI) were categorized as normal ( $<25$ , reference), overweight ( $25-29.9$ ) and obese ( $\geq 30$ ). Knee effusion was graded 0-3 (absent/mild/moderate/severe) on MRI and as absent/present on standardized physical examination (PE). Progression of MRI effusion ( $MRI_{eff}$ ) was defined as at least a one-grade increase at follow-up, in subjects with grade 1 or 2 at baseline. Incident  $MRI_{eff}$  was defined as grade  $\geq 1$  at follow-up in subjects with grade 0 at baseline. Because  $MRI_{eff}=1$  may reflect physiological joint fluid, grades 0 and 1 were collapsed to create a second model, where incident  $MRI_{eff}$  was defined as grade  $\geq 2$  at follow-up in subjects with grade 0 or 1 at baseline. Incident PE effusion ( $PE_{eff}$ ) was defined as present at follow-up in subjects without  $PE_{eff}$  at baseline. Exponential regression analyses were used to separately evaluate the associations of bBMI and pBMI with progression of  $MRI_{eff}$  and incidence of  $MRI_{eff}$  and  $PE_{eff}$ , adjusting for age, gender and Kellgren-Lawrence grade. Age decade-gender stratum sampling weights were used to obtain population based estimates.

**Results:** Progressive MRI<sub>eff</sub>, incident MRI<sub>eff</sub>≥1, incident MRI<sub>eff</sub>≥2, and incident PE<sub>eff</sub> were seen in 20%, 19%, 13%, and 20%, respectively. Baseline BMI≥30 was associated with a 3-fold increased risk of progressive MRI<sub>eff</sub> and incident MRI<sub>eff</sub>≥2, both with trends towards statistical significance (HR 3.31, 95% CI 0.98-11.16 and HR 3.37, 95% CI 0.98-11.53, respectively). Past BMI≥30 was a significant predictor of progressive MRI<sub>eff</sub> (HR 11.36, 95% CI 1.55-83.28) and incident MRI<sub>eff</sub>≥2 (HR 9.47, 95% CI 1.52-58.95). Baseline BMI 25-29.9 was associated with incident PE<sub>eff</sub> (HR 4.51, 95% CI 1.43-14.23), although this did not reach statistical significance for bBMI≥30 (HR 3.08, 95% CI 0.86-11.07). Past BMI was not associated with incident PE<sub>eff</sub>. Neither bBMI nor pBMI was associated with incident MRI<sub>eff</sub>≥1.

**Conclusion:** Obesity, including obesity in early adulthood, was a risk factor for incident and progressive knee effusion in this population-based symptomatic cohort. These findings add a new role for obesity, as obesity can aggravate knee OA by increasing the risk of knee effusion.

## 112

### **Using an ACPAC Trained Physiotherapist and a Standardized EMR Triage Assessment Tool to Efficiently and Accurately Detect Inflammatory Arthritis in a Community Rheumatology Office Setting**

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**Objective:** Objective: An immediate access rheumatology clinic was established at the Vienna General Hospital. An experienced rheumatologist conducted a 5 minute assessment on patients with potentially inflammatory disease to determine those that needed further rheumatology consultation and investigation. This resulted in good diagnostic accuracy by the assessing rheumatologist, shortened wait times for a rheumatology consultation, and earlier diagnosis and initiation of treatment. Due to the shortage of rheumatologists in Ontario, we proposed that the initial screen could be done by an allied health professional. An experienced ACPAC (Advanced Clinician Practitioner in Arthritis Care) trained physiotherapist conducted a 15 minute assessment on patients with suspected inflammatory arthritis to determine the priority of the rheumatology consultation. We evaluated the accuracy of the ACPAC therapist's ability to correctly identify patients with inflammatory arthritis.

**Methods:** Between January 2012 and March 2013, patients were referred to a solo community rheumatology practice in Brampton, Ontario, from local primary care physicians. The rheumatologist triaged the paper referrals, and those with suspected inflammatory arthritis were selected to be initially seen by the ACPAC physiotherapist. The physiotherapist's appointment consisted of a 15-minute assessment with findings documented on a standardized EMR form. The physiotherapist as per advanced directives ordered investigations. Patients in whom the physiotherapist suspected inflammatory arthritis were booked as priority to see the rheumatologist within 4 weeks. The remaining patients were booked as non-priority.

**Results:** At the time of this submission, 96 patients had been assessed by both the ACPAC physiotherapist and the rheumatologist. The physiotherapist designated 55 patients (57%) as priority and the remaining 41 patients as non-priority. In the patients booked as priority, the rheumatologist diagnosed inflammatory arthritis in 51 of the 55 (93%) patients. The remaining 4 patients had non-inflammatory arthritis. No patients

booked as non-priority were found to have inflammatory arthritis

**Conclusion:** Our novel approach using an experienced ACPAC trained physiotherapist to assess patients with inflammatory arthritis was efficient and correctly identified patients that needed prompt rheumatology consultation. This approach may serve as a model for other settings in which there is a need for health human resources in musculoskeletal care.

## 113

### **Mycobacterium Chelonae Septic Tenosynovitis**

Bindu Nair (University of Saskatchewan, Saskatoon); Regina Taylor-Gjevre (University of Saskatchewan, Saskatoon)

**Case Report:** Infections are a major cause of morbidity in patients with rheumatic disease, yet soft tissue infections may be difficult to recognize and diagnosis. We report the case of a 49 year old female found to have a mycobacterium chelonae septic extensor digital tenosynovitis. The patient presented with an acute swollen hand with the background history of seronegative rheumatoid arthritis for thirty-one years. She was on immunosuppressive treatment for her arthritis. Despite a series of imaging investigations including ultrasound, magnetic resonance imaging and nuclear imaging, the etiology of her presentation remained a diagnostic dilemma until she developed more focal swelling of a digital extensor tendon. Aspiration of fluid around the extensor tendon allowed for the identification of mycobacterium chelonae infection and antibiotic therapy to be appropriately tailored. This case illustrates the need to consider the possibility of atypical soft tissue infection in our rheumatoid arthritis population and also emphasizes that bacteriology study remains the gold standard for the diagnosis of infection, cautioning against a reliance on imaging investigations to exclude a septic process.

## 114

### **Segmental Arterial Mediolytic: A Rare Vasculitis Mimic**

Godfrey Lam (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

**Case Report:** BACKGROUND: Segmental Arterial Mediolytic (SAM) is an idiopathic non-inflammatory, non-atherosclerotic, and non-hereditary degenerative vasculopathy. It affects medium and large vessels, with predilection for branches of the celiac, superior mesenteric artery (SMA), and renal arteries. Clinical presentation usually involves rapidly progressive abdominal pain and hypotension secondary to aneurysmal rupture or dissection, with an acute phase mortality of up to 50%. Diagnosis involves imaging findings suggestive of SAM and excluding inflammatory, infectious or hereditary conditions with similar presentations, such as vasculitis, fibromuscular dysplasia or connective tissue related cystic medial necrosis. OBJECTIVE: (1) To describe a patient referred to rheumatology for management of abdominal vasculitis; (2) perform a literature review of SAM and its management. METHODS: We present a unique case of intra-abdominal SAM in a 68yo female who presented with an episode of syncope after a 3-week history of abdominal pain. She was admitted to the surgical service, and imaging was completed. CTA confirmed intra-abdominal hemorrhage secondary to a rupture of middle colic artery, a branch off the SMA. Aneurysms were also noted in the



branches of the celiac artery and inferior mesenteric artery. **RESULTS:** The middle colic artery was successfully coiled endovascularly to control bleeding. The patient was followed with serial CTAs, which showed expansion and eventual resolution of her multiple abdominal aneurysms without further surgical or medical treatment. No cranial aneurysms were identified. She was referred to Rheumatology for assessment of possible vasculitis. Further investigations revealed an ESR of 13, CRP of 1.4, negative ANCA, and a normal urinalysis and CBC. The remainder of the serologic and immunologic workup was within normal limits. Although no tissue was biopsied, she was diagnosed with SAM. Her condition was monitored, with serial imaging, and no medical treatment; specifically no corticosteroids were used. Two years after the initial diagnosis, her aneurysms have resolved, with no recurrence. **CONCLUSIONS:** While traditionally surgical intervention is warranted, recent evidence suggests endovascular management of life threatening complications of SAM appears to be safe and effective. This case underlies the natural history of SAM involving multiple branches of the splanchnic vasculature, and resolution without medical treatment. The distinction of SAM from systemic inflammatory vasculitides is important, since corticosteroids and immunosuppressive agents, which are necessary in the treatment of the inflammatory vasculitides, have no proven benefit in SAM.

## 115

### **Rheumatologists' Views and Perceived Barriers to using Patient Decision Aids in Clinical Practice**

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**Objective:** Patient decision aids (PtDAs) have been shown to improve patient's decision quality (1); however, little is known about rheumatologists' views about these tools. This study aims to explore rheumatologists' perception of PtDAs and their intention to use PtDAs in clinical practice, and to identify barriers to implementing PtDAs.

**Methods:** This study used a mixed methods approach. We conducted a cross-sectional online survey with all members of the Canadian Rheumatology Association (N=459). The survey asked about rheumatologists' intention of using PtDAs and the perceived barriers to implementing PtDAs in clinical practice. 10 survey respondents were invited to participate in a 30-minute telephone interview to further explore their views on PtDAs and shared decision making. Interview participants were purposefully sampled to achieve a balance in gender, years in clinical practice (< 2 years, 2-10 years, >10 years) and types of practice (solo/rheumatologist group practice, multidisciplinary practice).

**Results:** In August-September 2013, 153 participants responded to the survey (response rate=33.3%). Of those, 113 completed the questionnaire. 63 respondents (55.8%) were male, 54 (47.8%) were age 50 or older, and 55 (48.7%) practiced in a multidisciplinary setting. When asked their intention to use PtDAs, participants on average rated 5.7 (SD=2.8; 0=not likely, 10=very likely). 82% (n=93) felt that most rheumatologists were confident in guiding patients in making a treatment decision, and 57% (n=64) believed

most rheumatologists were unfamiliar with PtDAs. 67% (n=76) thought that the use of PtDAs would require reorganization of their practice/workflow. The top barriers to implementing PtDA were: 1) time constraints in explaining to patients how to use a PtDA, 2) unfamiliarity with the content in PtDAs, and 3) unfamiliarity whether a PtDA was available for a specific treatment decision. Preliminary analysis from the in-depth interviews further revealed rheumatologists' beliefs about PtDAs, including: 1) that these tools offered patient education rather than decision support, 2) the perceived limitation of treatment information in PtDAs, as it was based mainly on randomized controlled trials, 3) that PtDAs could impair rheumatologist-patient communication as patients might review the treatment information alone.

**Conclusion:** There is a sense of ambivalence among rheumatologists about using PtDAs. Our in-depth interviews further revealed potential misconceptions regarding the evidence, function and application of PtDAs in clinical practice. Further research to demonstrate the effectiveness of PtDAs for improving rheumatology practice is warranted. (1) Stacey D et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2011;(10).

## 116

### **Association of Ethnicity and Self-Reported Hip Pain among Caucasian and Chinese in Vancouver: A Population-Based Study**

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**Objective:** A previous uncontrolled study found a very low prevalence of hip OA among the Chinese. This study aims to estimate the prevalence of self-reported hip pain using telephone screening questions and explore the association between Chinese ethnicity and hip pain using the Caucasian population as a control.

**Methods:** This study was conducted within IMPAKT-HiP (Investigations of Mobility, Physical Activity, and Knowledge Translation in Hip Pain), a large multi-faceted study on the role of physical activity in hip disease. Participants were recruited from a cross-sectional telephone household survey in Metro Vancouver by a pooling company using a standardized questionnaire. Eligible participants were of Caucasian or Chinese descent and between 20 and 49 years old. They were considered as having hip pain if they reported pain, stiffness or discomfort in the groin or front of upper thigh in the past 12 months, plus one of the follow-up questions: 1) symptoms lasted >6 consecutive weeks, or 2) symptoms appeared on at least 3 occasions over the past 12 months. Logistic regression was used to assess the relationship between ethnicity and hip pain, after adjusting for age and sex.

**Results:** A total of 369,550 random digit calls were made, of which 3,092 households completed the survey (Caucasians: 2,350, 76.0%; Chinese: 741, 24.0%; other: 1). 64.5%

(n=1,516) of Caucasians and 68.4% (n=507) of Chinese were female. 58.3% (n=1370) of Caucasians and 53.0% (n=393) of Chinese were age 40-49. 375 (12.1%) reported having hip pain based on the screening questions. Of the Caucasian participants, 295 (12.6%) reported having hip pain. Among the Chinese participants, 80 (10.8%) reported the same. Logistic regression revealed that, compared to Caucasians, estimated odds of reporting 'pain, stiffness or discomfort in the groin or front of upper thigh in the past 12 months' was significantly lower in the Chinese population [OR = 0.78, 95% CI = 0.61-0.98], after adjusting for age and sex. When asked the follow-up questions, Chinese had a lower estimated odds of reporting hip pain, but it was not statistically significant [OR = 0.84, 95% CI = 0.64-1.10].

**Conclusion:** To our knowledge, this is the first controlled study of hip pain prevalence in the Chinese population. Compared to the Caucasian population, we found lower prevalence of hip pain among Chinese when used a single screening question; but not when specific questions related to the duration or frequency of symptoms were included. Further studies are needed to examine the source of hip pain.

## 117

### **Psoriatic Nail Changes are Associated with Clinical Outcomes in Psoriatic Arthritis**

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**Objective:** Psoriatic nail changes are common in patients with psoriatic arthritis (PsA), occurring in up to 85% of patients. This study aimed to characterize relationships between specific nail changes, active psoriasis and joint involvement.

**Methods:** PsA patients fulfilling the CASPAR criteria were assessed by their rheumatologist. Joint counts, axial measurements and physician global assessment of disease activity (MDGA) were recorded. Patients completed questionnaires regarding disease activity over the past year. Fingernails of patients were assessed, and high quality photographs were taken of patients' hands and fingernails. Photos were reviewed by a dermatologist for confirmation of nail and skin findings.

**Results:** 188 participants were included (52.4% male, mean age 53.8 years [SD 12.5]). The mean duration of psoriasis was 20.4 years (SD 15.4) and mean PsA duration 12.5 years (SD 11.7). 85.7% ever had skin disease, 89.9% ever peripheral arthritis and 12.7% ever axial arthritis. The mean tender joint count (TJC) was 2.5 (SD 4.8) and mean swollen joint count (SJC) 2.0 (SD 3.7). The mean Schober's was 4.4 cm (SD 1.5), mean occiput-to-wall distance 0.7 cm (SD 2.3) and mean chest expansion 4.1 cm (SD 1.5). The mean MDGA was 2.3 (SD 2.3). 91.5% had at least one nail change (78.7% at least one matrix change, 73.9% at least one nail bed change). The most common nail matrix changes were pitting (59.0%), leukonychia (42.0%) and rough onychorrhexis (23.9%). The most common nail bed changes were splinter hemorrhages (55.9%), onycholysis (51.6%) and oil spots (27.7%). Higher swollen joint counts were seen in those with distal interphalangeal or periungual psoriasis (p=0.001), total number of splinter hemorrhages (p=0.006) and any nail bed change (p=0.03). Higher tender joint counts were seen in those with rough onychorrhexis (p< 0.001), distal/periungual psoriasis (p=0.03), red spots in the lunula (p=0.001), nail crumbling (p=0.046), any nail matrix change (p=0.03) and any nail bed change (p=0.03). Those with any nail change had a significantly higher mean Schober's measurement than those without (p=0.01). Mean

MDGA was significantly worse in those with any nail matrix change ( $p=0.03$ ) or any nail bed change ( $p=0.002$ ).

**Conclusion:** Nail changes were common in this PsA population. Distal interphalangeal or periungual psoriasis, splinter hemorrhages, rough onychorrhexis and red spots in the lunula were associated with higher joint counts in PsA. Nail matrix and nail bed changes were associated with higher disease activity on MDGA.

## 118

### **Baricitinib, an Oral Janus Kinase Inhibitor, in the Treatment of Rheumatoid Arthritis: 52 Week Safety and Efficacy in an Open-Label, Long-Term Extension Study**

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**Objective:** Baricitinib is a novel, oral inhibitor of JAK1 and JAK2 in the JAK-STAT signaling pathway being investigated as a treatment for RA. In a phase 2b study, baricitinib treatment resulted in significant improvements in the signs and symptoms of RA versus placebo over 12 weeks, and these responses were maintained or improved for an additional 12 weeks of blinded treatment 1. Here we report 52 week safety and efficacy in an open label extension.

**Methods:** Patients (Pts) were initially randomized to placebo (PBO) or 1 of 4 once-daily (QD) baricitinib doses (1, 2, 4, or 8 mg) for 12 wks. Pts assigned to 2 mg, 4 mg or 8 mg continued assigned treatment and pts assigned to placebo or 1 mg were reassigned to 4 mg QD or 2 mg BID for an additional 12 weeks of blinded treatment. In the open label portion of the study, patients in 8 mg group continued to receive 8 mg QD and all other patients received 4 mg QD. Doses could be escalated to 8 mg QD at 28 or 32 weeks when  $>6$  tender and swollen joints were present. These analyses include 52-week data for pts treated in the open-label extension (non-responder imputation used for discontinued pts).

**Results:** Of the 212 pts eligible to participate, 201 (95%) entered the open label extension, 184 pts completed 52 weeks of treatment, 15 pts discontinued, and 2 pts had not yet completed 52 weeks. Among pts who remained on 4 mg ( $n=108$ ), TEAEs occurred in 57 (53%), SAEs in 14 (13%), infections in 34 (31%) and serious infections in 4 (4%). Among pts who received 8 mg at any time ( $n=93$ ), TEAEs occurred in 59 (63%), SAEs in 8 (9%), infections in 37 (40%) and serious infections in 2 (2%). No opportunistic infections or TB cases were observed. There was one death due to myocardial infarction in the 8 mg group. Among all open-label patients, the proportions achieving ACR20, ACR50, ACR70, CDAI Remission, SDAI Remission,  $\text{DAS28CRP} \leq 3.2$ ,  $\text{DAS28CRP} < 2.6$ ,  $\text{DAS28ESR} \leq 3.2$ ,  $\text{DAS28CRP} < 2.6$  or the ACR/EULAR Boolean remission at the start (week 24) were similar or increased at week 52. This increase was mainly due to enhanced clinical responses following dose escalation in patients who initially received PBO, 1 mg or 2 mg QD.

**Conclusion:** Clinical improvements observed at week 24 were maintained or improved during the open label extension. Safety signals were consistent with previously reported results of baricitinib.

119

**Inflammatory Myositis or Diabetic Myonecrosis?: A Case Study**

Ruchi Murthy (The University of Ottawa, Ottawa); Douglas Smith (The Ottawa Hosp, Ottawa)

**Case Report:** A 42 year old woman of Caribbean decent with a history of poorly controlled Type 2 Diabetes associated with retinopathy and nephropathy, hypertension and iron deficiency anemia presented with a one week history of bilateral quadriceps pain. The pain was deep, cramping in nature and associated with weakness. The pain progressively worsened and she was no longer able to ambulate. She denied any constitutional symptoms, recent travel or infectious prodrome. She had poor compliance with management of her medical conditions. On physical exam, her vitals were: BP 178/86, HR 108, RR 18 and she was afebrile. She had pitting edema and tenderness in both thighs. Hip flexor and extensor power was 3/5 bilaterally. She had normal upper extremity power. Reflexes were equal bilaterally. She had some decreased to pin-prick sensation on her feet. Cardiovascular, abdominal and head and neck examination were contributory. She was blind in her right eye due to retinopathy. Investigations on admission to hospital were: haemoglobin 65, ESR 130, CK 300, urea 13.7, and creatinine 157. Her HbA1c was 15.8% and glucose was 24.8. She also had nephrotic range proteinuria presumed to be related to her diabetic nephropathy. Her ANA was positive (1:1280, homogeneous), and anti-dsDNA was elevated at 161 IU/ml (normal<100). Anti ENA was negative and levels of C3 and C4 were normal. Her initial femur X-rays revealed an Erlenymer Flask deformity. MRI showed significant muscle edema in both anterior and posterior compartments of the thighs. EMG showed features that were suggestive of a myositis and simultaneously showed length dependant axonal neuropathy bilaterally in keeping with long standing diabetes. Initial muscle biopsy showed minor non-specific changes. Repeat biopsy showed necrotizing features with focal attenuation. The patient required two months of rehabilitation after discharge from hospital. Repeat ANA, anti-dsDNA, CRP and ESR eight months after her initial presentation were all normal. After two weeks of management with fluids and opioids, her symptoms of pain persisted limiting her range of motion to bed rest. She began to experience symptoms of allodynia and intolerance to opioids. A trial of high dose steroids was initiated and clinically she transiently improved. Her pain symptoms disappeared and she was able to move her legs; however, over the course of one week, the symptoms of pain recurred and she was again unable to ambulate. Though the case is very much in keeping with diabetic myonecrosis, the transient response to steroids combined with transient elevation in Lupus antibodies presented a challenge.

120

**Magnetic Resonance Imaging Substudy in a Phase 2b Dose-Ranging Study of Baricitinib, an Oral Janus Kinase 1/Janus Kinase 2 Inhibitor, in Combination with Traditional Disease-Modifying Antirheumatic Drugs in Patients with Rheumatoid Arthritis**

Youb Chalabi (Toronto); Charles Peterfy (Spire Sciences, San Francisco); Mark Genovese (Stanford University, Palo Alto ); Paul Emery (University of Leeds and Leeds Teaching Hospitals, Leeds); Peter Taylor (Oxford); Douglas Schlichting (Indianapolis); Scott Beattie (Indianapolis); William Macias (Indianapolis); Edward Keystone (Mount Sinai Hospital,

Toronto)

**Objective:** Primary results of this phase 2b study have shown that baricitinib reduces signs and symptoms of RA with no unexpected safety signals<sup>1</sup>. MRI was used to examine dose dependency of baricitinib on joint changes in a subgroup of patients (pts) with erosive RA and inadequate response to methotrexate (MTX).

**Methods:** In this randomized, double-blind, placebo-controlled trial, 301 pts with active, established RA on stable MTX were randomized 2:1:1:1:1 to placebo or 1 of 4 once-daily LY doses (1, 2, 4 or 8 mg) for up to 24 weeks. 208 pts (placebo [n=68], 1 mg [n=34], 2 mg [n=40], 4 mg [n=33], 8 mg [n=33]) with definitive radiographic erosion had MRI of the dominant hand/wrist at baseline, week 12 and week 24. Pts assigned to placebo or 1 mg were reassigned to an exploratory 4 mg or 2 mg twice daily group at week 12 and excluded from the 24-week analysis. Fat-suppressed, T1-weighted 3D gradient-echo and STIR images were obtained with and without gadolinium contrast using 1.5T MRI and a hand frame to ensure reproducible positioning. Images were scored using RAMRIS and a validated 9-point cartilage loss scale. Total inflammation (osteitis + 3x synovitis) and total joint damage (erosion + 2.5x cartilage loss) scores were calculated. ANCOVA adjusting for baseline score and dose group was used for analysis.

**Results:** Significant decrease in osteitis over 12 weeks in 15% of pts on placebo vs 29% and 29% on baricitinib 4 and 8 mg, respectively. Synovitis decreased in 18% of pts on placebo vs 33% and 29% of pts on 4 or 8 mg baricitinib. Bone erosion did not progress in 80% of placebo vs 96% and 88% of pts on 4 or 8 mg baricitinib. Significant decreases in adjusted mean synovitis, osteitis and total inflammation scores were observed in the 4 mg and 8 mg groups compared to placebo at week 12 that persisted to week 24. A trend in improvement in total joint damage was also observed for the 4 mg group. These MRI improvements correlated with significant improvements in tender and swollen joints in the 4 mg and 8 mg groups and with numeric decreases in median CRP.

**Conclusion:** MRI findings in this subgroup of pts with active erosive RA suggest dose-dependent suppression of synovitis, osteitis and total inflammation by baricitinib for the 4-mg and 8-mg groups at 12 and 24 weeks, corroborating previously demonstrated clinical efficacy of baricitinib.

## 121

### **Long-Term Safety and Efficacy of Certolizumab Pegol in Combination with Methotrexate in the Treatment of Rheumatoid Arthritis: 5-Year Results from a 24-Week Randomized Controlled Trial and Open-Label Extension Study**

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**Objective:** In the RAPID2 randomized controlled trial, certolizumab pegol (CZP) + MTX every 2 weeks (Q2W) improved signs and symptoms of rheumatoid arthritis (RA) over 24 weeks (wks). Previous results demonstrated long-term safety and efficacy of CZP+MTX over 3 yrs in RAPID2 open-label extension (OLE). We present the final report on long-term safety and efficacy of CZP+MTX over 5 yrs.

**Methods:** Eligible patients from RAPID2 were treated in OLE with CZP 400mg Q2W, reduced to 200mg Q2W after  $\geq 6$  months, + MTX. Combined safety data from RCT and OLE are reported for all patients treated with  $\geq 1$  dose of CZP (N=612). AEs and SAEs were assessed at each visit following first dose of CZP. DAS28(ESR), HAQ-DI and ACR20/50/70 are presented to Wk232 for CZP Completers (patients who completed RCT and enrolled onto OLE [N=342]) and CZP ITT population (all patients randomized to CZP in RCT [N=492]). Change from baseline in modified Total Sharp Score (mTSS) and % of patients with radiographic non-progression (mTSS change from RCT baseline  $\leq 0.5$ ) are reported to Wk128 for CZP Completers. Dose reduction efficacy data is presented for all Wk24 CZP. Completers who received CZP 400mg Q2W +MTX for  $\geq 6$  months in OLE, following which the CZP dose was reduced to 200mg Q2W over 132 wks of CZP exposure.

**Results:** Of 492 pts treated with CZP+MTX, 355 (72%) completed the RCT and 342 entered OLE, of which 215 remained after 232 wks from RCT baseline. Safety profile was consistent with previous reports. Most frequent AEs are reported. 19 patients (3.1%) died (IR=0.82) (including 5 malignancies, 4 cardiac disorders, 4 nervous system disorders, 4 injuries). No new safety signals were identified. Clinical improvements from RCT were maintained to Wk232 in CZP Completers and ITT Population, respectively: mean DAS28(ESR), 3.7 and 3.9; mean HAQ-DI, 0.96 and 1.06; ACR20/50/70, 68.4%/47.1%/25.1% and 65.9%/45.4%/24.2%. Radiographic progression in CZP-treated patients was minimal (mean mTSS change from RCT baseline to Wk24: 0.62, from RCT baseline to Wk128: 0.79; % of patients with radiographic non-progression at Wk24: 84.6%, Wk128: 73.2%). Clinical improvements were maintained in the dose reduction population (400mg to 200mg Q2W +MTX; N=288) from the first CZP 200mg treatment (DAS28[ESR]=3.5) through 132 wks of CZP 200mg Q2W (DAS28[ESR]=3.6).

**Conclusion:** In patients with active RA despite MTX, CZP+MTX maintained reduction in signs and symptoms of RA with a favorable long-term risk benefit ratio.

## 122

### **Etanercept-Methotrexate Combination Therapy Compared with Etanercept Monotherapy in Rheumatoid Arthritis Patients with Moderate or Severe Disease in the CAMEO Trial**

Edward Keystone (Mount Sinai Hospital, Toronto); Boulos Haraoui (Université de Montréal, Montréal); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Melanie Poulin-Costello (Amgen Canada Inc., Mississauga); Eric Trottier (Amgen Canada Inc., Mississauga); Andrew Vieira (Mississauga); Janet Pope (University of Western Ontario, London)

**Objective:** CAMEO is an open-label trial that sought to determine if withdrawing methotrexate (MTX) is as effective as continuing etanercept (ETN) + MTX after 6 months of ETN + MTX in patients with moderate disease activity (MDA) and severe disease activity (SDA). This pre-specified post-hoc analysis assessed month 12 response in patients with baseline (BL) MDA ( $3.2 < \text{DAS28} \leq 5.1$ ) and SDA ( $\text{DAS28} > 5.1$ ).

**Methods:** Patients with rheumatoid arthritis (RA) who were TNF inhibitor naïve and had active disease (defined as  $\geq 3$  swollen joints and disease activity severity [ $\text{DAS28} \geq 3.2$ ]) despite MTX ( $\geq 15$  mg/wk, or 10 mg/wk if intolerant) for  $> 12$  weeks were enrolled. Patients received combination therapy of ETN (50 mg/wk sc) + MTX for 6 months.

Randomization occurred at month 6. Patients were randomized to either continue combination ETN + MTX, or switch to ETN alone, for another 18 months. Here we present DAS28 from month 6 randomization to month 12 by BL disease activity of either MDA or SDA.

**Results:** 258 patients were enrolled (female: 76%; mean disease duration:  $8.9 \pm 8.4$  yrs; mean number of prior DMARDS:  $2.7 \pm 1.0$ ; prior oral prednisone: 52%). 205 were randomized at month 6 (BL SDA: 121 [59.0%]; BL MDA: 84 [41.0%]). At month 6, 70% more patients with MDA at baseline, compared to patients with SDA at baseline, had reached low disease activity (LDA)/remission (REM) (DAS28 < 3.2; 61.3% (49/80) vs. 35.8% (43/120); adjusted OR [95%CI] = 2.5[1.38-4.41]). MDA patients maintained stable DAS28 to month 12 whether they continued ETN + MTX at month 6 (mean DAS28 [95% CI] = 3.10[2.66-3.53]) or switched to ETN alone (mean DAS28 [95% CI] = 3.06[2.59-3.52]). In contrast, in patients with SDA, only those who were on the combination of ETN + MTX continued to improve to month 12 (mean DAS28 [95% CI] = 3.39[3.02-3.76]) compared to those who switched to ETN alone (mean DAS28 [95% CI] = 4.31[3.85-4.76]).

**Conclusion:** This analysis suggests that in a relatively high proportion of patients who have MDA when initiating treatment, it may be possible to withdraw MTX after 6 months of combination ETN + MTX, since more of these patients maintain LDA/REM. However, patients with initial SDA may need to continue combination therapy. This analysis provides important information on the disease state required to make a therapeutic adjustment in order to achieve and maintain LDA/REM.

## 123

### **Clinical and Radiographic Outcomes in Patients with Rheumatoid Arthritis Treated with Etanercept or Etanercept + Methotrexate: Two-Year Results from the Canadian Methotrexate and Etanercept Outcome Study (CAMEO)**

Boulos Haraoui (Université de Montréal, Montréal); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Edward Keystone (Mount Sinai Hospital, Toronto); Melanie Poulin-Costello (Amgen Canada Inc., Mississauga); Eric Trottier (Amgen Canada Inc., Mississauga); Andrew Vieira (Mississauga); Janet Pope (University of Western Ontario, London)

**Objective:** The CAMEO trial assessed whether withdrawing methotrexate (MTX) is as effective as continuing combination etanercept (ETN) and MTX following 6 months of ETN+MTX in rheumatoid arthritis (RA) patients with moderate or high disease activity (MHDA). The present analysis assessed clinical and radiographic data for up to 24 months from the CAMEO study.

**Methods:** TNF-inhibitor naïve patients with active RA (defined as  $\geq 3$  swollen joints and a Disease Activity Score [DAS]28  $\geq 3.2$ ) despite treatment with MTX ( $\geq 15$ mg/week, or 10mg/week if intolerant) for > 12 weeks were treated with ETN (50mg/week SC) and MTX for 6 months. Patients were then randomized (1:1) to switch to ETN monotherapy or to continue ETN+MTX for an additional 18 months. DAS28 was assessed at baseline and 6, 12, 18, and 24 months/early termination (24m/ET), and X-rays of the hands and feet were taken at baseline and 12 and 24m/ET.

**Results:** A total of 258 patients were enrolled, and 205 randomized to stop MTX and continue ETN monotherapy (n=98) or to maintain ETN+MTX treatment (n=107). Seventy-



six percent were females with a mean age of  $54.7 \pm 12.5$  years, disease duration of  $8.9 \pm 8.4$  years, and baseline DAS28 score of  $5.4 \pm 1.1$ . The mean baseline modified total Sharp score (mTSS) was  $38.1 \pm 52.7$  (n=198). Overall, patients who reached low disease activity (LDA) at month 6 maintained LDA at 24m/ET whether they were treated with ETN or ETN+MTX; those with MHDA treated with ETN monotherapy had worsening disease activity, while those treated with ETN+MTX had a sustained response. The mean change in mTSS from baseline to 24m/ET was similar between the ETN and ETN+MTX groups ( $0.4 \pm 1.9$  vs.  $0.0 \pm 1.4$ ). The proportion of patients with LDA showing no radiographic progression was similar between the ETN and ETN+MTX groups at both 12 (88% vs. 85%) and 24m/ET (86% vs. 87%). However, a higher number of patients with MHDA receiving ETN+MTX had no radiographic progression compared with ETN monotherapy at 12 (81% vs. 68%) and 24m/ET (76% vs. 64%).

**Conclusion:** These data clarify the role of long-term combination of ETN+MTX in maintaining optimal disease control. For patients who achieve LDA by 6 months, ETN monotherapy may provide an effective alternative to combination therapy for up to 24 months based upon clinical and radiographic outcomes. However, patients with MHDA may need to continue combination therapy, as clinical and radiologic response may be reduced when MTX is withdrawn.

## 124

### **Long-Term Safety of Tocilizumab in Patients with Rheumatoid Arthritis following a Mean Treatment Duration of 3.9 Years**

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**Objective:** To evaluate the long-term safety of tocilizumab (TCZ) in adults with RA.

**Methods:** Analyses were performed in all patients who received  $\geq 1$  TCZ dose in 1 of 5 placebo-controlled studies (OPTION, TOWARD, RADIATE, AMBITION, LITHE), a clinical pharmacology study or long-term extension studies. In addition, 6-month data were included from the phase 4 TCZ monotherapy study (ADACTA). Data were pooled and analysed from initial TCZ exposure to 2 May 2012 (cut-off).

**Results:** 4171 pts were included. Mean (median [range]) duration was 3.9 (5.1 [0.0-6.8]) y; total observation time was 16204.8 pt-y (PY). Rates of serious adverse events (SAEs), serious infections, myocardial infarction (MI) SAEs, stroke SAEs, hepatic SAEs and gastrointestinal (GI) perforations were stable over time. The overall rate of AEs leading to withdrawal was 4.9/100PY (95% CI, 4.6-5.3). Infections, laboratory abnormalities and neoplasms were the most common AEs leading to withdrawal (0.97/100PY, 0.87/100PY and 0.77/100PY). 8 pts withdrew due to anaphylaxis; these were previously reported.<sup>1</sup> Overall rates/100PY (95% CI) were 14.4 (13.9-15.0) for SAEs and 0.58 (0.47-0.71) for deaths. The most common SAEs were infections, which occurred at a rate of 4.4/100PY (95% CI, 4.1-4.8); the most common serious infection was pneumonia. Overall rates/100PY (95% CI) of MI SAEs, stroke SAEs and hepatic SAEs were 0.27 (0.20-0.36), 0.32 (0.24-

0.42) and 0.04 (0.02-0.09), respectively. The GI perforation rate was 0.20/100PY (95% CI, 0.14-0.29). The rate of GI perforations in pts who received or did not receive concomitant corticosteroids was 0.2/100PY (95% CI, 0.16-0.36) and 0.1/100PY (95% CI, 0.03-0.24), respectively. There were 204 confirmed malignancies, including 68 non-melanoma skin cancer (NMSC) cases, corresponding to an overall rate/100PY (95% CI) of 1.26 (1.09-1.44) and, excluding NMSC of 0.84 (0.70-0.99).

**Conclusion:** The safety profile of TCZ in the current analysis is consistent with that in previous analyses; it remained stable over a mean duration of 3.9 years with no new safety signals emerging.

## 125

### **Prevalence of Inflammatory Back Pain in PsA: The PREPARE Study**

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**Objective:** Up to 30% of patients with psoriasis (Ps) may develop psoriatic arthritis (PsA); spondylitis prevalence in PsA is approximately 25-30%. PREPARE, a multicenter, non-interventional study assessed PsA prevalence in patients presenting to dermatologists with Ps (285/949 had PsA, 117/285 = newly diagnosed; the Toronto Psoriatic Arthritis Screen [ToPAS] and Psoriasis and Arthritis Screening Questionnaire [PASQi] detected probable PsA in 42.9% and 45.1% of patients). Since PREPARE involved no formal assessment of inflammatory back pain (IBP), the focus of these post-hoc analyses was to determine if positive IBP correlated with PsA diagnosis as a useful screening tool.

**Methods:** Our analyses included patients with Ps who received either PASQi or ToPAS screening questionnaires during their dermatologist's visit. Patients were subsequently evaluated by a rheumatologist to establish/exclude a clinical diagnosis of PsA. Prevalence of IBP was identified by the PASQi and ToPAS questionnaires: PASQi back pain was defined by patients who "ever had back troubles" with stiffness lasting >30 minutes and IBP total score>4; ToPAS had 1 question addressing back pain occurrence lasting >3 months that was not injury related (although this was not included in the scoring of ToPAS). Cochran-Mantel-Haenszel (CMH) tests were used to analyze differences in proportions of positive IBP between PsA vs non-PsA groups. Kappa coefficients determined the agreement between PsA diagnosis and positive IBP.

**Results:** Of the patients, 85/341 (24.9%) had positive PASQi defined IBP while 146/337 (43.3%) had positive ToPAS defined IBP. Patients with PsA detected by a rheumatologist/PASQi/ToPAS/a combination had higher IBP prevalence than Ps patients with no indication of PsA (32.6%-55.2% vs 17.6%-38.9%; Table). Of the patients with detected PsA or IBP, there was a higher extent of activity impairment in patients with IBP than those without IBP (PsA: 22.4% vs 15.75%, P=0.003; PASQi: 19.1% vs 16.2% P=0.3651 and ToPAS 23.5% vs 13.4% P=0.0003). Work productivity impairment was significantly higher in patients with PsA vs non-PsA (16.5% vs 10.9%, P=0.012) and positive vs negative IBP as detected by the ToPAS screen (19.1% vs 9.3%, P=0.003). All kappa coefficients were < 0.2 indicating slight agreement between IBP and PsA as defined by PASQi, ToPAS or a rheumatologist.

**Conclusion:** In this study, Ps patients with PsA had increased IBP incidence compared to

those without PsA. Kappa coefficients indicate that IBP is not a good marker for PsA diagnosis in patients with Ps. However, the high incidence of IBP detected in Ps patients warrants further investigation.

## 126

### **Validation of the Ankylosing Spondylitis Disease Activity Score (ASDAS) and Effectiveness of Infliximab in the Treatment of Ankylosing Spondylitis over 4 Years: The Canadian Experience**

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**Objective:** To assess in a clinical practice the 4-year outcomes in patients with AS treated with infliximab and the performance of ASDAS, a new disease activity measure in AS.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab as first biologics or after having been treated with a biologic for less than 6 mos. AS patients treated with infliximab between 2005 and 2012 were included. Descriptive statistics were produced for clinical outcome measures and patient reported outcomes at baseline and follow-up assessments over four years. Within-group changes were assessed for statistical significance with the paired-samples Student's t-test. The correlation of ASDAS with BASDAI and BASFI was assessed with the Pearson correlation coefficient. The correlation of these measures with MDGA was assessed with the Spearman's rho.

**Results:** A total of 230 AS patients who had at least one follow-up assessment were included in this analysis, with a mean (SD) age of 45.7 (11.5) years and mean (SD) disease duration since diagnosis of 10.0 (10.1) years. At the time of enrollment, mean (SD) patient parameters were: C-reactive protein (CRP) = 16.9 (20.2) mg/dL, erythrocyte sedimentation rate (ESR) = 25.8 (20.2) mm/hr, morning stiffness = 74.6 (40.2), health assessment questionnaire (HAQ-DI) = 1.20 (0.61), physician global assessment of disease activity (MDGA) = 6.6 (1.9), BASDAI = 6.4 (2.1), BASFI = 6.1 (2.5), and ASDAS = 3.8 (1.0). By 6 mos of treatment significant improvements ( $P < 0.01$ ) were observed in all clinical and patient outcome parameters studied, which were sustained or further enhanced over 48 months of treatment. Similar significant changes were observed in ASDAS, BASDAI, and BASFI over time providing evidence of construct validity and sensitivity to change. A strong positive linear correlation between ASDAS and BASDAI ( $r=0.85$ ;  $P < 0.001$ ) and BASFI ( $r=0.76$ ;  $P < 0.001$ ) was observed. The correlation of MDGA was strong with ASDAS ( $\rho=0.73$ ;  $P < 0.001$ ) and BASDAI ( $\rho=0.70$ ;  $P < 0.001$ ) and moderate with BASFI ( $\rho=0.64$ ;  $P < 0.001$ ). The proportion of patients with very high disease activity (ASDAS  $> 3.5$ ) decreased from 62.4% at baseline to 6.9% at 48 months.

**Conclusion:** Treatment with infliximab over four years is effective in reducing symptom severity and improving outcomes in patients with AS. Furthermore, the data from this

registry confirm the validity and sensitivity to change of the ASDAS score in a real-world AS cohort.

127

### **In RA, 14-3-3 $\eta$ Positive Serum is Associated with More Severe Disease and its Levels Inform Response to Anti-TNF Therapy**

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**Objective:** Serum 14-3-3 $\eta$  is 1) an RA diagnostic marker 2) an independent predictor of RA development in arthralgia patients, and 3) in early RA, informs radiographic progression risk. Extracellular 14-3-3 $\eta$  behaves as a proinflammatory molecule that induces itself and is induced by TNF $\alpha$ . This study investigated whether a) 14-3-3 $\eta$  positive patients have more severe disease and b) if 14-3-3 $\eta$  informs TNF therapy response.

**Methods:** Serum 14-3-3 $\eta$  levels were measured at baseline and 15 weeks in 74 RA patients who were refractory to DMARDs and candidates for TNF therapy. 14-3-3 $\eta$  positivity for diagnosis was based on  $> 0.19\text{ng/ml}$ , and the change in 14-3-3 $\eta$  was calculated by subtracting the 15 week measurement from baseline. Pearson correlations were performed to determine the relationship between 14-3-3 $\eta$  and clinical/serological measures. EULAR criteria were used to define a good EULAR response, which 15 patients (20%) achieved and 59 did not. Mann Whitney U-tests were used to compare differences between Good responders and not. ROC curve analysis was used to identify a 14-3-3 $\eta$  cut-off that could discriminate between responder groups. Contingency analysis was used to determine the association between 14-3-3 $\eta$  and therapy response.

**Results:** Of the 74 patients, 66 (89%) were 14-3-3 $\eta$  positive. Baseline 14-3-3 $\eta$  titres did not correlate with baseline clinical (DAS, HAQ) or serological measures (CRP, ESR). 14-3-3 $\eta$  positive patients had significantly higher median HAQ (2.1 vs 1.1,  $p=0.019$ ), CRP (19.4 vs 7.0mg/l,  $p=0.030$ ), and ESR (43 vs 24mm/hr,  $p=0.014$ ) than 14-3-3 $\eta$  negatives. A decrease in 14-3-3 $\eta$  post-treatment titres, reflected a greater change in HAQ (0.9 vs 0.5,  $p=0.045$ ) with the change in ESR approaching significance (12 vs 6mm/hr,  $p=0.078$ ). Of the available clinical and serological measures, only baseline ESR (20 vs 45mm/hr,  $p< 0.001$ ) and 14-3-3 $\eta$  (0.72 vs 2.52ng/ml,  $p=0.029$ ) were expressed at significantly lower levels in good EULAR responders. Subset analysis of the good EULAR responders revealed that a high correlation existed between the change in 14-3-3 $\eta$  and the change in ESR ( $r=0.89$ ,  $p< 0.00001$ ), CRP ( $r=0.68$ ,  $p=0.006$ ) and DAS ( $r=0.56$ ,  $p=0.009$ ). ROC AUC analysis ( $p=0.03$ ) confirmed that lower 14-3-3 $\eta$  levels correspond with Good EULAR response yielding a 14-3-3 $\eta$  cut-off of  $< 0.38\text{ng/ml}$ . At this cut-off, contingency analysis returned a significantly higher likelihood of achieving a Good response to TNF therapy (LR=9.26,  $p=0.002$ ) with 14-3-3 $\eta$  levels  $\leq 0.38\text{ng/ml}$ .

**Conclusion:** 14-3-3 $\eta$  seropositivity ( $\geq 0.19\text{ng/ml}$ ) is associated with more severe disease. Lower baseline 14-3-3 $\eta$  levels and a post-treatment decrease correspond with a higher likelihood of achieving a Good EULAR response to anti-TNF therapy.

128

### **Serum 14-3-3 $\eta$ is an RA Specific Diagnostic Marker that Predicts RA Development in Arthralgia Patients**

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**Objective:** 14-3-3 proteins bind to and regulate the biologic activity of various intracellular proteins. The 14-3-3 $\eta$  isoform is expressed at higher levels in patients with arthritis compared to healthy individuals. This study examined 413 subjects to determine (a) the specificity of 14-3-3 $\eta$  serum expression for RA and (b) if 14-3-3 $\eta$  may predict RA development in arthralgia patients.

**Methods:** To examine the specificity for RA, serum 14-3-3 $\eta$  was measured in 135 RA patients (who were on standard DMARDs but biologically naïve) and 130 age- and gender-matched controls (55 presumed healthy individuals, 65 with autoimmune diseases, 5 with osteoporosis, and 5 with gout). A ROC curve was generated yielding likelihood ratios (LR) for various 14-3-3 $\eta$  serum concentration cut-offs. To examine 14-3-3 $\eta$  expression in arthralgia, 148 consecutive patients of whom 44 (30%) developed RA within 5 years and 104 did not, were selected from the prospective Reade cohort of ACPA and/or RF positive arthralgia patients. Age and gender did not differ between the groups. Two-tailed t-tests and Mann-Whitney u-tests were run to compare group-differences in serum concentrations. Univariate and multivariate regressions were used to identify serologic variables associated with RA development.

**Results:** Specificity of 14-3-3 $\eta$  for RA. Median 14-3-3 $\eta$  serum concentrations were significantly higher in RA versus controls, 1.12 versus 0.12 ng/ml ( $p < 0.0001$ ). The area under the ROC curve was 0.85 (95%CI 0.80 to 0.90;  $p < 0.0001$ ). A best 14-3-3 $\eta$  cut-off level of 0.19 ng/ml provides a positive likelihood ratio (LR+) of 5 and a negative likelihood ratio (LR-) of 0.27 for RA versus all controls. With 14-3-3 $\eta$  levels above 1.30 and 2.18, LR+ was 10 and 50, and LR- was 0.55 and 0.62, respectively. Prediction of RA. Median 14-3-3 $\eta$  levels were significantly higher in the arthralgia group that developed RA, 0.90 versus 0.03,  $p < 0.004$ . Univariate analysis indicated that 14-3-3 $\eta$  positive patients had a higher likelihood of developing RA (LR=5.7,  $p=0.002$ ) with titres also being significantly associated with the development LR=4.8,  $p < 0.03$ . ACPA titres (LR=5.3,  $p < 0.03$ ), but not RF as associated with RA development. Multivariate analysis revealed that 14-3-3 $\eta$  was an independent predictor of RA development ( $p < 0.04$ ) together with ACPA and other clinical variables.

**Conclusion:** 14-3-3 $\eta$  is an RA diagnostic marker whose serum expression precedes, by at least 5 years, arthralgia patient diagnosis for RA by ACR/EULAR classification criteria. Serum 14-3-3 $\eta$  independently predicts the development of RA and further improves prediction when added to ACPA.

## 129

### Impact of Adherence to Treat-to-Target of Rheumatoid Arthritis in Real World

#### Practice: Data from the International RA BIODAM Program

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Joanne Homik (University of Alberta, Edmonton); Rana Dadashova (Edmonton); Mark Tempest (Edmonton)

**Objective:** A recent Canadian study showed that treating to target (T2T) in established RA did not differ from routine care in terms of therapeutic end point achievement for patients remaining on treatment. However, this study did not ascertain adherence to T2T and assess the impact of non-adherence to T2T on clinical endpoints. We aimed to assess the impact of adherence to T2T in real world practice across 10 countries participating in the RA BIODAM program.

**Methods:** RA BIODAM is an international multicenter (35 sites, 620 patients) 2-year program aimed at the clinical validation of biomarkers reflecting structural damage endpoints in RA. Active RA patients are enrolled and systematically assessed for disease activity with a prompt to make major treatment changes (standard DMARD and/or anti-TNF) in order to achieve a DAS target of  $\leq 2.4$ . Patients with early and established RA are evaluated every 3 months for DAS, HAQ, RAID, SF36, RF, CRP, and serum/urine biosamples and every 6 months with radiography to determine whether change in RA biomarkers are consistently associated with change in damage. An internet-based data entry and management system (IDEMS) was custom designed to automate calculation of the DAS and alert sites to the requirement for treatment change. If a treatment change is not made a reason for that decision is required. IDEMS also automates calculation of RA outcomes and attainment of remission (DAS, CDAI, SDAI, ACR Boolean). We compared RA outcomes and attainment of remission stratified by adherence to T2T and according to treatment category (DMARD, anti-TNF).

**Results:** As of September 2013, 382 patients have been recruited of whom 73 have completed at least 15 months follow-up. For the entire cohort, adherence to T2T was 52% and non-adherence 37% for at least 1 study visit (54% and 36% in Canada), unknown in 11%. Reasons for non-adherence were physician decision current treatment acceptable (70%), physician decision (other) (12%), patient decision (9%), physician decision due to concern for adverse event (2%), other non-specific (7%). By cumulative probability plot, 6-month change in DAS was superior in T2T adherent patients. Area under the curve analysis showed more improvement in swollen/tender joint count, patient/physician global, HAQ, RAID, SF36 in T2T adherent patients. Remission was attained in 40% (DAS), 12% (CDAI), 13% (SDAI, ACR Boolean) and was more frequent in T2T adherent patients irrespective of therapy.

**Conclusion:** Adherence to T2T is associated with improved RA outcomes. There remains a substantial gap in implementation even in protocol-specified clinical settings.

## 130

### ECG Abnormalities in a Cohort of Systemic Sclerosis Patients

Alaa Dekis (Jewish General Hospital - McGill University Health Centre, Montreal); Murray Baron (McGill University and Jewish General Hospital, Montreal); Marie Hudson (McGill University and Jewish General Hospital, Montreal); Thao Huynh (Montreal)

**Objective:** Systemic sclerosis (SSc) is a chronic autoimmune rheumatic disease characterized by small-vessel vasculopathy, fibrosis of skin and visceral organs, and the presence of autoantibodies. Cardiac involvement, resulting from one or more of these pathological processes, is one of the most frequent complications of SSc, affecting up to 80% of SSc patients. Prognosis of symptomatic patients is poor (hazard ratio for death 2.8, 95% CI 2.1-7.2; Ioannidis, 2005]. Although electrocardiographic (ECG) abnormalities have been

frequently reported in SSc, previous studies have been limited by small sample sizes and uncertainty regarding which ECG abnormalities were assessed and how those were defined. Not surprisingly, results have been inconsistent. We undertook this study to determine the prevalence of ECG abnormalities in a large sample of SSc patients using a standardized approach to ECG reporting.

**Methods:** We conducted a cross-sectional study of SSc subjects in the Canadian Scleroderma Research Group. Baseline ECG were obtained and read by a single, experienced cardiologist, blinded to the subjects' clinical status.

**Results:** Clinical data and ECGs from 833 subjects were available: 86.1% females, mean age 56.4 years and disease duration 11.3 (9.3) years, 97.4% fulfilled the 2013 ACR/EULAR criteria for SSc, 57.4% had limited cutaneous and 38.7% had diffuse cutaneous disease. The prevalence of cardiac conduction abnormalities were: first degree atrioventricular block (3.8%), complete right bundle branch block (RBBB) (3.0%), left bundle branch block (LBBB) (1.7%), incomplete RBBB (0.6%), incomplete LBBB (0.1%) and left anterior fascicular block (3.0%). Only a minority of patients had arrhythmia with atrial fibrillation in 0.6% of patients and paced rhythm in 0.5%. The prevalences of dilation/hypertrophy of cardiac chambers were left atrial enlargement (9.3%), right atrial enlargement (0.1%), left axis deviation (4.0%), right ventricular hypertrophy (1.7%) and left ventricular hypertrophy (0.6%). Finally, repolarisation abnormalities in the lateral leads (16.0%) and inferior (11.3%) leads were relatively frequent.

**Conclusion:** This study provides robust data on the type and frequency of ECG abnormalities in SSc. Repolarisation abnormalities and chamber enlargement were frequent, whereas conduction abnormalities and arrhythmias were less common. However, the clinical significance of these ECG abnormalities remains unknown. Although ECG are easily accessible and non-invasive tests, further studies comparing SSc to age- and sex-matched normal individuals, and assessing evolution of ECG abnormalities over time and clinical outcomes of subjects with selected ECG abnormalities will be needed to determine the diagnostic and prognostic value of ECG in SSc. Those studies are underway.

## 131

### **Patient Medication Knowledge and Satisfaction with Inflammatory Arthritis Medication Information as Justification for Pharmacist-Led Education Program**

Alexandra Charlton (Alberta Health Services, Calgary); Carolyn Johns (Calgary); Dianne Mosher (University of Calgary, Calgary); Claire Barber (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary)

**Objective:** Since March 2012, we have offered medication education classes for patients with inflammatory arthritis (IA). These classes are led by our clinic pharmacist and provide information on disease modifying anti-rheumatic drugs (DMARDs) and biologic agents. This study will assist us in developing appropriate education materials and ensure that we are serving the needs of our patients. The objectives are to describe patient perceptions of the medication information provided at their clinic visit and to determine what sources of medication information are being accessed after patients leave the clinic.

**Methods:** An 8-question, paper-based questionnaire was developed and distributed to patients immediately prior to attending the classes. The questionnaire captured the sources of the medication information received by the patient and satisfaction with same. No identifying demographic information was captured in the surveys.

**Results:** A total of 243 patients have taken the DMARD (n=113) or Biologic (n=130) classes since their inception. Our data was collected over a 4 month period, where seventy patients agreed to complete the questionnaire. Patients reported receiving medication information in the clinic from a variety of sources: nurse (57.7%), physician (64.2%), or other (residents/medical students, pharmacist and physiotherapist (1%)). Nearly half of the patients (45.6%,) reported receiving too little medication information during their clinic visit. Thirty-eight percent of patients found the information given to them to be too simplistic and a further seventeen percent found it too complex. Seventy- three percent reported receiving information about both the risks and benefits of the medications, but only about one third (35.3%) of the patients were comfortable taking their medications prior to attending the classes. The remainder reported some degree of anxiety or fear around taking their medications. The Internet was the most frequently reported outside source of medication information (31.4%). Only 17% of patients received medication information from their community pharmacist, two of which reported that they perceived that information to be negative.

**Conclusion:** Patients with IA receive medication information in clinic, however, they report that it is often not sufficiently detailed and as a result, turn to sources in the community. Frequently patients resort to the Internet for information that is not always validated. As a result, our pharmacist-led medication classes are focused on addressing the issues that have been identified by the patients in this survey. Future work will involve a formal evaluation of patient satisfaction with the medication education being provided by our classes.

## 132

### **Rheumatologists of Tomorrow: One School's Story**

Alfred Cividino (McMaster University, Hamilton); Nader Khalidi (Mc Master University, Hamilton); Lynne Lohfeld (McMaster University, Hamilton)

**Objective:** In July of 2012, the McMaster Rheumatology program conducted an internal review of its education program built around findings from individual interviews and documents. The goal was to identify strengths and gaps in the program, hallmarks of success, as well as ways to increase interest in Rheumatology by learners and better support faculty and clinical practitioners.

**Methods:** We collected data from key documents, feedback from Internal Medicine residents completing an anonymous survey, and individual interviews with faculty (n=10), fellows (n=5) and administrators (n=8)

**Results:** The interviews provided information on respondents' background and current roles as a practitioner, educator or learner, opinions about Rheumatology programs in general, key features of McMaster's Rheumatology program, ways to increase the number of rheumatologists, and final thoughts. Documents revealed no deficits in the formal curriculum. Survey results indicated residents viewed the rotation as outstanding (6.1 on a 7-point scale), with high points awarded to staff ("friendly, supportive, excellent teachers") and the structured mix of clinical exposure to patients in a variety of settings as well as case-based learning and musculoskeletal exams. Fellows described the department as collegial with "happy mentors and excellent educators" who treat residents and fellows with respect and support learners' clinical and research development. They suggested more opportunities for electives and shadowing rheumatologists, more assistance to fellows setting up a new practice, and changing the face of research to include more basic science and medical education research. Faculty echoed these views and also emphasized the need for interdisciplinary



models of care offered in a single setting, the need to collaborate with other programs on interdisciplinary research, and the advantages of having a centralized research facility to reduce costs and increase efficiency.

**Conclusion:** Overall the study participants viewed McMaster's Rheumatology program as having strong educational and research components. The next step is to refocus on a more collaborative way of working, both locally and nationally, that include working to increase the number of rheumatologists in Canada. Supported by a CIORA grant.

### 133

#### **A Comparison of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) Trial Design: Ways to Improve the Number of Positive Trials in SLE**

Amy Miles (Western University and U of Toronto, London); Janet Pope (University of Western Ontario, London)

**Objective:** Recent SLE RCTs were examined for potential design flaws and compared to rheumatoid arthritis (RA) RCT over the same time period to suggest modifications to SLE RCTs that could help improve the potential success rate of future SLE trials.

**Methods:** RA and SLE biologics RCTs published between 2005 and July 2013 were identified using PubMed. Inclusion criteria, study design, outcome measures, sample size calculations, patient baseline characteristics steroid use in the protocol and results were extracted and compared.

**Results:** Twenty-two RA RCTs and eight SLE RCTs were included. All RA RCTs used either a partial or continuous measure of improvement. SLE RCTs used SLEDAI, BILAG, SLAM, SRI and BICLA. RA trials were larger (543 vs 376 participants). Concomitant corticosteroid use was stable in 100% of RA trials while all SLE RCTs allowed dose tapering. RA trials were mostly in methotrexate or DMARD inadequate responders whereas SLE trials allowed for the presence or absence immunosuppressives within all trials. Sample sizes in RA were determined on a change in disease activity or proportion meeting a disease state. Positive trials were found in 100% of RA RCTs and 25% of SLE RCTs.

**Conclusion:** The potential insensitivity of SLE disease activity indices to partial improvements may result in type II errors in SLE RCTs. Varying concomitant pharmacotherapy, especially corticosteroid use, in SLE may blunt observed treatment effects. Steroid tapering should be considered a trial outcome in isolation. More realistic sample size calculations are needed in SLE.

### 134

#### **Hospitalization Rates Associated with Systemic Lupus Erythematosus in Canada: Temporal Trends and Provincial Variations from 2006-2010.**

Neerav Monga (GlaxoSmithKline, Inc., Mississauga); Amyn Sayani (GlaxoSmithKline, Inc., Mississauga); Marni Freeman (GlaxoSmithKline, Inc., Mississauga); Jorge Ross Terres (GlaxoSmithKline, Inc., Mississauga)

**Objective:** Systemic Lupus Erythematosus (SLE) is a complex autoimmune disorder that primarily affects women of childbearing age, and poses a significant burden on the Canadian health care system. The rate and length of stay (LOS) of hospitalizations (HOSP) for SLE patients across Canada has not been well documented. The purpose of this study was to describe rates of hospitalization in Canadian patients with SLE from 2006 to 2010 by region, gender, age and LOS.

**Methods:** Population-based data for SLE HOSPs across Canada was obtained from the Canadian Institute for Health Information's Discharge Abstract and Hospital Morbidity databases between 2006 and 2010, using ICD-10 coding. Annual population size was obtained from Statistics Canada. Data were grouped by geographical regions: British Columbia (BC), Prairies (PR: Alberta/Manitoba/ Saskatchewan), Ontario (ON), Quebec (QC), Maritimes (MR: Nova Scotia/Prince Edward Island/ Newfoundland/New Brunswick), and Territories (TERR). Hospitalization rates were reported by age and by province, standardized to 2006 population levels. LOS was reported by gender and province.

**Results:** SLE HOSP rates (reported per 100,000) across Canada remained relatively stable over time (2006: 2.6; 2010: 2.2). PR and BC had the highest HOSP rates in 2006 (3.5 and 3.0, respectively). However, while BC rates remained stable to 2010 (3.2), PR showed the highest drop in rates in 2010 (2.1). HOSP rates in TERR doubled between 2006-2010 (2006: 0.9; 2010:1.8). Females had higher rates than males (3.5 vs. 0.9 in 2010), but decreased over the same time frame (2006: 4.2; 2010: 3.5). HOSP rates for males remained relatively stable over time. Patients under 19 had the lowest HOSP rates (1.3 in 2010) while those in their 20s had the highest rate (2006: 4.1; 2010: 3.5). Lower HOSP rates were reported for the elderly (>60 yrs; 2006:1.9; 2010: 2). On average, LOS from 2006-2010 varied: 26.5% of patients stayed 1-3 days, 20.8% stayed 4-6 days, 22.2% stayed 7-11 days and 30.5% stayed 12+ days with more males having longer LOS than females (36.8% vs. 27.8% in 2006; 34.7% vs. 26.9% in 2010).

**Conclusion:** SLE HOSP from 2006-2010 was relatively stable at a national level, however, regional differences were observed most notably in BC, PR, and TERR. This may be due to variations in access to health care resources, the multiple manifestations of SLE, and/or limited access to GP/Specialists. Further research is needed to examine the underlying cause of HOSPs, particularly in the male population (longer LOS) and in TERR.

## 135

### **Comparing Drug Survival between Five Tumor Necrosis Factor Inhibitors in Patients with Psoriatic Arthritis**

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**Objective:** To compare the drug survival rates of etanercept, adalimumab, infliximab, golimumab, and certolizumab pegol when used as first and second Tumor Necrosis Factor- $\alpha$  inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA).

**Methods:** We conducted a chart review in a community office of two rheumatologists in the Greater Toronto Area. Charts dating back to 2001 were scanned in May-July 2013 for any patients diagnosed with psoriatic arthritis and subsequently treated with one or more of the TNFis under study. Demographic information, DMARD use, and TNFi treatment details were extracted from the charts of eligible patients. We assessed for any significant differences in baseline characteristics (age, gender, disease duration, rheumatoid factor positivity, concomitant DMARD use, and comorbidity status) between the treatment groups. Drug survival rates, proportions of first and secondary failures, and median survival times were measured for each drug, for both their use as first and second TNFi therapy. Drug survival was compared between the TNFis in their use as first and second TNFi agents with Kaplan-Meier survival analysis and log rank tests.

**Results:** We included 134 patients in the analysis. There were no significant differences in

demographics between the treatment groups. None of the included patients used certolizumab pegol as a first or second TNFi. Our analysis found: 1) When used as first TNFi therapy, survival rates were 42% (27/65), 44% (19/43), 47% (8/17), and 78% (7/9) for etanercept, adalimumab, inxlifimab, and golimumab respectively. In the same order, secondary failures were found to occur in 88%, 81%, 100%, and 50% of patients. Median survival times were 53 months (CI: 32.0-74.0), 33 months (CI 4.5-61.5), and 38 months (CI: 9.0-67.0), for etanercept, adalimumab, and inxlifimab. 2) When used as the second TNFi therapy, survival rates were 69% (9/13), 52% (16/31), 75% (3/4), and 50% (3/6) for etanercept, adalimumab, inxlifimab, and golimumab respectively. In the same order, secondary failures occurred in 80%, 50%, 67%, and 0% of patients. Median survival times were 28 months (CI: 0.0-67.9) and 20 months (CI: 0.0-49.4) for adalimumab and golimumab. The log-rank tests yielded insignificant p-values, measuring at 0.305 for first TNFi and 0.771 for second TNFi.

**Conclusion:** Our findings indicate that regardless of whether they are used as the first or second TNFi agent for the treatment of PsA, there are no differences in drug survival of etanercept, adalimumab, infliximab, and golimumab. Further research is necessary to discern how certolizumab pegol and newer biologics compare.

## 136

### **What is the Internal Consistency of the Disease Activity Score (DAS)-28 in Rheumatoid Arthritis Patients Treated in a Real-World Setting?**

Andrew Chow (Credit Valley Rheumatology, University of Toronto, McMaster University, Mississauga); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Regan Arendse (Saskatoon); Dalton Sholter (124 Street Medical Group, Edmonton); Denis Choquette (Institut de Rhumatologie de Montréal, Montreal); Isabelle Fortin (Centre de santé et de services sociaux de Rimousk, Rimouski); Boulos Haraoui (Université de Montréal, Montréal); Emmanouil Rampakakis (JSS Medical Research & McGill University, St. Laurent); Francois Nantel (Janssen, Toronto); Allen Lehman (Janssen Inc., Toronto); May Shawi (Janssen Inc., Toronto); Susan Ottawa (Janssen Inc., Toronto)

**Objective:** The DAS-28 is used in clinical decision making and research as an outcome assessment for patients with RA. The tool measures clinical, patient centric and inflammatory components of disease activity. Simplification or improvement of the tool would be important in facilitating its use in real-world settings. The objective of this analysis was to assess the internal consistency of the DAS-28 components and contrast these upon replacing patient global assessment (PtGA) with HAQ-DI in RA patients treated in a Canadian real-world setting.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or golimumab as first biologics or after having been treated with a biologic for < six months. Patients with RA treated with infliximab or golimumab who were enrolled between 2002-2012 and had a maximum of 60mons of follow-up were included in this analysis.

**Results:** A total of 510 patients evaluated over 3,817 visits were included. Mean follow up was ~20 months. The overall correlation between TJC and SJC was high ( $r=0.746$ ), whereas the correlations of ESR with TJC ( $r=0.187$ ) and SJC ( $r=0.212$ ) were poor. The correlation between patient assessment of disease activity (PtGA) was poor with ESR ( $r=0.190$ ) and modest for TJC ( $r=0.519$ ) and SJC ( $r=0.487$ ). Internal consistency was low [Cronbach's alpha (CA)=0.482] and Intra-Class Correlation Coefficient (ICC)=0.205]. All item-item correlations, ICC and CA deteriorated with time over the 60-month follow up period. The correlations of TJC ( $r=0.454$ )

and SJC ( $r=0.367$ ) with HAQ-DI were lower when compared to those with PtGA while the correlation of ESR ( $r=0.260$ ) was higher with HAQ-DI. Replacement of PtGA with HAQ-DI would result in lower internal consistency ( $CA=0.337$ ) suggesting modest improvement in validity. The slopes measuring rate of change over time for the DAS-28 items showed acceptable internal consistency ( $ICC=0.638$ ). Item-item correlations were low for the ESR-slope with PtGA-Slope ( $r=0.262$ ), TJC-Slope ( $r=0.240$ ) and SJC-Slope ( $r=0.300$ ); PtGA-slope had moderate correlation with SJC-Slope ( $r=0.512$ ) and TJC-Slope ( $r=0.570$ ). When compared to PtGA, HAQ-DI-Slope had comparable correlations with the slopes of the DAS-28 components.

**Conclusion:** There is poor cross sectional and longitudinal correlation between the DAS-28 components indicating that they are measuring related but discriminating concepts of disease activity. The exception being SJC and TJC and therefore exclusion of one of these measures may be considered. Replacement of PtGA with HAQ within the DAS-28 would not provide any significant statistical benefits however it could offer practical benefits (i.e. reduce measurement workload) without loss of validity of DAS-28.

137

### **Low Socioeconomic Status (SES) as Measured by Education is Not Predictive of Poor Patient Outcomes in Systemic Lupus Erythematosus (SLE): Data from the 1000 Canadian Faces of Lupus**

Angela George (Western University - Rheumatology, London); Janet Pope (University of Western Ontario, London); Christine Peschken (University of Manitoba, Winnipeg); Earl Silverman (The Hospital for Sick Children, University of Toronto, Toronto); Christian Pineau (McGill University Health Centre, Montreal); Douglas Smith (The Ottawa Hosp, Ottawa); Michel Zummer (CH Maisonneuve-Rosemont, Montreal); Ann Clarke (McGill University, Montreal); Sasha Bernatsky (McGill University, Montreal); Marie Hudson (McGill University and Jewish General Hospital, Montreal); Carol Hitchon (University of Manitoba, Winnipeg); Paul Fortin (CHU de Québec Research Centre - CHUL, Québec)

**Objective:** We wanted to determine whether socioeconomic status, as measured by education, had an impact on disease activity (measured by SLAM-2, SLEDAI-2K) or disease damage (measured by SLICC SDI) in patients with systemic lupus erythematosus (SLE).

**Methods:** Data was gathered from the 1000 Canadian Faces of Lupus, a multi-center, prospective cohort database and included adult SLE patients from June 2005 onward. Socioeconomic status, as measured by education was defined as being either low (did not complete high school) or high (completed high school or further). The relationship between socioeconomic status, as measured by education and SLE outcomes were evaluated using one-way ANOVA and logistic regression analyses.

**Results:** 484 patients met inclusion criteria (mean age 47 years, 91.5% female, mean disease duration of 10 years). Of the included patients, 80.4% had completed high school education or higher and 19.6% had not completed high school. One-way ANOVA analyses of education level to SLE outcomes of disease activity (SLAM-2 and SLEDAI-2K) and disease damage (SLICC) demonstrated the following: SLICC,  $p = 0.986$ , SLAM-2,  $p = 0.332$  and SLEDAI-2K,  $p = 0.011$ . Further logistic regression analysis of SLEDAI-2K did not demonstrate significance with multiple variables including age,  $p = .831$ , gender,  $p = .950$ , ethnicity,  $p = .700$  and disease duration,  $p = .467$ .

**Conclusion:** Socioeconomic status, as measured by education, does not appear to have an impact on SLE patient outcomes as measured by disease activity (SLAM-2 and SLEDAI-2K) or disease damage (SLICC).

138

**Mortality in Canadian Systemic Sclerosis Patients: Cause for Alarm.**

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**Objective:** Systemic sclerosis (SSc) is a relatively rare but serious connective tissue disease associated with increased mortality. A first Canadian study conducted between 1979-90 on 237 SSc patients in Ontario reported a standardized mortality ratio (SMR) of 4.69 (Abu-Shakra et al. 1995), whereas a second study conducted between 1984-99 on 309 French Canadian SSc patients reported an SMR of 2.69 (Scussel-Lonzetti et al. 2002). Examining trends in mortality over time can assist in monitoring disease burden and evaluating the effectiveness of treatment. The aim of this study was to quantify mortality in a large contemporary cohort of Canadian SSc patients.

**Methods:** This study consisted of subjects followed in the Canadian Scleroderma Research Group (CSRG) cohort between 2005 and 2012. Using data from Statistics Canada data for the general population, we calculated SMR and Years of Life Lost (YLL) in the whole cohort, which consists of both prevalent and incident cases, as well as in the subset of incident cases defined as subjects recruited within 5 years of disease onset.

**Results:** Among the 1132 subjects in the CSRG cohort, 86% were female, mean age was  $55.7 \pm 12$ , mean disease duration was  $10.8 \pm 9.5$ , and 35.6% had diffuse cutaneous SSc (dcSSc). Of these, 151 (13.3%) died over a mean follow up time of  $3.7 \pm 2$  years. In Cox regression analysis, male sex, dcSSc, pulmonary hypertension and interstitial lung disease were independent predictors of death. Age- and sex-adjusted SMR was 3.7 (95% CI 3.2, 4.2). YLL from birth were 19.8 in females and 16.7 in males and from age of disease onset were 21.6 for females and 19.5 for males. Of the 405 incident subjects, 81% were female, mean age was  $51.1 \pm 12.6$ , mean disease duration was  $2.3 \pm 1.3$ , and 41.8% had dcSSc. Of these, 53 (13.1%) died over a mean follow up time of  $3.5 \pm 2.1$ . In Cox regression analysis, older age and pulmonary hypertension were independent predictors of death. Age- and sex-adjusted SMR was 4.7 (95% CI 3.6, 5.7). YLL from birth were 21.1 for females and 19.7 for males, and from age at disease onset were 23.8 for females and 22.9 for males.

**Conclusion:** Mortality in Canadian SSc patients is substantial and has not improved in over 30 years. Prevalent cohorts underestimate mortality in SSc by failing to capture early deaths. Novel research to improve our understanding of SSc is imperative if we aspire to improve outcomes for patients with this devastating disease in a meaningful way.

139

**Practical Learning about Inflammatory Arthritis Improves the Precision of Patients' Referral in Rheumatology. Results of PRADA, a Regional CME Activity in Sherbrooke (Québec)**

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(Université de Sherbrooke, Sherbrooke)

**Objective:** Context: Patients with early Inflammatory Arthritis (IA) initially consult with primary care family physicians (FPs). There is evidence that recognition of EIA and the consequent referral in rheumatology are too often delayed. The importance of early management of IA by rheumatologists is well established. Objective: Evaluate the impact of a hands-on educational program about inflammatory arthritis (IA) directed to FPs aiming at early recognition and referral of IA patients to an academic rheumatology center.

**Methods:** Methods: The PRADA (Programme de reconnaissance et acheminement rapide de patients avec arthrite) educational activity consisted in interactive workshops with real patients presenting different types of arthritis (rheumatoid arthritis, spondyloarthritis). The learning activity was combined with the recommendation of use of a practice enabler: a standard referral form specific for suspected IA. To measure the impact of the learning intervention, we analyzed subsequent referral letters to our Rheumatology Department. Referrals from physicians who attended workshops training (trained FPs) were compared to a control group of regular referrals (control group). The primary endpoint was the clinical validation of IA by the rheumatologist. A secondary endpoint was the pertinence of the complementary investigation, categorised as complete versus incomplete.

**Results:** Results: 115 family physicians from 14 regional medical centers were trained. During the following two years, 73 consecutive referral letters coming from trained FPs were compared to 154 referral letters from the control group. IA was confirmed in 70,8% of the trained FPs' referrals vs 50,7% in the controls' referrals ( $p=0,03$ ). The pertinence of the paraclinical complementary investigation was also higher in the trained group than in the control group: 35,6% vs 3,4% ( $p<0,001$ ). In the subgroup of trained physicians that used the standard referral form, the level of a complete complementary workup reached 59,4%.

**Conclusion:** Conclusions: PRADA, a practical, hands-on educational program, helped FPs from the Sherbrooke area to recognize inflammatory arthritis more consistently, to complete an adequate initial workup and to refer affected patients to rheumatology. Establishing and continuing this type of learning activity may improve referrals and early diagnosis and treatment of IA patients by rheumatologists. Supported by a CIORA grant.

## 140

### Survey of Practice Patterns in the Diagnosis and Management of Systemic Lupus Erythematosus in Canada

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**Objective:** Systemic Lupus Erythematosus (SLE) is a heterogeneous autoimmune disease with multiple factors affecting care including the degree of disease activity and damage, socioeconomic status, and geographical variability in care provision across Canada. Therefore, Canadian SLE experts in collaboration with the Canadian Rheumatology Association (CRA) are evaluating existing practice patterns of SLE care in Canada to inform future recommendations for the diagnosis and management of SLE in Canada.

**Methods:** A survey of 63 questions in English and French was developed after piloting with the CRA and the Canadian Network of Improved Outcomes in SLE (CaNIOS). The survey monkey questionnaire was e-mailed to active members of the Canadian Rheumatology Association (CRA) in November 2012.

**Results:** The 176 respondents (Male 49%), included general adult rheumatologists (85%) and pediatric

rheumatologists (10%), with the largest proportion (26%) having been in practice for 11-20 years, and 65% practicing in academic/teaching hospitals. The clinical manifestations cited by respondents as occurring most often in their SLE patients were musculoskeletal (41% of respondents); cutaneous (26%); fatigue (24%) and renal (6%). In clinical assessments, swollen/tender joint counts (reported by 77% and 70% of respondents respectively) and MD global assessment (36%) were used much more often than SLE-specific disease activity (e.g. SLEDAI) and damage indices (i.e. SLICC). Only 9% of responders reported calculating formal cardiovascular risk scores. The most common frequency for monitoring disease activity in a stable patient was every 6 months (reported by 39%). Of 147 responders, hydroxychloroquine (99% of respondents) was most commonly used for non-renal SLE. Twenty-six (26) percent of responders reported that 6 to 10% of SLE patients required a minimum low dose prednisone indefinitely. The most common agent reported as first-line induction for class 3/4 nephritis was cyclophosphamide IV (50%) and mycophenolate mofetil was reported most commonly (33%) for second line treatment.

**Conclusion:** Considerable variability exists in diagnosing, monitoring and treating SLE patients in Canada. These data have informed a recently formed Canadian SLE Working Group to develop Canadian SLE recommendations with an aim to ensure that every SLE caregiver is aware of what the standard-of-care should be in diagnosing, monitoring and treating SLE patients.

141

#### **Improved Clinical Control of a Challenging Case of Behçet's Disease with Rituximab Therapy**

Barbara Zhao (University of Alberta Canada, Edmonton); Anna Oswald (University of Alberta, Edmonton)

**Case Report:** Behçet's disease (BD) is a rare form of vasculitis in North America. Like other rare diseases, there is no high quality evidence for biologic use beyond case reports/series and thus therapy remains controversial. We report the case of a patient who failed to respond to conventional therapy with colchicine and NSAIDs. She responded to steroids but failed to tolerate steroid tapers despite azathioprine, methotrexate, infliximab and etanercept and required chronic Prednisone up to 20 mg daily due to recurrent severe mucosal ulcers with fever, erythema nodosum (EN) and arthritis. She received cyclophosphamide for another indication but even then failed steroid taper. After 3 courses of rituximab, she showed marked clinical improvement and was able to reduce Prednisone to 8 mg and to return to school and work. A review of disease mechanisms and clinical literature is presented for those facing challenging cases where evidence is limited.

142

#### **Causes of Mortality in Lupus Patients followed Prospectively at the University of Toronto Lupus Clinic**

Barry Sheane (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objective:** A bi-modal pattern of mortality in SLE has been described whereby death within the first years after diagnosis was associated with active lupus and infection, while death in later years was associated with atherosclerosis and corticosteroid use. The aim of this study was to re-examine the causes of mortality in lupus patients followed prospectively at a large lupus clinic between 1970 and 2013.

**Methods:** Causes of death were recorded and acquired from autopsy reports (n=48), discharge summaries

(n=64), hospital notes (n=23), and death certificates (n=20). Causes were divided into 5 categories: active lupus, atherosclerosis-related (acute myocardial infarction, congestive cardiac failure (as a direct result of coronary artery disease), or stroke, all in the absence of active SLE), infection, malignancy and 'other'.

**Results:** Of 264 patients known to have died, causes of death were established in 206 cases. Mean disease duration at time of death was  $14.6 \pm 11.8$  years, with 47 (23%) dying within 5 years of and 62 (30%) dying 20 or more years after diagnosis. Mean age at death was  $52.6 \pm 17.5$  years, with 56 (27%) dying before the age of 40. Infection was responsible for the majority of deaths (n=71 (34.5%)), followed by active SLE (n=38 (18.4%)), AS (n=38 (18.4%)), malignancy (n=24 (11.7%)) and 'other' (n=60 (29.1%)). Renal failure in inactive SLE (n=6) and bowel perforation (n=5) were among 'other' causes. There was a significant decline in the number of death attributable to infection and active SLE with increasing disease duration: 49% (n=23) and 34% (n=16) of deaths in those with SLE for less than 5 years were due to infection and active lupus, respectively, compared with 26% (n=16) and 15% (n=9) of deaths in those with SLE for 20 or more years ( $p=0.01$ ). Atherosclerosis was increasingly responsible for death with increasing disease duration: 13% (n=5) with less than 5 years disease duration, compared with 23% (n=14) after 20 years of SLE ( $p=0.11$ ). Malignancy also increased in prevalence as a cause of death with greater disease duration ( $p=0.13$ ).

**Conclusion:** Within the first 5 years of disease onset, infection and active SLE account for over 80% of deaths in lupus. Despite a significant reduction as a cause of death over time, infection remains the single biggest killer in those with disease over 20 years. Atherosclerosis replaces active SLE as the next most important cause of death in lupus patients with increasing disease duration.

## 143

### **How often are Core Variables Required to Calculate Common Disease Activity Scores Measured in the Routine Care of Rheumatoid Arthritis Patients?**

Bindee Kuriya (Mount Sinai Hospital, University of Toronto, Toronto); Binu Jacob (University Health Network, Toronto); Jessica Widdifield (University of Toronto, Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Treat-to-target (T2T) is a therapeutic strategy in rheumatoid arthritis (RA) that has been associated with improved outcomes. T2T relies on objective measurement of disease activity at regular intervals with escalation of treatment until remission or low disease activity is achieved. In clinical trials, variables needed to assess disease activity are routinely collected but whether the same is done in clinical practice is uncertain. We aimed to determine the frequency of core variable collection needed to calculate disease activity scores of RA patients followed in routine care.

**Methods:** All patients (N=2081) enrolled in the Ontario Best Practices Research Initiative since its inception in 2009 were included in this study. OBRI is a clinical registry of RA patients with both early and established disease and are treated according to the discretion of the rheumatologist. We determined the frequency by which components required to calculate common composite disease activity scores (DAS28, SDAI, CDAI) were collected and documented during the first 6 consecutive visits: physician global health assessment (MDGA), patient global health assessment (PtGA), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tender joint count-28 (TJC) and swollen joint count-28 (SJC). Results are reported as the % of measured variables, expressed as the number of measured components divided by the number of patients at each visit.

**Results:** At entry into the cohort, 77% of patients were female with mean (SD) age 57 (13) years, and the



majority (85%) was Caucasian. Patients had moderate disease activity according to both mean (SD) DAS28 4.5 (1.5) and CDAI scores 21(14). Over subsequent visits, the % measurement was consistent for most variables with the exception of ESR and CRP, which had a higher frequency of measurement at cohort entry (visit 1) than subsequent visits. Documentation of TJC and SJC assessment was universally high at each visit and ranged from 92-96%. MDGA (range 85-89%) and PtGA (range 88-90%) were similar. Missing data was greatest for values of CRP (missing range 29-40%).

**Conclusion:** Measurement of core variables required to assess RA disease activity are collected in a majority of RA patients followed in routine clinical practice. Objective measures such as TJC and SJC have near perfect collection. MDGA and PtGA are missing in ~15% of visits and measurement of inflammatory markers are sub-optimal which may limit calculation of composite scores that drive T2T strategies and comparison of disease activity to other cohorts. Further work determining potential barriers to collection of these variables is needed.

## 144

### **All-Cause Mortality for Patients with Rheumatoid Arthritis in a Universal Public Health Care System**

Jessica Widdifield (University of Toronto, Toronto); Michael Paterson (Institute for Clinical Evaluative Sciences, Toronto); Sasha Bernatsky (McGill University, Montreal); Bindee Kuriya (Mount Sinai Hospital, University of Toronto, Toronto); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Simon Hollands (Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Studies evaluating trends in rheumatoid arthritis (RA) mortality over time have produced inconsistent results. Our aim was to estimate all-cause mortality in RA between 1996-2009, assess changes in mortality over time, and to compare mortality rates in RA with the general population.

**Methods:** We studied all residents in Ontario, Canada's most populous province (N~13 million). Patients with RA were identified using the Ontario RA administrative Database (ORAD), a population-based research cohort generated from administrative data using a validated RA case definition. Linking to vital statistics data, we estimated annual all-cause mortality in RA by dividing the number of deaths among RA patients by the number of RA patients in each year. To compare mortality rates over time, we standardized for age and sex using the 2001 Ontario census population estimates. Age specific and age-and-sex standardized all-cause mortality estimates are expressed as the number of deaths per 1,000 RA patients for each year of the study period. The age-and-sex-standardized all-cause mortality estimates were compared in terms of relative percentage change between 1996 and 2008. We compared changes in mortality over time in RA patients, to estimates of mortality in the general population, over the same period. Finally, standardized mortality ratios (SMRs) were calculated, which provides the ratio of the mortality rate in RA patients versus the age and sex matched general population mortality.

**Results:** Age-and-sex standardized all-cause mortality ranged from 13.0 deaths per 1,000 RA patients (95%CI 12.2,13.9) in 1996 to 9.2 deaths per 1,000 RA patients (95%CI 8.4,10.0) in 2010. In 2008, the age-standardized rate for RA females was 8.8 deaths per 1,000 (95%CI 8.0,9.6) compared to 12.1 deaths per 1,000 (95%CI 10.3,14.2) in males, and rates were higher among males than females in all age groups. Age-specific all-cause mortality in RA patients increased with increasing age. Comparing RA mortality trends to the general population (Figure), since 1996, all-cause mortality decreased for RA by a relative 21.4%, with a smaller decrease (13.4%) in the general population. The SMRs for RA patients in 2000, 2004, and 2008 were 1.50 (95% CI 1.43-1.57), 1.43 (95%CI 1.37-1.50), and 1.41 (95%CI 1.35,1.47) respectively.

**Conclusion:** All-cause mortality for patients with RA has decreased over the past decade but remains elevated compared to the general population. Our results suggest 40-50% more deaths among RA patients compared to the general population. SMR estimates over the past decade do suggest the mortality gap may

be slowly narrowing.

145

### **Cigarette Smoking and Disease Activity in Rheumatoid Arthritis Patients: Results from Ontario Best Practice Research Initiative (OBRI)**

Binu Jacob (University Health Network, Toronto); George Tomlinson (Toronto General Research Institute, Toronto); Pooneh Akhavan (Mount Sinai Hospital, University of Toronto, Toronto); Xiuying Li (University Health Network, Toronto); Angela Cesta (University Health Network, Toronto); Sandra Couto (Toronto); Carol Mously (Toronto); OBRI Investigators (Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Smoking has been shown to be a significant risk factor for developing rheumatoid arthritis; however its impact on disease activity has conflicting evidence. The aim of this study was to assess the effect of smoking on disease activity in rheumatoid arthritis (RA) patients.

**Methods:** Data from the Ontario Best Practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care, were examined. All patients whose smoking status was reported at baseline were included in the study. Patients were divided into three groups based on their smoking status: Never, Past and Current smokers. The demographic, clinical laboratory and therapeutic features were compared according to their smoking habits. Physician reported disease activity measures such as tender joint counts (TJC), swollen joint counts (SJC), disease activity score 28 joints (DAS28), clinical disease activity index (CDAI) and patient reported disease activity score of rheumatoid arthritis disease activity index (RADAI) were considered as the outcomes. Differences between the groups were compared using chi-square test for categorical parameters, or analysis of variance (ANOVA) for continuous parameters. Multivariable analysis was performed for each outcome to assess the impact of smoking on disease activity when adjusted for potential confounders including patient demographics and rheumatoid factor (RF). When there was an overall difference in an outcome according to smoking status, Tukey-adjusted pair wise comparisons were made between groups.

**Results:** A total of 2,090 patients with a mean (SD) age 57.3 (12.9) years were included in the study and 77% were females. There were 343 (16.4%) current smokers (men-22.1% and women-14.8%), 812 (38.9%) past smokers (men-50.5% and women 35.5%) and 935 (44.7%) never smokers (men-27.4% and women-49.7%) in the cohort. A significantly higher proportion of RF positives were found in current smokers (76.7%) compared to past (70.9%) and never smokers (64.5%),  $p=0.0003$ . More DMARDs and less biologics were used at baseline in smokers; however it was not statistically significant. Current cigarette smokers found to have significantly higher mean TJC (7.4 vs. 6.3,  $p<0.001$ ), SJC (7.1 vs. 6.4,  $p<0.001$ ), CDAI (24.3 vs. 21.5,  $p<0.001$ ), and RADAI (4.5 vs. 3.7,  $p<0.001$ ) than non-smokers, after adjusting for patient sex, age and RF. There was no difference in DAS28 scores between the groups.

**Conclusion:** Smokers have worse disease activity outcomes than non-smokers in RA patients, after adjusting for measured confounders.

146

### **Methods Used in Standardizing Drug Names: Experience from OBRI Study**

Jimmy Nguyen (University Health Network, Toronto); Binu Jacob (University Health Network, Toronto); Pooneh Akhavan (Mount Sinai Hospital, University of Toronto, Toronto); OBRI Investigators (Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Standardization of medication data eliminates collection errors and provides a hierarchical organization to facilitate safety and efficacy comparisons between individual drugs, classes of drugs, and broader groupings. The objective was to code medication data from the Ontario Best Practices Research

Initiative (OBRI) cohort using currently available systems.

**Methods:** The OBRI collects long-term treatment information from a broad range of rheumatoid arthritis (RA) patients. We used the Anatomical Therapeutic Chemical (ATC) code of drug products from the Health Canada Drug Product Database (HC-DPD) which has complete information for all active and discontinued products available in Canada. An appropriate ATC code was selected for each drug based on trade, generic, chemical names, dosage form, and indication. For drugs with multiple ATC codes, the most appropriate code was selected that accurately represented the medication, its route of administration, and the pathology it is intended to treat. For drugs with unmatched codes, broad new categories were introduced into the dictionary while preserving the structure of the ATC system. The ingredients within each unmatched drug product were identified then assigned a new ATC code. For those drugs which were 'unable to code', we used the WHO Criteria to develop a new coding system classify them meaningfully within the ATC classification system structure.

**Results:** There were 2081 RA patients in the OBRI cohort with 8845 unique medication entries. Using H-DPD only, 2415(27.3%) entries were unable to code. These mainly included food products, probiotics, fatty acids, and oils.

**Conclusion:** Existing HC-DPD is capable of coding the majority of therapeutic agent's observational studies but still a portion of entries cannot be coded using this system alone. In this study creating new codes using WHO classification allowed an appropriate coding that can be used by other groups. This standardized medication data facilitates drug utilization studies.

147

#### **Adherence to RA Medications as Reported by Patients and Rheumatologists in the Ontario Best Practices Research Initiative (OBRI)**

Angela Cesta (University Health Network, Toronto); Xiuying Li (University Health Network, Toronto); Sandra Couto (Toronto); Binu Jacob (University Health Network, Toronto); OBRI Investigators (Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** The World Health Organization (WHO) has identified five dimensions of adherence; social/economic related, therapy related, patient related, condition related, and health system related factors. The objective of this study was to look at reported non-adherence in patients participating in the OBRI.

**Methods:** In the OBRI database, 311 patients reported 407 occurrences of either not taking their RA medications as prescribed or not starting a recently prescribed RA medication. Patient reported reasons for these occurrences were categorized according to the WHO dimensions. OBRI patients who completed 2 years of patient reported data (N = 901) were also categorized as either adherent (N = 638, 71%) or non-adherent (n = 263, 29%). Patients were considered non-adherent if their rheumatologist reported "patient decision" as the reason for the discontinuation of an RA medication or if the patient reported any of the following to their interviewer: i) not taking their RA medications as prescribed, ii) stopped taking their prescribed RA medication, or iii) not started taking an RA medication prescribed by their rheumatologist. The adherent and non-adherent groups were compared with respect to demographics, socio-economic status, and disease outcome scores, at baseline. Patient reported global, RADAI (Rheumatoid Arthritis Disease Activity Index) and HAQ (Health Assessment Questionnaire) were also reported for the assessment at which the patient reported non-adherence.

**Results:** Patient related, health system related, therapy related, condition related, and socio economic related factors accounted for 41%, 24%, 18%, 6%, and 4% of the reasons patients reported for not taking their RA medications. At baseline assessment, non-adherent patients were significantly younger, reported higher household incomes, and higher education levels ( $p < 0.05$ ). No significant differences were found

with respect to RA duration, smoking, private vs public insurance, number of co-morbidities, patient reported global, RADA and HAQ scores. At the time of the reported non-adherence, patients reported significantly lower globals, RADA and HAQ scores compared to their baseline assessments ( $p < 0.0001$ ).

**Conclusion:** Patient's perceived needs for treatment, their concern about side effects, and forgetting to take their medications were the most common reasons reported for not taking RA medications as prescribed or for not starting a recently prescribed RA medication. One third of the OBRI patients reported non-adherence. The decrease in patient reported global, RADA and HAQ at the time of the reported non-adherence suggests that patients may be discontinuing the use of their RA medications when experiencing low disease activity.

## 148

### **Use of MEDSCHECK Program Among Rheumatoid Arthritis Patients – Results from Ontario Best Practice Research Initiative (OBRI)**

Apoorva Kelkar (University Health Network, Toronto); Sandra Couto (Toronto); Binu Jacob (University Health Network, Toronto); OBRI Investigators (Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** The MedsCheck program is one of many professional services offered by Ontario community pharmacists. It consists of a one-on-one interview between a pharmacist and a patient to review patients' medications. It is designed to encourage patients to better understand their medication therapy, and to ensure they can experience benefit from their medications by taking them correctly. Any patient with a valid Ontario Health Card who is currently taking a minimum of 3 prescription medications for a chronic condition is eligible to receive a Medscheck review. The aim of this study was to identify the number of patients who are participating in the Ontario Best Practices Research Initiative (OBRI) who reported receiving a Medscheck review within the last year

**Methods:** From the OBRI clinical registry of rheumatoid arthritis (RA) patients ( $N = 2081$ ), 733 patients who were currently suffering from 3 or more chronic medical conditions were deemed eligible for this study. From the eligible patients, 20% were randomly selected ( $N = 121$ ) to be contacted using a telephonic survey. The selected patients ( $n = 121$ ) were contacted directly by an OBRI telephone interviewer to determine whether they had received a Medscheck review by their local pharmacy. The patient questionnaire was created in collaboration with the Ontario Pharmacist's Association (OPA).

**Results:** Out of the 121 eligible RA patients, the telephone interviewers were able to contact 105 patients. The mean (SD) age of patients was 62.4 (10.4) years and 84 (69%) were females. The mean (SD) disease activity score at baseline was 4.8 (1.4). Of these 105 patients, 32% reported that their pharmacist had performed a MedsCheck review with them in the last one year. Thirty patients (88%) reported that the review took between 15-30 minutes and on an effectiveness scale of 1-10 (10 = extremely effective), 41% reported that they found the review extremely effective at addressing their medical concerns. Lastly, 79% of the patients reported that they would not be interested in a pharmacist review program that solely focused on their arthritis medications.

**Conclusion:** Our review highlights that the Ontario MedsCheck is currently underutilized in a cohort of rheumatoid arthritis patients. Of interest, a good proportion of patients who did experience this service found it extremely effective at addressing their medical concerns. These results may be useful for practicing pharmacists to advocate for an increased awareness and usage of the Ontario MedsCheck medication review for patients.

### Characterizing T cell Profiles in Patients with Ankylosing Spondylitis

Blerta Green (Case Western Reserve University School of Medicine, Cleveland); Eric Gracey (Toronto); Ammepa Anton (Toronto); Robert Inman (University of Toronto, Toronto)

**Objective:** In this study, we analyzed the number of different T cell subsets and cytokine production in patients with ankylosing spondylitis (AS) and compared the results with those of healthy controls (HC).

**Methods:** 39 patients with AS and 31 age-matched healthy controls were included. Peripheral blood mononuclear cells were obtained from fresh blood samples and stained for surface markers, or stimulated for 5 hours with phorbol 12-myristate 13-acetate/ionomycin and stained with antibodies to analyze their cytokine production (IL-7a and INF $\gamma$ ) through flow cytometry.

**Results:** The frequency of CD4<sup>+</sup>IL-17a<sup>+</sup> T cells was significantly higher in male patients with AS compared to male healthy controls, but there was no difference between females. The frequency of CD4<sup>+</sup> INF $\gamma$ <sup>+</sup> T cells was significantly lower in AS patients compared to HC. AS patients show a trend of higher CD4<sup>+</sup> CD103<sup>+</sup> T cells, and significantly higher CD4<sup>+</sup> CCR6<sup>+</sup> T cells in the peripheral blood.

**Conclusion:** Our findings favor a pathogenic role for Th17 in AS. Th1 cells do not seem to contribute in the pathogenesis of this disease. Our study also implicates gut homing receptors in the pathogenesis of AS.

### The Knowledge-To-Action Cycle (KTAC): A Canadian Model to Guide the Dissemination and the Implementation of the Bilingual People Getting a Grip on Arthritis Self-Management Program

Lucie Brosseau (University of Ottawa, Ottawa); George Wells (University of Ottawa, Ottawa); Sydney Brooks (The Arthritis Society - Ontario Division, Toronto); Mary Bell (Sunnybrook Health Sciences Centre, Toronto); Gino De Angelis (University of Ottawa, Greely); Laurianne Loew (Gatineau)

**Objective:** Question: What are the best multifaceted strategies to implement the Ottawa Panel guidelines using the Canadian Implementation Model called the Knowledge-To-Action Cycle? Design: Between 2006 and 2012, four implementation studies including randomised controlled trials were conducted to facilitate the adoption of self-management interventions to rheumatoid arthritis and osteoarthritis.

**Methods:** Participants: Over 200 arthritic individuals participated to examine the efficacy/feasibility of various implementation strategies to facilitate the adoption of effective self-management interventions including walking programs, Tai Chi, therapeutic exercises etc. Ethics approval was obtained for all trials. Interventions: The intervention group used affordable technologies like social media for three months. The control group received unsupervised assistance to use the effective self-management programs. Outcome measures: The primary outcome was adherence to the self-management programs. Secondary outcomes were knowledge acquisition and self-efficacy. Measures were taken before and after program training and after three months.

**Results:** Results: After 3 months, participants were more compliant in the intervention group compared to the self-directed group ( $p < 0.012$ ). Knowledge acquisition scores improved among participants with a mean difference of 1.8 ( $p < 0.01$ ) when compared from baseline to immediate post-intervention. Self-efficacy towards self-management interventions was maintained from immediate post-intervention to three months

follow-up, and confidence improved as the study progressed.

**Conclusion:** Conclusion: The strategies used in the two studies were effective in improving program adherence, knowledge acquisition, and self-efficacy months later. The Knowledge-To-Action Cycle provided milestones to conduct these implementation studies.

## 151

### **The Non Pharmacological Management of Osteoarthritis & Rheumatoid Arthritis**

Lucie Brosseau (University of Ottawa, Ottawa); Karine Toupin-April (Childrens Hospital of Ontario, Ottawa); Gail Paterson (The Arthritis Society, Ottawa); Gino De Angelis (University of Ottawa, Greely); Laurianne Loew (Gatineau)

**Objective:** Question: The objectives of the review were: to assess the quality of the clinical practice guidelines on non-pharmacological management of osteoarthritis and rheumatoid arthritis using the Appraisal of Guidelines Research and Evaluation (AGREE II) tool; and to summarize the recommendations based on only high-quality existing clinical practice guidelines.

**Methods:** Design: A systematic review in a narrative format synthesising data from existing guidelines. Two pairs of evaluators were trained to assess the guidelines. A reliability study using intraclass correlation coefficients (ICC) was performed on the subtotal scores for each of the six AGREE II domains. Ethics approval was not required for this review. Clinical Practice Guidelines: A systematic search of scientific literature databases from 2001 to 2013 for evidence identified 17 guidelines for osteoarthritis and 12 for rheumatoid arthritis. Intervention: Only the recommendations on non-pharmacological interventions were considered. Outcome measures: The AGREE II instrument was used to appraise all 29 included guidelines.

**Results:** Results: All guidelines effectively addressed a minority of AGREE II domains. The overall quality of the included guidelines, according to the 7-point AGREE II scoring system, is  $5.1 \pm 0.27$  for rheumatoid arthritis and  $5 \pm 0.41$  for osteoarthritis. Therapeutic exercises, patient education, Transcutaneous Electrical Nerve Stimulation, and weight control are commonly recommended by the high-quality guideline. The two evaluators had intraclass correlation coefficient values ranging from 0.86 (good) to 0.95 (high).

**Conclusion:** Conclusion: Non-pharmacological interventions were superficially addressed in more than half of the guidelines. Thus, guidelines creators should use the AGREE II criteria when developing guidelines.

## 152

### **The Implementation of Ottawa Panel Evidence-Based Clinical Practice Guidelines for Aerobic Walking Programs in the Management of Osteoarthritis: The PEP (Participant Exercise Preference) Study**

Laurianne Loew (University of Ottawa, Ottawa); Gino De Angelis (University of Ottawa, Greely); Lucie Brosseau (University of Ottawa, Ottawa)

**Objective:** Osteoarthritis (OA) is the most common disabling disorder affecting joints, such as the knees and hips (Klippel et al. 2008) with over 4.4 million Canadians suffering from this joint disease (Statistics Canada, 2011). The main objective of this pilot RCT was to evaluate the effect of participants' exercise preference. We did examine the hypothesis that participants who follow their preferred aerobic walking program: 1) supervised (S) or 2) unsupervised (U), combined with a BI component, will be more encouraged and satisfied, thus enhancing their walking adherence through the 9-month study period, compared to individuals who do not obtain their preferred choice of aerobic walking program, among people diagnosed with knee OA.

**Methods:** This is a single blind RCT with a two-stage, two-group parallel design, based on a patient

treatment preferences model (Cahill et al. 1996). Sixty four (32 in each group) adult individuals with OA were recruited in Ottawa, through local newspapers and by telephone. The selected participants were randomized to one of two groups: (1.1) a 9-month supervised community-based walking program with BI (WB<sub>S</sub>), or (1.2) a 9-month self-directed unsupervised walking program supplemented with a multifaceted BI (WB<sub>U</sub>).

**Results:** Adherence to walking exercise was assessed at 3, 6 and, 9 months, and influencing factors determining adherence were also identified at 3 months. We secondly evaluated if favorable effects on clinical outcomes as well as drop-out rate were demonstrated among participants who presented a preference, either supervised or unsupervised and who obtain their preferred choice of program compared to participants who did not obtain their preferred choice of program through the 9-month study period.

**Conclusion:** Older individuals with OA who received a supervised structured community-based aerobic walking program combined with a multifaceted BI (WB<sub>S</sub>) demonstrated greater adherence rate compared to a self-directed unsupervised/unstructured walking program supplemented with a multifaceted BI (WB<sub>U</sub>). It addresses questions of clinical and scientific importance to identify the main strategies to promote the long-term adherence of community-based walking program. It also guides clinical decision-making of health professionals in rehabilitation sciences, by implementing an evidence-based walking program in existing health organizations (e.g. Public Health: City of Ottawa). Therefore, preference for improving adherence rates is an innovative approach that addresses a new knowledge gap.

## 153

### **Eosinophilic Cystitis: A Case Report and Review of the Literature**

Carrie Ye (Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

**Case Report:** Background: Eosinophilic cystitis is a rare inflammatory condition of the bladder characterized by eosinophilic infiltration of the bladder wall. Although most often diagnosed by the urologist performing the bladder wall biopsy, patients may be referred to rheumatology for further work-up and treatment for a localized hypereosinophilic condition. Objective: (1) To describe a patient referred to rheumatology for management of severe eosinophilic cystitis; (2) perform a literature review of eosinophilic cystitis and its management. Methods: A chart review of the patient was performed. A PubMed search was completed using key words: “eosinophilic cystitis”, “hypereosinophilia”, “steroid”, “antihistamine”, and “immunosuppressant”. Results: MB, a previously healthy 43-year-old man, presented with acute urinary retention requiring catheter insertion. He was diagnosed with benign prostatic hypertrophy and completed green laser surgery for partial removal of his prostate. From the initial catheter insertion, he developed gross hematuria, pelvic discomfort and urinary frequency. These symptoms continued after catheter removal post-operatively. Over six months, the patient lost forty pounds. He was treated with multiple courses of antimicrobials without relief before admission to hospital with anemia and gross hematuria. He underwent cystoscopy with biopsy of his bladder wall, confirming eosinophilic cystitis. MB was referred to rheumatology for further investigation and management. In the absence of a systemic eosinophilia and other organ involvement, MB was diagnosed with isolated eosinophilic cystitis, not part of a hypereosinophilic syndrome. After reviewing the literature for potential causes and management of eosinophilic cystitis, he was started on oral prednisone and an antihistamine (cetirizine). Within 2 weeks of initiating this therapy, the gross hematuria had resolved and the urinary frequency had improved. Conclusion: Eosinophilic cystitis is a rare condition that a rheumatologist may be asked to manage. There are fewer than 200 reports of this condition in the literature. It can occur as part of a hypereosinophilic syndrome or independently. This unusual inflammatory condition appears to respond to immunosuppression and antihistamines. Knowledge and understanding of the hypereosinophilic syndromes is a part of rheumatology practice, and management of these patients requires collaboration with

urology for treatment.

## 154

### **Therapeutic Options in Fibroblastic Rheumatism: Case Report and Review of the Literature**

Carson Chin (University of British Columbia, Vancouver); Iman Hemmati (Department of Medicine, University of British Columbia, Vancouver); Peter Phillips (Vancouver); John Kellsall (Mary Pack Arthritis Center and St Paul's Hospital, Division of Rheumatology, University of British Columbia, Vancouver)

**Case Report:** Objective: Presentation of a case of a rare inflammatory arthritis, fibroblastic rheumatism (FR), and review of the literature focusing on therapeutic options. Method: A comprehensive review of the English medical literature was completed on FR for its clinical features, diagnosis and treatment with a specific focus on therapeutic options. Treatment outcomes in the literature are reported and recommendations based on the review of literature are provided. Results: FR is a rare dermatoarthritis characterized by cutaneous nodules and polyarthritis. FR is rare and treatment recommendations are based solely on case reports. We present a case of a 33-year-old female with inflammatory arthritis, cutaneous nodules, and flexion contractures of her fingers. Diagnosis of FR was made based on clinical features and biopsy showing spindle cell proliferation and increased cellularity. Treatments in the past have included prednisone, methotrexate, hydroxychloroquine, NSAIDs, TNF blocking agents, and interferon alpha among several others. Treatment response is unpredictable with varying degrees of success. On literature review, methotrexate has shown the most promise in the treatment of FR. Conclusion: In our experience, adalimumab in combination with prednisone showed good clinical response and was found to be superior to methotrexate with significant improvement of arthritis and nodules.

## 155

### **Ankylosing Spondylitis Remission with Imatinib**

Catharine Dewar (Lions Gate Hospital, North Vancouver); Stephen Nantel (Leukemia/Bone Marrow Transplant Program of B.C., Vancouver); David Spouge (Lions Gate Hospital, North Vancouver)

**Case Report:** A 40 year old man with HLA-B27 positive AS since age 22 was poorly controlled with NSAIDs or low dose prednisone. His BASDAI was 8.4 with 4 hours of morning stiffness, and his CRP was 12.59 mg/L. He had suffered from sinusitis with facial cellulitis and septicemia in Feb. 2006 and his white cell count (WCC) was 16.0 giga/L with a left shift read as infection. He recovered with intravenous antibiotics and was being considered for infliximab 'biologic' therapy for AS when a repeat WCC was done 3 months later. This showed 79.2 giga/L WCC: with 58.6 neutrophils, 2.4 basophils, 2.9 metamyelocytes, 6.5 myelocytes, 1 NRBC and occasional blasts. Bone marrow aspirate 1 week later confirmed Philadelphia chromosome positive chronic myelogenous leukemia (CML), with an abnormal M:E ratio of 10:1. Discontinuation of prednisone and short-term therapy with hydroxyurea normalised the WCC. Treatment with 400 mg daily imatinib was started within 2 weeks. He achieved a cytogenetic remission of CML within 3 months with a 2.43 log reduction in BCR/ABL1 transcript. Repeat bone marrow aspirate showed a normal M:E ratio of 2.5:1. He achieved the target 4.0 log reduction of BCR/ABL1 transcript in Sept. 2010. Unexpectedly, his AS symptoms slowly improved and his use of NSAIDs diminished and then stopped completely. His BASDAI improved to 1.0 with no morning stiffness. An MRI scan done in March 2013 showed no bone marrow edema and no inflammation in the spine or sacroiliac joints on Fast STIR images. Clinical improvement with imatinib was reported in 3 HLA-B27 positive AS patients in an uncontrolled study in 2006 (K. Eklund et al; Rheumatology 45:1575-76). Unfortunately, MRI imaging was not used in this small study to confirm the spinal anti-inflammatory response to imatinib. Our patient is the first case in the world literature with a major molecular response to imatinib for CML, along with a clinical and



radiological remission of his AS. We estimate the likelihood of finding a patient with concurrent AS and CML to be less than 1 in 100 million. This exceedingly rare patient may have serendipitously opened up a new avenue for 'biologic' therapy of AS. Further study of AS patients using imatinib or other selective tyrosine kinase inhibitors implicated in the pathogenesis of inflammation, is clearly needed.

156

### **Impact of Socioeconomic Status on Survival in Connective Tissue Disease Associated and Idiopathic Pulmonary Arterial Hypertension**

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**Objective:** Poorer health outcomes for persons with chronic diseases have been reported in association with lower socioeconomic status (SES). No such evaluation exists for patients with connective tissue disease associated pulmonary arterial hypertension (CTD-PAH). We evaluated the impact of SES on survival of patients with CTD-PAH and idiopathic PAH (IPAH).

**Methods:** A retrospective cohort study of patients attending the University Health Network Pulmonary Hypertension Programme and the Toronto Scleroderma Program was conducted. Using postal codes and census information for median household income, SES (low, middle, high) was assigned to each individual. Kaplan Meier curves were used to compare survival in different SES groups.

**Results:** 600 patients (n=445 CTD, n=155 IPAH) were identified. There were 209 deaths (n=177 CTD, n=32 IPAH). CTD-PAH patients stratified by SES had 5-year survival of 81.4% (95%CI 68.7%, 96.3%) for high SES, 87.9% (95%CI 77.2%, 100%) for middle SES and 74.1% (95%CI 62.2%, 88.3%) for low SES. IPAH patients stratified by SES had 5-year survival of 84.4% (95%CI 73.5%, 96.9%) for high SES, 89.2% (95%CI 79.7%, 100%) for middle SES and 75.7% (95%CI 64.4%, 89.0%) for low SES. IPAH patients with low SES had worse survival (log rank test p=0.03), and CTD-PAH patients had similarly findings that bordered on statistical significance (log rank test p=0.08).

**Conclusion:** Socioeconomic inequalities appear to impact survival. Further research is required to understand the underlying basis for these findings.

157

### **Erosion Case Definition and Scoring Reliability Exercise using a New Outcome Measurement Tool, High-Resolution Peripheral Quantitative Computed Tomography, in Rheumatoid Arthritis**

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**Objective:** High-resolution peripheral quantitative computed tomography (HR-pQCT) is a novel imaging instrument for bony damage in rheumatoid arthritis (RA). Agreement on a case definition for pathologic

erosions is required given the sensitivity of HR-pQCT for detecting cortical bone disruptions. The reliability of erosion detection and measurement between readers is crucial to evaluate with this new technology, as HR-pQCT is undergoing validation as an outcome measurement tool.

**Methods:** HR-pQCT images of the 2<sup>nd</sup> and 3<sup>rd</sup> metacarpophalangeal joints of RA patients and control subjects were used in an iterative process to achieve consensus on a case definition for erosions. This case definition was applied by 11 independent readers to score 82 joints. Each surface (radial, ulnar, palmar, dorsal) of the proximal phalanx and metacarpal head were characterized for image quality, the presence of a cortical break, the appearance of the cortical defect (physiological or pathological) and a total count of the number of pathologic erosions. Pathologic erosions were further characterized in 2 perpendicular planes for their maximum width and depth.

**Results:** The case definition of erosion was based on the size and shape of the defect so as to eliminate physiological (eg vessel channel) defects. Of the 656 surfaces analyzed in the reliability exercise, 6 (0.9%) were felt to be of inadequate quality for analysis by the 10 readers and were removed. Inter-reader reliability for erosion detection was excellent with a kappa score of 0.9024 ( $p < 0.0001$ ), with higher kappa scores between experienced readers. Images with discrepant scoring by more than 2 readers were reviewed as a group a second time, with resolution of all cases except for 2 which were lower quality images with multiple bony pathologies overlapping each other (eg vessel channels with superimposed osteophytes masquerading as erosions). Erosion size ranged from 0.16 to 0.89 mm in maximal width and 0.028 to 0.801 mm in maximal depth, with up to 6.3% variability in measurement between readers.

**Conclusion:** We have devised a new case definition for erosions visualized with a novel sensitive imaging tool. Inter-reader reliability for erosion detection and measurement is high, yielding promise to use HR-pQCT as an outcome measurement tool for bony damage.

## 158

### **Serological Analysis of Patients with Positive Anti-CCP Antibodies Referred through a Rheumatology Triage System**

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**Objective:** Antibodies to cyclic citrullinated peptide (CCP) are generally considered to be a highly specific (>90%) and sensitive (~70%) biomarker for the diagnosis of rheumatoid arthritis (RA). The objective was to determine the serological profiles of patients referred through a central triage system for evaluation of a positive anti-CCP test and to determine the potential value of serological profiles in assessing the urgency of referrals and the clinical diagnosis.

**Methods:** Cases that met three criteria were included in the study: 1) referred to Rheumatology Central Triage from July 2009-December 2012 (n=20,389); 2) reason for referral was a “positive anti-CCP” (n=568); 3) were evaluated by specialists at Foothills or Rockyview Medical Centres (n=315). An administrative serological database was used to retrieve specific anti-CCP test results. Where ANA or ENA serological information was absent from the initial referral, serological tests were retrospectively performed by technologists with >7 years of experience. on sera retrieved from storage. ANA was by immunofluorescence on HEp-2000 cells (ImmunoConcepts, Sacramento, CA) and ENA by addressable laser bead immunoassay (FIDIS: BMD, Paris, France).

**Results:** Of the 315 anti-CCP positive referrals, 79% (n=250) were high positive (< 60 absorbance units AU); 5.4% (n=17) were moderately positive (40-59 AU) and 15.2% (n=48) were low positive (20-39AU). The average anti-CCP value was 118.20 AU (range of 19.851 - 415.13). The three most common primary ANA patterns were nuclear speckled (n=93; 42.8%), homogeneous speckled (n=92; 42.3%), and nucleolar

(n=37; 17.1%) with titres ranging from 1/160-1/5120. Thirty-five patients [12.5%] had a positive ENA with the four most common specificities being anti-Ro52/TRIM21 [n=15; 6.1%], anti-SS-A/Ro60 [n=9; 3.6%], anti-topoisomerase I (Scl-70) [n=5; 2.0%] and SSB/La [n=3, 1.2%]. Of note, 1 [2.3%] tested positive for anti-dsDNA.

**Conclusion:** More than 10% of patients referred through a central triage system for evaluation of a positive anti-CCP and the possible diagnosis of RA had a variety of other definable autoantibodies that may provide additional information to the clinician. The consulting rheumatologist's diagnoses are currently being compiled to determine the positive predictive value of anti-CCP in accurately identifying RA patients as well as demographic and other clinical parameters.

## 159

### **Obesity and Rheumatoid Arthritis: A Systematic Review**

Christopher Sparks (University of Liverpool, Liverpool); Robert Moots (University of Liverpool, Liverpool); Nicola Goodson (University of Liverpool, Liverpool)

**Objective:** Background Obesity may be an inflammatory condition. Increasing adiposity results in heightened production of adipokines, which in turn can regulate inflammation. In the past, research in rheumatoid arthritis (RA) has viewed BMI as a demographic variable that requires omission or adjustment on further analysis. More recently, however, the potential disease and treatment modifying effect of obesity in RA have become recognised and studies have focussed on investigating possible associations between increasing adiposity and disease characteristics. Objectives We undertook a systematic review of the published literature to assess the strength of the effect that obesity may have on RA disease characteristics, addressing the effect of obesity on (a) risk of developing RA; (b) disease activity; (c) radiographic joint damage (RJD); and (d) disability in RA.

**Methods:** Web of Science (SCI-EXPANDED and CPSI-SI), European League Against Rheumatism (EULAR) abstract archive and American College of Rheumatology (ACR) meeting indexes, were searched using keywords: “rheumatoid arthritis AND”; “obesity”; “obese”; “overweight”; “body mass index”; “adiposity”; “adipose tissue”; “body fat”; “body composition”; “waist circumference”. Review articles, case reports and studies primarily focussing on biochemical pathways/adipokines were excluded. Further hand searches of reference lists were also performed. Identified cohort and case-control studies were scored using the Newcastle-Ottawa Quality Assessment Scale.

**Results:** Eight hundred and twelve studies were identified and screened, with 56 relevant to the review. Six out of 9 (1 cohort, 5 case-control) studies identified a positive association between obesity and risk of developing RA; 3 large-scale cohort studies found no relationship between obesity and development of RA. A range of findings have been observed with regards to obesity and disease activity, with 2 cohort and 2 cross-sectional studies identifying a modest positive association between increasing BMI and disease activity, whilst 6 cross-sectional studies found no significant relationship. The majority (8 out of 9 studies) of the current evidence base observed an inverse association between obesity and RJD; findings of this relationship being specific to ACPA or RF positivity were not replicated consistently. Eight out of 9 studies assessing the effect of obesity on disability identified a positive association between increasing BMI or obesity and self-reported disability scores, with further evidence from 11 abstracts supporting this.

**Conclusion:** Obesity appears to have an inverse association with RJD and a positive association with disability. Current evidence is inconclusive in regards to the effects of obesity on risk of developing RA, and on RA disease severity.

## 160

## **Bisphosphonates for Steroid-Induced Osteoporosis: A Meta-Analysis**

James Yeung (University of Alberta, Edmonton); Claire Allen (University of Alberta, Edmonton); Joanne Homik (University of Alberta, Edmonton)

**Objective:** To assess the efficacy of bisphosphonates for the prevention and treatment of corticosteroid-induced osteoporosis using a Cochrane Collaboration systematic review and meta-analysis.

**Methods:** We searched MEDLINE and EMBASE databases and International Pharmaceutical Abstracts (IPA) via OVID (January 1997 to June 2013) for relevant articles and conference proceedings. We included randomized clinical trials satisfying the following criteria: 1) prevention or treatment of corticosteroid-induced osteoporosis; 2) adults taking a mean steroid dose of 7.5 mg/day or more; 3) active treatment included bisphosphonates of any type alone or in combination with calcium or vitamin D; 3) Comparator treatment included a placebo with or without calcium or vitamin D; and 4) reporting relevant outcomes. We excluded trials dealing with transplant-associated osteoporosis. The primary outcome of interest was the change in bone mineral density (BMD) at the lumbar spine and femoral neck at 12 months. Data were analyzed with data from an existing Cochrane review by the same author (1) using a fixed-effects model.

**Results:** A total of 31 trials with 2603 patients are included in the meta-analysis for BMD change at the lumbar spine, and a total of 24 trials with 1969 patients are included in the meta-analysis for BMD change at the femoral neck. Twenty seven and twenty one trials in the respective analyses above were new or updated publications since the original meta-analysis. There were 15 prevention trials and 16 treatment trials and for this analysis both types of trials were combined. Results are reported as a weighted mean difference of the percent change in BMD between the treatment and placebo groups. Overall, the active treatment groups reported stabilization or increase in BMD, while the placebo groups showed decreased BMD over the study period. At the lumbar spine, the weighted mean difference of BMD between the treatment and placebo groups was 2.76% (95% CI 2.58, 2.94). At the femoral neck, the weighted mean difference was 2.44% (95% CI 2.19, 2.69).

**Conclusion:** On average, bisphosphonate use resulted in a 2.4-2.8% increase in bone density as compared to treatment with calcium or vitamin D alone over a one-year period. We conclude that bisphosphonates are effective at preventing and treating corticosteroid-induced bone loss at both the lumbar spine and femoral neck.1 Homik J et al. A meta-analysis on the use of bisphosphonates in corticosteroid-induced osteoporosis. *J Rheumatol* 26(5): 1148-57, 1999.

## **161**

### **Inflammatory RANK-Expressing Neutrophils Resorb Bone in K/BxN Arthritis**

Daniel Rusu (Centre de Recherche en Rhumatologie et Immunologie, Centre de Recherche du CHUQ, Quebec); Isabelle Allaeys (Quebec); Irina Gymnina (Quebec); Patrice Poubelle (Quebec)

**Objective:** Abnormal local bone destruction leads to functional handicap in rheumatoid arthritis (RA). Osteoclasts, the bone-degrading cells, regulate bone resorption through their expression of RANK. Inflammatory neutrophils which massively infiltrate RA joints (*Arthritis Rheum* 40:217) express RANK (*Arthritis Res Ther* 9:R25). To demonstrate that RANK-expressing neutrophils resorb bone in vivo, a specific deletion of RANK in neutrophils will be set up in mice and K/BxN arthritis will be induced. The K/BxN arthritis is pathophysiologically similar to RA (*Trends Mol Med* 10:40), and neutrophils are the main cell implicated in its initiation and progression (*J Immunol* 167:1601). Generation of conditional

knockout (CKO) mice for RANK specifically in neutrophils, induction of arthritis into CKO mice by K/BxN serum transfer, and evaluation of bone destruction by micro-computer tomography (CT) of affected joints will be specific objectives.

**Methods:** CKO mice (C57BL/6) with RANK-deleted neutrophils were obtained by crossing a Cre knock-in mouse (Elane<sup>tm1(cre)Roes</sup>) in which Cre recombinase is expressed selectively in neutrophils under the control of their membrane elastase promoter, and a floxed RANK mouse in which RANK exons 2 and 3 are flanked by two loxP sites. In the offsprings from intercrosses between the two strains, Cre-loxP site-dependent recombination occurs only in neutrophils expressing Cre gene, thereby deleting RANK gene in neutrophils. The induction of K/BxN arthritis in CKO mice (RANK<sup>-/-</sup>-Cre<sup>+/-</sup>) and in control mice (RANK floxed<sup>+/+</sup>; ElaneCre<sup>+/-</sup>) was performed by injecting arthritogenic serum from K/BxN mice. Inflammatory arthritis was evaluated (clinical score, paw thickness), and mice were sacrificed after 10 days. To quantify bone destruction, micro-CT of involved joints was performed, and results were expressed as BV/TV (bone volume/tissue volume).

**Results:** 1- Viable CKO mice (RANK<sup>-/-</sup>; Cre<sup>+/-</sup>) were generated and validated (genotype). 2- Induction of K/BxN arthritis in (RANK<sup>+/+</sup>) and (ElaneCre<sup>+/-</sup>) control mice has led to a significant (p< 0.05) bone loss of 15% and 16% in involved joints, respectively, as compared to mice treated with PBS instead of arthritogenic serum. 3- K/BxN arthritis in CKO mice (RANK<sup>-/-</sup>; Cre<sup>+/-</sup>) did not induce bone loss in inflammatory joints.

**Conclusion:** 1- K/BxN arthritis provoked local bone destruction in Cre knock-in mice and in floxed RANK mice. The deletion of RANK in neutrophils protected against abnormal bone destruction in joints affected by K/BxN arthritis. 2- This is the first study which brings evidence that neutrophils can be bone-degrading cells directly implicated in bone destruction of inflammatory arthritis through their expression of RANK.

## 162

### **Tuberculous Myositis Presenting as a Relapse of Dermatomyositis**

David Shaw (University of Western Ontario, London); Sherry Rohekar (University of Western Ontario, London)

**Case Report:** Tuberculous myositis is a rare complication of infection with *Mycobacterium tuberculosis*, and symptoms can mimic idiopathic inflammatory myositis. We present a case of a 53 year-old man with a 12 year history of biopsy-confirmed dermatomyositis (DM) who was re-referred to our office for relapse of his symptoms after successful therapy of DM using prednisone. He had elevated creatinine kinase and inflammatory markers, and was re-started on high-dose prednisone and methotrexate. He shortly thereafter required admission to hospital for pain and swelling of the right leg and arm. Imaging and surgical biopsy of the leg swelling revealed muscle necrosis, and culture revealed *Mycobacteria tuberculosis* infection. CT imaging of the thorax revealed multiple calcified granulomata. He was diagnosed with tuberculous myositis, and treatment of his tuberculosis with standard therapy in addition to prednisone and intravenous immunoglobulin (IVIg) resulted in improvement of his DM symptoms. This case report reviews the existing literature regarding tuberculous myositis in patients with co-existing rheumatologic diseases.

## 163

### **Glucocorticosteroids and Mortality Risk in Rheumatoid Arthritis - Results of a Population Based Study**

Diane Lacaille (Arthritis Research Centre of Canada and University of British Columbia, Richmond); Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Richmond); Eric Sayre

(Arthritis Research Centre of Canada, Richmond); Michal Abrahamowicz (McGill University, Montreal); John Esdaile (Arthritis Research Center of Canada and Division of Rheumatology, University of British Columbia, Richmond)

**Objective:** Glucocorticosteroids (GC) are frequently used in the management of rheumatoid arthritis (RA). Potential side-effects could increase mortality risk, yet suppression of disease activity could reduce mortality risk. We evaluated the association between exposure to GC and risk of mortality in RA, using a population-based incident RA cohort with administrative health data.

**Methods:** Using administrative billing data, we assembled a population-based cohort including all incident RA cases between 01/1996 and 03/2006, followed until 03/2010. Cases with GC use prior to RA onset were excluded. Administrative data were obtained on all medications since 09/1995; MD visits, hospitalizations, and tests since 01/1990. The Cox proportional hazard model (PHM) was used to estimate risk of death associated with GC exposure. Time analyzed was from index RA date to death or end of follow-up. GC exposure was defined as any dispensed prescription for oral GC during follow up, and was measured using three time-dependent exposure variables, in separate models, representing current dose (in mg prednisone equivalent), past cumulative dose and past cumulative duration of exposure. We used propensity scores (PS) to control for the observed differences between GC users and non-users, calculated at the time of initiating GC, using markers of RA severity, as well as co-morbidities increasing risk of death. Variables for which there was residual imbalance across PS quintiles were also included as covariates in the model. PHM analyses were also adjusted for age, gender, calendar year of inclusion, PS, as well as time-dependent variables representing exposure to RA medications that could influence mortality risk (MTX, biologics and NSAIDs).

**Results:** Our sample includes 18,215 incident RA cases (mean (SD) age: 57.2(17.1), 66.5% females) providing 128,799 person-years of follow-up, with 5,326 RA cases (29.2%) exposed to GC. We observed 2,881 deaths. Exposure to GC was associated with an increased risk of death in all models [aHR (95%CI) =1.22 (1.21;1.24) per 5 mg of current dose; 1.11 (1.10;1.12) per 1 gm of cumulative dose; and 1.30 (1.26;1.35) per 1 yr of cumulative duration, all  $p < 0.0001$ ]. Limitations of our study are those inherent to observational study, including possible effect of residual or unmeasured confounding, and selection bias from non-random allocation of treatment.

**Conclusion:** In our population-based cohort, exposure to GC was associated with a significant increase in mortality. Given the increased mortality risk of RA, this has important implications for health care providers and people with arthritis.

## 164

### **Risk of Venous Thromboembolism in Individuals with Dermatomyositis and Polymyositis**

Erin Carruthers (Arthritis Research Centre of Canada, Richmond); Eric Sayre (Arthritis Research Centre of Canada, Richmond); Kamran Shojania (University of British Columbia, Vancouver); Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Richmond)

**Objective:** Data on the risk of venous thromboembolism (VTE) including deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients with dermatomyositis (DM) and polymyositis (PM) at the population level are lacking. To fill this knowledge gap, we estimated the risk of newly recorded VTE among incident cases of DM and PM compared to controls from the general population, using physician billing and hospitalization databases that cover the entire population of British Columbia.

**Methods:** We identified a retrospective cohort (1996-2010) of adults with incident DM and PM, and up to 10 age-, sex- and entry-time-matched controls from the general population. DM and PM cases were defined as follows: a) new diagnosis of DM or PM on at least two visits within a two-year period by a non-rheumatologist physician; or b) diagnosis of DM or PM on at least one visit by a rheumatologist or from hospitalization. We created DM and PM cohorts and corresponding control cohorts after excluding individuals with prevalent VTE at baseline. Our outcome was first newly recorded VTE from an outpatient visit (DVT only), hospital (VTE), or death certificate (VTE). In addition, for nonfatal events, we required the use of anticoagulant medications within six months of the VTE event. We estimated relative risks (RRs) comparing DM or PM cases with the comparison cohort before and after adjusting for potential risk factors.

**Results:** We identified 355 and 443 cases with incident DM and PM, respectively. After adjusting for risk factors, both DM and PM cases were associated with a significantly increased risk of VTE (RR= 7.1 (95%CI 2.8-18.3) and RR= 7.4 (95%CI 3.6-15.2), respectively). Similar results were seen for DVT (RR= 8.7 (95%CI 2.8-27.3) and 5.6 (95%CI 2.0-15.7)). However, risk of PE was statistically significant only in PM (RR= 7.0 (95%CI 2.9-17.0)). When assessing the time trends since diagnosis we found that risk of VTE was significantly higher within the first year of diagnosis (RR=16.1 (95%CI 4.4-64.2) and RR= 25.3 (95%CI 9.0-81.0) for DM and PM, respectively) and progressively attenuated over time. Similar time trends were observed for DVT and PE individually.

**Conclusion:** This is the first population-based study to demonstrate an increased risk of VTE in patients with DM and PM, especially within the first year of diagnosis. This calls for increased vigilance in monitoring VTE, a potentially preventable complication in individuals with DM and PM.

## 165

### **The Role of Biological Agents in the Management of Large Vessel Vasculitis (LVV): A Systematic Review and Meta-Analysis**

Mohammed Osman (University of Alberta, Edmonton); Christian Pagnoux (Mount Sinai Hospital, Toronto); Donna Dryden (University of Alberta, Edmonton); Dale Storie (University of Alberta, Edmonton); Joanne Homik (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

**Objective:** Background: Giant cell arteritis (GCA) and Takayasu's arteritis (TAA) are large vessel vasculitides (LVV) for which corticosteroids (CS) are the mainstay for treatment. In patients unable to tolerate CS, biological agents have been used to manage LVV with variable efficacy. Objective: To systematically review the efficacy (remission and reduction of CS use) and safety of biological agents in patients with LVV.

**Methods:** Methods: We searched 5 electronic databases (inception to October 2012) and conference abstracts with no restrictions. Two reviewers independently selected studies, extracted data and assessed methodological quality. Our protocol was registered in PROSPERO.

**Results:** Results: We included 25 studies (3 RCTs, 5 cohort studies, 17 case series). 98 GCA and 113 TAA patients received biological agents. The RCTs using anti-TNF agents (infliximab, etanercept and adalimumab) did not suggest a benefit in GCA. GCA patients receiving tocilizumab, in case series, achieved remission and reduction of corticosteroid dose (mean difference = -16.55 (95% CI: -26.24, -6.86). Patients with refractory TAA treated with infliximab discontinued CS 52 % of the time. Remission was variably defined and the studies were clinically heterogeneous which precluded further analysis.

**Conclusion:** Conclusion: Tocilizumab may be effective in the management of LVV, although the evidence comes from case series. Infliximab may be effective in patients with refractory TAA. This study emphasizes a complete review, with the most recent findings of biological treatment in LVV. Future studies

defining remission as clinical, serological and radiographic assessments are necessary in order to more clearly establish a role for biological agents to treat LVV.

166

### **Neuropsychiatric Systemic Lupus Erythematosus: Association with Global Disease Activity**

Emma Morrison (Halifax); Stephanie Carpentier (Halifax); Emily Shaw (Halifax); Steve Doucette (Halifax); John Hanly (Dalhousie University, Halifax)

**Objective:** To determine if patients with neuropsychiatric (NP) events attributed to systemic lupus erythematosus (SLE) have higher global disease activity than patients with NP events not attributed to SLE.

**Methods:** Patients were recruited from an academic lupus clinic. Global disease activity was measured with the SLE disease activity index 2000 (SLEDAI-2K) and organ damage with the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (SDI). NP disease was defined using the ACR case definitions. A priori decision rules were used to determine the attribution of NP events to SLE and non-SLE causes and this was done independently of completion of SLEDAI-2K forms.

**Results:** There were 68 patients [age (mean  $\pm$  SD)  $40.8 \pm 15.2$  years, 85% female, 94% Caucasians] with 126 NP events. SLEDAI-2K scores in patients with NP events attributed to SLE were higher than in patients with NP events attributed to non-SLE causes (mean  $\pm$  SD:  $12.1 \pm 6.3$  vs.  $5.9 \pm 5.1$ ;  $P < 0.0001$ ). This difference persisted when NP variables were removed from the SLEDAI-2K (mean  $\pm$  SD:  $7.4 \pm 5.4$  vs.  $5.5 \pm 4.6$ ;  $P = 0.04$ ). Group differences in SLEDAI-2K scores occurred in patients with CNS (mean  $\pm$  SD:  $7.5 \pm 5.6$  vs.  $5.4 \pm 4.7$ ;  $P = 0.035$ ) and diffuse (mean  $\pm$  SD:  $8.9 \pm 5.8$  vs.  $5.4 \pm 4.8$ ;  $P = 0.005$ ) NP events, rather than in patients with PNS (mean  $\pm$  SD:  $6.8 \pm 4.8$  vs.  $7.0 \pm 2.8$ ;  $P = 0.91$ ) and focal (mean  $\pm$  SD:  $6.0 \pm 4.8$  vs.  $6.2 \pm 2.9$ ;  $P = 0.91$ ) events. There were no significant differences in total SDI scores comparing NP events due to SLE vs. non-SLE causes (mean  $\pm$  SD:  $2.1 \pm 1.8$  vs.  $1.7 \pm 1.7$ ;  $P = 0.28$ ) even when NP variables were omitted.

**Conclusion:** Increased global SLE disease activity in organs outside of the nervous system is associated with concurrent NP events attributed to SLE, particularly for diffuse NP and CNS NP events. The findings have diagnostic and therapeutic implications for SLE patients with NP events and inform pathogenetic mechanisms underlying NPSLE.

167

### **Rheumatological Causes of Subglottic Stenosis – A Case Series**

Evelyn Kwok (University of Alberta, Edmonton); Paul Davis (University of Alberta, Edmonton); Anna Oswald (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

**Case Report:** Introduction: Subglottic stenosis is the narrowing of the airway below the level of the vocal folds. Etiologies for subglottic stenosis include trauma, infection, autoimmune, neoplastic, congenital and idiopathic. Subglottic stenosis due to autoimmune diseases is rare. We report three cases of subglottic stenosis observed by the Rheumatology Division at the University of Alberta. Objectives: To review the case presentations of a series of patients with a possible autoimmune basis for their subglottic stenosis.

Case Series: Case 1: A 54 year-old male with biopsy-proven subglottic stenosis secondary to sarcoidosis presented with relapsing episodes of respiratory distress. Despite treatment with systemic corticosteroids and methotrexate, the patient was hospitalized on four occasions with respiratory distress and eventually required placement of a permanent tracheostomy. Case 2: A 51 year-old female with a history of juvenile idiopathic arthritis presented with stridor, shortness of breath on exertion, sinusitis and hematuria and was found to have subglottic stenosis. A diagnosis of granulomatosis with polyangiitis (Wegener's) was made on a clinical basis, however both subglottic and renal tissue pathology was inconclusive. Her disease was



managed with systemic corticosteroids and multiple cycles of cyclophosphamide. Despite this she had multiple exacerbations and required repeated dilatation of her subglottic stenosis. Case 3: A 34 year-old female presented with a fifteen year history of relapsing symptoms of shortness of breath and cough found to be due to stenosis involving initially the subglottic region which then progressed to involve both mainstem bronchi. Biopsy has shown evidence of inflammation on pathology. Despite a tracheal resection, multiple tracheostomies, and bronchoscopic dilatations of her subglottic stenosis and systemic corticosteroid therapy her disease has been poorly controlled. Conclusion: Though rare, subglottic stenosis is a potentially life-threatening manifestation of rheumatological disorders that warrants prompt recognition and management. Localized treatment remains the mainstay of therapy and response to systemic immunosuppression is often poor. The differential diagnosis of this condition is broad, and close clinical evaluation and assessment are required for diagnosis and management. Disease control is often difficult to achieve and exacerbations are common; therefore, close clinical follow-up of these patients is warranted.

168

### **The Development of Psoriasis in Patients on Biological Response Modifiers**

Francois Gagnon (University of Ottawa, Ottawa); Jacob Karsh (University Of Ottawa, Ottawa)

**Objective:** This study investigated (1) the type of psoriasis induced with a biological response modifier (BRM) and (2) the type of psoriasis induced according to the underlying disease treated.

**Methods:** Pharmaceutical companies provided information on the development of psoriasis associated with their respective BRMs from internal and external databases. Data was obtained for the following medications: golimumab, infliximab, adalimumab, etanercept, abatacept and rituximab. Data from clinical trials, open-label extensions and prospective cohort studies were reviewed.

**Results:** Presentation of the data by disease and psoriasis subtype was not explicitly reported in all the studies reviewed. A prospective study evaluating the efficacy of TNF inhibitors for various rheumatological conditions reported 8 adverse events (5.3%) of psoriasis, 5 cases of psoriasis vulgaris and 3 cases of palmoplantar pustulosis, in patients with rheumatoid arthritis or ankylosing spondylitis. An association with a particular TNF inhibitor was not observed. Two prospective studies assessing the efficacy of TNF inhibitors for rheumatoid arthritis reported 25 cases (0.2%) of psoriasis, 13 of which were caused by adalimumab, and 3 cases (1.0%) of psoriasis of the vulgaris, palmoplantar pustulosis and guttate subtypes induced by adalimumab therapy. Phase III trials conducted with golimumab for psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis produced 5 cases (0.8%) of psoriasis vulgaris in the placebo arms and 6 cases (0.4%) of psoriasis of the vulgaris (4 cases), nail and pustular subtypes in the treatment arms. Trials conducted with infliximab produced a total of 29 cases (1.8%) and 86 cases (1.5%) of psoriasis in the placebo and treatment arms respectively. A trial investigating etanercept for the treatment of psoriasis reported 2 cases (1.8%) of new-onset pustular and guttate psoriasis and one case of psoriasis exacerbation. Data from 8 clinical trials evaluating the anti-T-cell agent abatacept for rheumatoid arthritis produced a long-term psoriasis incidence rate of 0.57p-y. A phase II trial evaluating the anti-B-cell agent rituximab for chronic fatigue syndrome reported 2 cases (13.0%) of psoriasis exacerbation.

**Conclusion:** This study did not elucidate a clear association between the type of psoriasis induced as an adverse event of BRM therapy and a specific BRM agent or a particular underlying disease. More data is required to further investigate this relationship, including more precise adverse event reporting practices classifying psoriasis cases by their specific subtype.

169

### **Giant Cell Arteritis in an HIV Patient: A Case Report and Review of the Literature**

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(Department of Medicine, University of British Columbia, Vancouver); Kenneth Blocka (The University of British Columbia, Vancouver)

**Case Report:** Objectives: To describe a rare case of giant cell arteritis (GCA) in an HIV positive patient 2. Review of literature on large vessel vasculitis associated with HIV. Method: A rare case of HIV positive patient with biopsy proven aortitis was presented. English medical literature was reviewed for HIV and large vessel vasculitis with focus on GCA and its manifestations in HIV patients. Results: Our patient is a 66 years old Caucasian HIV positive male, with weakly positive ANA, anti-CCP, myeloperoxidase ANCA titers, who was on HAART treatment for 15 years with undetectable viral load. He was found to have progressive asymptomatic ascending aortic aneurysm and underwent elective surgical aortic repair. The pathology result revealed GCA. His CRP which was elevated (160 mg/L) prior to surgery was normalized post operation. Based on literature review, large elastic artery involvement in HIV is uncommon and not well documented. Most large artery involvement in HIV patients has an infective etiology. Non-infective cases are usually secondary to leucocytoclastic vasculitis of the vasa vasora or periadventitial vessels. Conclusion: We describe an extremely rare case of ascending aortitis in an HIV positive patient consistent with GCA based on pathology. The growing use of HAART has led to increased life expectancy in HIV patients along with increased probability of concordant autoimmune diseases including vasculitis. GCA although rare should be considered in the differential diagnosis of large vessel involvement in patients with HIV.

## 170

### **Does Socioeconomic Status Affect Outcomes in Early Rheumatoid Arthritis? Data from a Multi-Site Canadian Inception Cohort**

Grace Yang (Western University and U of Toronto, London); Vivian Bykerk (Toronto); Gilles Boire (Université de Sherbrooke, Sherbrooke); Carol Hitchon (University of Manitoba, Winnipeg); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Diane Tin (Southlake Regional Health Centre, Newmarket); Boulos Haraoui (Université de Montréal, Montréal); Edward Keystone (Mount Sinai Hospital, Toronto); Janet Pope (University of Western Ontario, London); CATCH Investigators of Canada (Canada)

**Objective:** To assess the impact of socioeconomic status (SES) on outcomes in patients with early inflammatory arthritis using data from the Canadian Early Arthritis Cohort (CATCH) study.

**Methods:** There were 2023 patients recruited to a prospective incident cohort study, and allocated to low- or high-SES groups based on education and income. Outcomes at baseline and 12 months were analyzed in relation to SES including the Disease Activity Score (DAS28), Simplified Disease Activity Index (SDAI), pain, patient global assessment scale (PTGA), the Health Assessment Questionnaire Disability Index (HAQ), and the SF12-v2 Health Survey using correlations and regression analyses.

**Results:** The CATCH population had 43% with high school education or less and 37% in the low-income group (< \$50,000 Canadian per annum household income). The low-education group had higher DAS28 ( $p=0.045$ ) at baseline but was non-significant at 12 months and lower physical component score on SF12-v2 at baseline ( $p=0.018$ ) and 12 months ( $p=0.024$ ). Patients in the low-income group presented with higher HAQ ( $p=0.017$ ), pain ( $p=0.035$ ), PTGA ( $p=0.004$ ), and SDAI ( $p=0.022$ ). Low-income vs. high-income groups were associated with an odds ratio (OR) above the median for: HAQ 1.220 (95% CI 1.013-1.470), PTGA 1.284 (95% CI 1.067-1.546), and SDAI 1.240 (95% CI 1.018-1.509). The predictive value of low income for HAQ persisted at 12 months, OR 1.304 (95% CI 1.018-1.669) but not for other variables.

**Conclusion:** Low SES is associated with higher disease activity, poorer physical function, more pain, higher PTGA, and higher HAQ at baseline. Physical function and HAQ remain worse at one-year follow-up in this population.

171

### **A Screening Failure**

Greg Marcotte (University of British Columbia, Vancouver); Kamran Shojania (University of British Columbia, Vancouver); Andrew Chalmers (Mary Pack Arthritis Treatment Program, Vancouver)

#### **Case Report:**

Anti-Tumor Necrosis Factor (TNF) agents confer an increased risk of latent *Mycobacterium tuberculosis* infection (LTBI) activation. Canadian guidelines recommend screening for LTBI prior to anti-TNF therapy. Immunosuppression is known to reduce the sensitivity of both the TB skin test (TBST) and interferon gamma release assays (IGRA) in observational studies. We report a case of TB pleuritis in a patient on adalimumab despite negative pre-treatment screening for LTBI. A 61 year old female, originally from India, was diagnosed with sero-negative rheumatoid arthritis (RA) in 2011. She was initially treated with methotrexate, sulfasalazine and hydroxychloroquine, and subsequently trialed on methotrexate and leflunomide after inadequate treatment response. Due to continued symptoms, adalimumab was recommended. In February 2012 the patient was reviewed by TB control for LTBI screening. The patient had no known history of TB contacts although she was born in India and had intermittent return travel. At the time of screening she remained on methotrexate and leflunomide. A CXR was normal and a TBST was non-reactive. An IGRA, recommended for further risk stratification, was negative. Adalimumab was subsequently started without TB prophylaxis. In September 2012 the patient developed shortness of breath. Investigations revealed both pericardial and pleural effusions with cultures positive for TB. She had no interval return to India or new TB contacts. Repeat TBST was positive. Repeat IGRA was non-reactive. TB treatment was initiated and adalimumab was suspended. This case illustrates the importance of continued vigilance in patients on anti-TNF therapy with negative LTBI screening in whom initial screening was performed in the setting of immunosuppression. This is particularly relevant given current provincial drug coverage requirements which demand the documented failure of multiple disease modifying anti-rheumatic drugs prior to anti-TNF funding. Consequently, patients are routinely variably immunosuppressed during LTBI screening which may reduce the sensitivity of screening. We propose that LTBI screening be routinely performed at the time of initial RA diagnosis, and prior to DMARD initiation, in order to increase screening sensitivity. Additionally, previous vaccination history should be reviewed and immunizations updated at the time of initial diagnosis. We also propose that re-screening with serial IGRAs and/or TBST may be a useful approach in patients with negative LTBI screening when risk factors for false negative screening exist. Further study is warranted to delineate the ultimate cost-effectiveness of routine re-screening in this setting. Overall, clinicians are reminded of the potential for active TB in all patients receiving anti-TNF therapy.

172

### **Evaluation of the New ACR/EULAR Criteria for the Classification of Systemic Sclerosis in the Canadian Scleroderma Research Group Cohort**

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**Objective:** Background: New classification criteria for systemic sclerosis (SSc) have recently been published and reported to have high sensitivity and specificity. In this study, we aimed to determine the sensitivity of these new 2013 criteria in an independent cohort of SSc subjects, and to compare it to the sensitivity of the 1980 Preliminary classification criteria for SSc. We hypothesized that gains in sensitivity

in the 2013 criteria would be greatest in patients with limited disease, disease of short duration and anti-centromere antibodies. We also assessed the magnitude of the contribution of individual items of the 2013 criteria to the overall sensitivity of those criteria.

**Methods:** Method: SSc subjects are included in the Canadian Scleroderma Research Group cohort if they have a diagnosis of SSc according to an experienced rheumatologist. Clinical and serological data are collected using a standardized data collection protocol and entered into a database. The variables included in the 2013 and 1980 classification criteria for SSc were extracted. Sensitivity was determined by dividing the number of subjects who fit a set of criteria to the total number of subjects in the cohort. Sensitivities in selected clinical sub-groups were also determined. In patients who did not have the 2013 major criterion of skin thickening proximal to the metacarpophalangeal joints (MCPs), we tested the importance of the minor criteria by re-calculating sensitivity after removing individual criterion, alone or in combination.

**Results:** Results: A total of 724 SSc patients were included in the study. The majority were females (86%), mean age was 55.8 years, mean disease duration was 10.9 years, and 59% had lcSSc. Overall, the sensitivity of the 2013 criteria was higher (98.3%) than that of the 1980 criteria (88.3%). This pattern was consistent among a number of sub-groups, including those with lcSSc (98.8% versus 85.6%), anti-centromere antibodies (98.9% vs 79.8%), disease duration  $\leq 3$  years (98.7% vs 84.7%) and no skin involvement proximal to the MCPs (97% vs 60%). In the latter sub-group, removing Raynaud phenomenon and sclerodactyly from the 2013 criteria reduced the sensitivity to 77% and 78%, respectively. Removing both sclerodactyly and puffy fingers reduced the sensitivity to 61%.

**Conclusion:** Conclusion: Overall, the 2013 classification criteria for SSc are substantially more sensitive than the 1980 criteria. The improvement in sensitivity is most striking among sub-groups known to have been missed by the 1980 criteria. The addition of Raynaud phenomenon and puffy fingers to the 2013 criteria accounts for important gains in sensitivity.

## 173

### **Development of a Biologic Safety Screening Tool: Pre-Implementation Chart Review**

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**Objective:** In order to improve quality of care and patient safety, we have undertaken a project to increase compliance with screening and vaccination prior to use of biologics as per published guidelines. This chart review is the first phase of a three phase project with the objective of determining what percentage of patients with inflammatory arthritis on biologics at our centre have received the recommended screening and vaccinations. The second phase is the development and implementation of a Biologics Safety Screening Tool to be used in all the patients prior to starting biologics at our centre. Based on the literature, guidelines and consultation with experts in Rheumatology (doctors and nurses) and Infectious Diseases, we developed a tool to increase compliance and facilitate documentation of screening for infections, malignancy and autoimmune diseases, as well as appropriate vaccinations. The third phase will consist of a post-implementation chart review to assess compliance with guidelines.

**Methods:** We retrospectively reviewed charts of 50 randomly selected patients who started treatment with a biologic for the first time in our tertiary care rheumatology clinic between August 1, 2011 and August 1, 2013. Electronic and office charts were reviewed.

**Results:** Diseases include rheumatoid arthritis (n=24), ankylosing spondylitis (n=11), psoriatic arthritis (n=11), undifferentiated spondyloarthropathy (n=1), systemic lupus erythematosus (n=2), and dermatomyositis (n=1). Mean age of patients was 52 years (range 19 to 77) with 68.0% females. Prior to initiation of a biologic, 86.0% of patients were treated with at least one DMARD. The initial biologic was

etanercept (n= 28), adalimumab (n=16), rituximab (n=3), tocilizumab (n= 2) and belimumab (n= 1). Surprisingly, 39.0% and 43.9% of patients had no documented Hepatitis B or Hepatitis C serology respectively. Ten percent of patients had documented HIV testing (recommended only in high risk groups). Results of tuberculin skin test and chest imaging were missing in 14.0% and 10.0% of patients respectively. Ninety four percent of patients had no record of counseling or reception of influenza or pneumococcal vaccine. Zoster vaccine was documented to be discussed in 4.0% of patients, received in 6.0% of patients, and not recorded in 90.0% of patients. Primary care providers were not contacted for missing information. **Conclusion:** Despite several guidelines addressing screening and vaccination in patients treated with biologics, there is room for improvement in compliance and documentation of this process even in a tertiary care centre.

## 174

### **Efficacy and Safety of Adalimumab in Pediatric Patients with Enthesitis Related Arthritis**

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**Objective:** Enthesitis related arthritis (ERA) is a subcategory of juvenile idiopathic arthritis (JIA), which primarily affects peripheral joints and entheses but also can involve the sacroiliac joints and spine. The objective of this study was to evaluate the efficacy and safety of adalimumab versus placebo in children and adolescents with ERA.

**Methods:** This 12-week, phase 3, multicenter, randomized, double-blind, placebo-controlled study of adalimumab (24 mg/m<sup>2</sup> BSA up to 40 mg every other week) assessed ERA (ILAR criteria) patients aged  $\geq 6$  to < 18 years with active disease ( $\geq 3$  active joints [swelling or loss of motion + pain/tenderness] and enthesitis in  $\geq 1$  location) not responsive to  $\geq 1$  NSAID and  $\geq 1$  DMARD. Patients completing the double-blind study could receive open-label adalimumab for up to 144 weeks. The primary endpoint was % change from baseline in the number of active joints with arthritis (AJC) at week 12. Secondary variables included enthesitis count (EC), tender and swollen joint counts, and American College of Rheumatology Pediatric 30/50/70 responses. Results are summarized through 52 weeks of treatment. Safety was assessed in terms of adverse events (AE), laboratory values, and vital sign measurements.

**Results:** 46 patients (mean age: 12.9 $\pm$ 2.9 years; mean duration of ERA symptoms: 2.6 $\pm$ 2.3 years; mean AJC: 7.8 $\pm$ 6.6; mean EC: 8.1 $\pm$ 8.4) were randomized 2:1 to adalimumab (n=31) or placebo (n=15). No patient discontinued during the double-blind period; however, 7 patients early escaped to open-label adalimumab. The % change from baseline at week 12 in AJC was significantly greater in the adalimumab group versus placebo (-62.6 $\pm$ 59.5 vs -11.6 $\pm$ 100.5, P=0.039). Most secondary variables showed numerically greater, but not statistically significant improvements at week 12 in favor of adalimumab versus placebo. Treatment response was maintained with continued adalimumab therapy up to 52 weeks (% change from baseline at week 52 in AJC, -88.7 $\pm$ 26.1). During the double-blind period, AE incidence rates were similar (adalimumab/placebo [%]: any AE [67.7/53.3], serious AE [3.2/0, 1 patient in the adalimumab group (abdominal pain and headache)], and infectious AEs [29.0/20.0]). Among patients who received  $\geq 1$  adalimumab dose through week 52, any AE, serious AEs, and infectious AEs were reported in 91.3%, 10.9%, and 76.1%, respectively. No deaths, TB, or malignancies were reported.

**Conclusion:** Adalimumab reduced the signs and symptoms of ERA at week 12, and efficacy was sustained up to 52 weeks. The safety profile observed in pediatric patients with ERA was consistent with that observed in children aged  $\geq 4$  years treated for polyarticular JIA.

## **Thromboembolism in Rheumatology: Investigation of the Risks of Deep Vein Thrombosis and Pulmonary Embolism in Inflammatory Arthritis, Connective Tissue Diseases, Vasculitis and Myositis**

Jason Lee (Western University, London); Janet Pope (University of Western Ontario, London)

**Objective:** Non-cardiac thromboembolic vascular phenomena are increasingly recognized as endothelial diseases due to underlying inflammatory processes. The baseline incidence of venous thromboembolic events (VTE) in the general population is estimated to be 0.1% – 1% with high morbidity and mortality. Most rheumatologic diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) are innately inflammatory conditions that increase the risk of thromboembolic events. We performed a meta-analysis investigating the risk of developing deep vein thrombosis (DVT) and/or pulmonary embolisms (PE) in patients with inflammatory arthritis, vasculitis, SLE, myositis, and connective tissue diseases (CTD) such as Sjogren's syndrome, myositis and systemic sclerosis.

**Methods:** A comprehensive search was conducted using PubMed, Embase, Cochrane Databases, and Medline to identify full text English publications related to rheumatologic inflammatory diseases and VTE. Studies were reviewed and data regarding prevalence and rates of DVTs and PEs were extracted. Descriptive statistics, tests for heterogeneity and random effects models were performed to obtain pooled estimates for VTE in individual and pooled inflammatory rheumatologic diseases and compared with age, sex and comorbidity matched population where possible.

**Results:** Three thousand nine hundred and twenty nine studies were found and most were excluded due to lack of rate or incidence/prevalence of VTE. Twenty-two studies remained for analysis. Eight studies of RA identified a total of 5,273,942 patients and 891,530,181 controls with a prevalence of 2% (95% CI: 0.02 – 0.03). Odds Ratio of RA patients developing a DVT/PE was 2.23 (95% CI: 2.02 – 2.47) compared to age, sex, and comorbidity matched population. Six studies of SLE included 36,582 patients with a prevalence of 9% (95% CI: 0.06 – 0.11). Three Sjogren's syndrome studies with 16,180 subjects demonstrated a VTE prevalence of 3% (95% CI: 0.02 – 0.03). Four studies of dermatomyositis and/or polymyositis (N=8,245) resulted in a VTE prevalence of 4% (95% CI: 0.02 – 0.06). Overall, all inflammatory rheumatologic diseases were associated with relatively high rates of VTEs.

**Conclusion:** This meta-analysis is the first to recognize the high risk of venous thromboembolic events in patients across all inflammatory rheumatologic diseases. Although we provide strong evidence for this elevated risk in the rheumatology patient population, not all diseases were represented. Furthermore, evidence for prevention is lacking.

## **On the Precipice: A Prospective Exploration of Medical Students' Expectation of the Transition from Pre-Clinical to Clinical Training**

Jason Soo (Edmonton); Pamela Brett-MacLean (Edmonton); Marie Cave (Edmonton); Anna Oswald (University of Alberta, Edmonton)

**Objective:** Background: Medical learners face many transitions. While several professional bodies have called for blurring of the continuum, the majority of schools still follow a traditional Flexnerian structure leading to a critical preclinical/clinical training transition. Some schools attempt to ease this transition through increased clinical/interpersonal skills teaching. Others have had success with near peer mentors and transition specific courses. However, students still face difficulties in this transition. The majority of the literature reports students' perceptions after experiencing the transition to clinical training. However, retrospective accounts may not give accurate depictions of students' expectations prior to the

experience. **Objective:** We prospectively explored pre-clinical students' perceptions of their upcoming transition to clerkship.

**Methods:** 160/165 end-of-second-year medical students wrote narrative reflections and 79/165 completed a questionnaire on their upcoming transition. Narratives were separately analyzed by four authors and then discussed to identify a final thematic framework using parsimonious category construction. Descriptive statistics were applied to the questionnaire data.

**Results:** We identified 2 main thematic categories: 1) Evaluations, with sub-themes on experiences of preclinical training, specific learning strategies and supportive relationships; 2) Expectations, where a broader range of themes included emotional tensions, performance fears, patient relationships, contextual learning, life balance and career choices. Questionnaire data revealed mixed accuracy of expectations with incongruities around expectations of minimal independent study.

**Conclusion:** By prospectively exploring preclinical students' expectations of the transition to clinical training we identify expectations and misconceptions that could be addressed with future curricular interventions.

177

### **High Prevalence of Obesity Among Early and Established Rheumatoid Arthritis**

Maria Bazan Bardales (McGill University, Montreal); Ines Colmegna (McGill, Montreal); Susan Bartlett (McGill, Montreal); Carol Hitchon (University of Manitoba, Winnipeg)

**Objective:** Rheumatoid arthritis (RA) is characterized by early, accelerated atherosclerosis leading to increased disability, morbidity and mortality. Inflammation and traditional cardiovascular (CVD) risk factors contribute to poor outcomes, and obesity further increases risks of CVD, diabetes and disability. New sex-specific RA cutpoints for obesity have been proposed. We estimated the prevalence of obesity among Canadian RA patients using the existing and new thresholds.

**Methods:** Patients receiving care during 2011-13 at two university centers were included. Height and weight were measured and selected demographic (age, sex, tobacco use), RA (duration, RF+, CCP+, ESR, CRP, tender + swollen joints) and patient reported outcomes (patient global, HAQ, morning stiffness) were obtained at the visit. Patients were classified according to WHO criteria and proposed new RA cutpoints, and results were compared with 2008 StatsCan data.

**Results:** Participants were 200 RA patients (106 from Winnipeg, 94 from Montreal) who were mostly female (76%) with a mean  $\pm$  SD age of  $56.9 \pm 15.3$  yr, median [IQR] RA duration of 5 [6] yr (29% < 2 yrs) and HAQ of .7 [IQR 1]. 83% were RF+ and 63% anti-CCP+. Groups did not differ between sites by age, sex or BMI, however, patients in Montreal were more likely to have early RA (38 vs 20%;  $p = .001$ ) and less likely to have smoked (31% vs. 66%,  $p < .001$ ). Women were significantly younger than men ( $56 \pm 16$  vs  $61 \pm 14$ ;  $p = .025$ ) and less likely to report tobacco use (47 vs. 68%;  $p = .023$ ). RA duration, HAQ and BMI was similar between sexes. Using WHO criteria, 34% of the RA patients were obese; women with RA had higher rates of obesity than men (see table). Using the proposed RA cutpoints, 55% were classified as obese, and men with RA had higher rates of obesity than women. Demographic and RA characteristics were not significantly ( $p > .05$ ) different between obese and non-obese patients. Although HAQ was only weakly associated with BMI ( $r = .311$   $p < .001$ ), obese patients had more than twice the odds of HAQ scores  $\geq 1$  (OR 2.3 95% CI 1.2, 4.2).

**Conclusion:** Our results suggest that Canadian RA patients are more likely to be obese than their peers and men appear to be at particular risk. Obesity in RA is associated with greater rates of self-reported disability. Identifying and addressing obesity among newly and established RA patients may be relevant to reduce the excess CVD- morbidity and mortality associated with this disease.

### **Intra-Articular Corticosteroids Injections in the Lower Extremities: How do Ankles Respond?**

Jean-Philippe Proulx-Gauthier (Montreal Children's Hospital, Montréal); Claire MA LeBlanc (Montreal Children's Hospital, Montréal); Gaëlle Chédeville (Montreal Children's Hospital, Montreal)

**Objective:** The primary objective of this study is to describe the proportion of JIA patients who failed to demonstrate a clinical response to intra-articular corticosteroids injection (IAS) in the lower extremities. We hypothesized that, by 3 months following the procedure, the non-response rate would be higher in the ankle joint compared to other joints. A secondary objective is to determine the time to flare following IAS.

**Methods:** JIA patients 0-18 years old followed at the Montreal Children's Hospital undergoing IAS (blindly or with fluoroscopy) in the lower extremities from January 1<sup>st</sup> 2005 to December 30<sup>th</sup> 2012 were included in a retrospective cohort study. Data obtained through chart review encompassed demographics, IAS method, and response to IAS. Response was evaluated at 6 weeks, 3 months, 6 months, 12 months and 24 months post-procedure. Patients without available data for at least 3 months following intervention were excluded. Non-response to IAS was determined within the first 3 months after IAS. Time to flare was assessed in subsequent visits up to 24 months.

**Results:** Data from 50 patients included in our study are presented. Median age at diagnosis was 5.3 years with 66% affected with oligoarthritis and 62% of female gender. The mean age at the time of IAS was 8.9 years. Triamcinolone hexacetonide was administered in 98.3% of cases. IAS were performed in 64 knees, 38 ankles and 18 subtalar joints. At 3 months post IAS, 34.2% of ankles, 16.7% of subtalar joints and 9.4% of knees failed to demonstrate a clinical response. The median time to flare after IAS was 7.7 months for the ankles, 6.8 months for the subtalar joints and 7.6 months for the knees. Only one patient developed a complication (subcutaneous atrophy).

**Conclusion:** To date, we report a higher rate of non-response following blind IAS ankle injections compared to other lower extremities joints. Future analysis of the entire cohort will assess the factors associated with a non-response to IAS as well as the factors associated with a longer duration of remission. Our findings may reflect inaccurate needle placement and/or non-treatment of associated tenosynovitis and suggest the need to modify the approach to IAS in the ankles by performing ultrasound-guided injections to improve outcomes.

### **Needs Assessment in the Context of the Novel PAASSER Program to Ameliorate Care in Rheumatology**

Jean-Pierre Raynauld (Montreal Rheumatology Institute, Montreal); Denis Choquette (Université de Montréal, Montréal); Michèle Ouellet (Montreal Rheumatology Institute, Montreal); Anaïs Lacasse (Université du Québec en Abitibi-Témiscamingue, Rouyn-Noranda)

**Objective:** Describe the perceptions and referral practices to rheumatology of primary care physicians regarding patients with musculoskeletal disorders (MSD) ahead of the startup of the PAASSER Program (French acronym for Programme d'Accès et d'Amélioration des Soins de Santé En Rhumatologie).

**Methods:** In 2009, primary care physicians within the catchment region of the Institut de rhumatologie de Montréal (IRM), Québec Canada, were approached by mail and invited to participate to individual face-to-face interviews. Using a standardised questionnaire, these interviews were conducted to measure the characteristics of physicians' medical practice, referral patterns to rheumatology, as well as their needs and any perceived barriers to the referral of MSD patients to rheumatology.

**Results:** A total of 21 primary care physicians accepted to participate in the study. Among these, 81% worked in private primary care settings, and only a minority (23.8%) used algorithms for MSD screening



and management. The most common MSD treated by respondents were rheumatoid arthritis (95.2%), ankylosing spondylitis (71.4%), systemic lupus erythematosus (52.4%), and psoriatic arthritis (47.6%). Many primary care physicians (52.4%) referred 5 percent or less of their MSD patients to rheumatology. They reported that reasons for non-referral were related to delays, complexity of referrals, strict eligibility criteria, or perceived impossibility to obtain an appointment. Indeed, 76.2% of respondents considered delays to consultation in rheumatology were problematic. Prior to the launch of the PAASSER Program, only 14.3% of physicians used the IRM's standardised referral form. Reasons provided for the low usage of the IRM's form included a lack of knowledge about the form and/or the IRM itself, primary care physicians using their own form, a lack of time to complete the form, or the perception that the available form was useless/bothersome/too extensive. A majority of respondents expressed a desire for rheumatologists to offer greater support in the structure of specific and personalized MSD treatment plans (61.9%).

**Conclusion:** These preliminary results suggested the need for a reorganization of rheumatology referrals to the IRM and were used to develop and implement the PAASSER Program. This novel program has been implemented at the IRM since December 2010 and its effectiveness is currently being evaluated in a pragmatic trial.

## 180

### **Impact of Missing Anti-Cyclic Citrullinated Peptide (CCP) Antibody Serology on Clinical Outcomes in Early Rheumatoid Arthritis: Results from CATCH (Canadian Early Arthritis Cohort)**

Jenny Shu (Western University, London); Vivian Bykerk (Toronto); Boulos Haraoui (Université de Montréal, Montréal); Carter Thorne (Southlake Regional Health Centre, The Arthritis Program, Newmarket); Edward Keystone (Mount Sinai Hospital, Toronto); Gilles Boire (Université de Sherbrooke, Sherbrooke); Carol Hitchon (University of Manitoba, Winnipeg); Diane Tin (Southlake Regional Health Centre, Newmarket); Janet Pope (University of Western Ontario, London); all CATCH investigators (U of T, Toronto)

**Objective:** Anti-cyclic citrullinated peptide (CCP) antibody presence and titre are part of the ACR RA criteria. The test is not universally covered in Canadian provinces. We wondered if missing anti-CCP would impact the quality of care of Canadians with early inflammatory arthritis using data from the Canadian Early Arthritis Cohort (CATCH) study, especially when initiating treatment (over the first 3 months).

**Methods:** A total of 2191 patients were recruited into a prospective cohort study, and allocated to any of 3 groups: seropositive (Rheumatoid Factor (RF)+ and/or CCP+), seronegative (RF- and CCP-) and missing anti-CCP ((RF- with missing anti-CCP). Main outcomes in antibody serology groups include proportion fulfilling 2010 ACR RA criteria, DAS28, HAQ-DI, mean number of DMARDs, and proportion on methotrexate or corticosteroids. Adjustments were made for baseline age, sex, symptom duration, and smoking status if  $p < 0.1$  from Pearson's Chi-squared or Analysis of variance (ANOVA) tests.

**Results:** At baseline, there were 42.0% RF+, and 33.6% CCP+, 33.0% CCP-, and 33.4% missing CCP, so seropositive were 52.4%, seronegative 24.9%, and missing CCP 19.3%. A higher proportion of the seropositive fulfilled 2010 ACR/EULAR RA criteria relative to both seronegative groups ( $p < 0.001$ ; OR 5.28 [95% CI 4.20, 6.64] and missing anti-CCP ( $p < 0.001$ ; OR 4.49 [95% CI 3.51, 5.74]). In comparison to the missing anti-CCP group at 3 months, both seropositive and seronegative groups had higher mean number of DMARDs ( $p < 0.001$ ; respective OR 1.88 [95% CI 1.45, 2.43] for seropositive and OR 1.82 [95% CI 1.36, 2.44] for seronegative), proportion on corticosteroids ( $p = 0.01$ ; OR 1.46 [95% CI 1.08, 1.97] for seropositive and  $p = 0.04$ ; OR 1.42 [95% CI 1.01, 1.99] for seronegative), and proportion on methotrexate ( $p < 0.001$ ; respective OR 1.88 [95% CI 1.43, 2.48] for seropositive and OR 1.66 [95% CI 1.22, 2.26] for seronegative). There were no statistically significant differences amongst groups with

respect to: mean DAS28 at 3 months ( $p=0.96$ ), change in mean DAS28 over 3 months ( $p=0.12$ ), and mean HAQ-DI at 3 months ( $p=0.053$ ).

**Conclusion:** The missing anti-CCP group was less likely to fulfill RA criteria and are also treated differently in that they were prescribed fewer DMARDs, less methotrexate, and less steroids so a potential care gap exists. However their mean DAS28, change in DAS and HAQ-DI were not different at baseline and 3 months. The impact over the long term of missing CCP in seronegative RF needs further exploration.

## 181

### **Getting a Grip on Arthritis Online: Web-Based Continuing Health Education Improves Rural/Remote Primary Care Providers' Satisfaction and Confidence with Managing Arthritis**

Mary Bell (Sunnybrook Research Institute, Toronto); Lisa Fleet (St. John's); Elizabeth Badley (Health Care and Outcomes Research, Toronto Western Research Institute; Dalla Lana School of Public Health, University of Toronto, Toronto); Vernon Curran (St. John's); Marlene Del Pino (Winnipeg); Karen Gordon (Ottawa); Sydney Lineker (The Arthritis Society, Toronto); Anne Lyddiatt (Ontario Biologics Research Initiative, Ingersoll); Lynn Moore (The Arthritis Society, Toronto); Karla Simmons (St. John's); Raquel Sweezie (Toronto); Peter Tugwell (Institute of Population Health, University of Ottawa, and the Division of Rheumatology, Department of Medicine, University of Ottawa, Ottawa); Ed Ziesmann (Toronto)

**Objective:** Rural/remote primary care providers are often challenged with delivering optimal arthritis care and accessing relevant up-to-date information. Getting a Grip on Arthritis Online, a web-based continuing health education program with case-based content, was recently developed to address these issues. An evaluation of the program's effectiveness in improving primary care providers' confidence and satisfaction with their ability to manage arthritis was performed.

**Methods:** Online learning modules were developed for Osteoarthritis (OA) and Rheumatoid Arthritis (RA) based on a needs assessment with primary care providers. The program was piloted in two predominantly rural/remote areas of Canada with documented arthritis prevalence and health human resource shortages. A mixed methods evaluation was performed. This included 1) paired samples analyses of pre/post measurements of confidence and satisfaction with ability to manage arthritis and 2) an evaluation of module content and design. Confidence and satisfaction were measured on 10 point numerical rating scales (0=not satisfied/not at all confident; 10=extremely satisfied/confident).

**Results:** Participants represented various professions, including physiotherapists, occupational therapists, nurses, and family physicians (OA module,  $n=34$  participants; RA module,  $n=30$ ). After taking the modules, satisfaction with ability to manage arthritis improved significantly (OA  $p=0.016$ ; RA  $p<0.001$ ). Significant increases in confidence with different aspects of arthritis care were also observed. After taking the OA module, participants' confidence improved for the comprehensive musculoskeletal examination ( $p=0.025$ ), prescribing/recommending corticosteroids ( $p=0.020$ ), ordering/recommending serological tests ( $p=0.002$ ), and managing common musculoskeletal conditions ( $p=0.026$ ). After taking the RA module, participants' confidence improved for prescribing/recommending joint injections of the knee ( $p=0.038$ ), DMARDs ( $p=0.012$ ), and corticosteroids ( $p=0.019$ ). The majority of respondents agreed that the modules were consistent with stated objectives (OA=97.5%; RA=97.1), addressed their learning needs (OA=87.2%; RA=94.3%) and were relevant to practice (OA=80%; RA=91.4%). The planned use of relevant resources in practice and with patients highlighted the participants' commitment to change.

**Conclusion:** With knowledge gained from the online modules, participants reported an increase in both satisfaction and confidence with managing arthritis. The modules were also relevant to practice and the content addressed their learning needs. The case-based format simulated interaction with 'real' patients and

enabled participants to practice their diagnostic and management skills. Participant feedback highlighted the need for additional information relevant to professions other than physicians to better capture the importance of inter-professional care. This feedback will be incorporated into the next version with plans for national roll out in 2014.

182

### **The Effects of a Community-Based, Post-Rehabilitation Exercise Program after Total Hip and Knee Replacement: A Feasibility Study**

Marie Westby (Mary Pack Arthritis Program, Vancouver); Kim Hall (Osteoarthritis Services Integration System, Richmond); Natalie Grant (Evergreen Community Health Centre, Vancouver)

**Objective:** To 1) investigate the effects of a community-based, post-rehabilitation exercise program on physical function, health-related quality of life (HRQoL) and physical activity (PA) level in individuals after total joint replacement (TJR) of the hip or knee and 2) establish procedural feasibility.

**Methods:** A controlled before-and-after design was used to evaluate the effects of a fitness instructor-led exercise program for older adults who had elective TJR within the previous 6 months. We recruited participants through posters and brochures in an outpatient physiotherapy department of a regional hospital and during telephone registration for the Joint Replacement Recovery (JR2) program. The JR2 program consists of group land- and pool-based exercises 2x/week over 6 weeks and focuses on improving strength, balance and endurance. Individuals who chose to participate in JR2 were compared to matched subjects who chose not to using four outcome measures: 1) 6-Minute Walk Test (6-MWT); 2) Stair Climbing Test (SCT); 3) Hip/Knee Osteoarthritis Outcome Score (HOOS/KOOS); and 4) Rapid Assessment of Physical Activity (RAPA) at baseline and post-test (6 weeks). A physiotherapist blinded to group assignment performed all assessments. Feasibility data included recruitment and retention rates, adherence, adverse events and outcome assessor blinding. Participant demographic, RAPA and feasibility data were analyzed using descriptive statistics. We used paired t-tests to assess within-group changes and the mean difference (MD) to determine effect sizes with 95% confidence intervals for other outcomes.

**Results:** Over 12 months, 16 individuals were recruited (JR2 n=12, control n=4). All JR2 participants and 3 control participants (94% in total) completed baseline and post-test assessments. Insufficient control group data prevented between-group comparisons. JR2 group 6-MWT and SCT mean change scores were statistically ( $p < .001$  both) and clinically significant (6-MWT MD=67.11 metres [39.22, 95.00]; SCT MD=-4.48 secs [-2.46, -6.49]). Only the HOOS/KOOS HRQoL subscale improved significantly ( $p < .02$ ) and was clinically important (MD=13.45 [4.2, 22.7]). The RAPA revealed that 50% of JR2 participants improved their PA  $\geq 1$  level. JR2 adherence (attendances) was satisfactory (74%). No adverse events were reported. Outcome assessor blinding was problematic in 69% of participants.

**Conclusion:** A community-based exercise program may enhance physical recovery and HRQoL after TJR beyond that achieved with outpatient rehabilitation. Refinement of study design and methods are necessary before undertaking a larger trial to establish effectiveness. Limited healthcare resources necessitate additional research to determine the role of community-based programs after TJR.

183

### **Cumulative Exposure to Elevated Inflammatory Markers is Associated with Increased Burden of Atherosclerosis in Psoriatic Arthritis Patients: A Cohort Study**

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Dafna Gladman (University of Toronto, Toronto)

**Objective:** Cardiovascular morbidity is increased in patients with psoriatic arthritis (PsA). It is unclear whether the cumulative burden of inflammation contributes to cardiovascular risk. We aimed to investigate whether a higher burden of arthritis and psoriasis over time is associated with the development of atherosclerotic plaques in patients with PsA..

**Methods:** A retrospective cohort analysis was conducted in patients attending a large PsA clinic. Patients were assessed at 6-12 month intervals according to a standard protocol. The cumulative effect of inflammation was measured by a time-adjusted arithmetic mean (AM) of all available measurements from the first visit to the clinic. The following variables were considered as predictors: Psoriasis Activity and Severity Index (PASI), Erythrocyte Sedimentation Rate (ESR), total leukocyte counts (TLC), Tender and Swollen joint count (TJC, SJC), C - reactive protein (CRP), Psoriatic Arthritis Disease Activity Score (PASDAS) and Disease Activity for PsA (DAPSA). An ultrasound assessment of the carotid arteries was performed and Total Plaque Area (TPA) was measured. This measure represented the extent of atherosclerosis and was considered the outcome of interest. TPA was stratified into 4 categories: 1) TPA=0 (no plaques), 2)  $0 < \text{TPA} \leq 0.1 \text{ cm}^2$ , 3)  $0.1 < \text{TPA} \leq 0.4 \text{ cm}^2$ , 4)  $\text{TPA} > 0.4 \text{ cm}^2$ . The association between the various AM variables and TPA categories was assessed using logistic ordinal regression model adjusted age and gender.

**Results:** A total of 235 patients with PsA were analyzed. Patients in higher TPA categories were older at the time of assessment ( $p < 0.001$ ), were more likely to be smokers ( $p = 0.008$ ), hypertensive ( $p = 0.002$ ), diabetics ( $p < 0.001$ ) and were older at the onset of psoriasis ( $p < 0.001$ ) and PsA ( $p < 0.001$ ). In a multivariable regression model adjusted for age and sex, AM-ESR was associated with higher TPA categories (category 3 vs. 1 Odds Ratio (OR) 1.04, 95% Confidence Interval (CI) 1, 1.08,  $p = 0.04$ , category 4 vs. 1 OR 1.05, 95% CI 1.01, 1.1,  $p = 0.02$ ). The following variables were also associated with higher probability of having severe atherosclerosis (being in TPA category 4 vs. 1): AM-TLC (OR 1.45, 95% CI 1.09, 1.92,  $p = 0.01$ ) and AM-DAPSA (OR 1.08, 95% CI 1.02, 1.14,  $p = 0.009$ ). A trend for an association was observed between AM-PASDAS and being in the highest TPA category (OR 1.73,  $p = 0.06$ ). No significant association was found between AM-PASI, AM-CRP, AM-TJC, AM-SJC and damaged joint count and TPA.

**Conclusion:** An exposure to increased cumulative inflammation is associated with the development of atherosclerotic plaques in patients with PsA.

184

### **Invasive Fungal Disease in Systemic Lupus Erythematosus: A Systematic Review of Disease Characteristics, Risk Factors, and Prognosis**

Linda Wang (University of Alberta, Edmonton); Claire Barber (University of Calgary, Calgary); Andrew Johnson (University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary)

**Objective:** Invasive fungal disease (IFD) is a life-threatening complication of systemic lupus erythematosus (SLE) and/or its treatment. We conducted a systematic review to characterize IFD in SLE, and identify risk factors and outcomes.

**Methods:** Medline, Embase, and Web of Science were searched up to June 2013 using MeSH terms and keywords pertaining to two major themes: SLE and IFD. Adult cohorts, chart reviews, case reports, and autopsy studies in English were included. Inclusion by two independent reviewers (LRW & CEB, kappa=

0.87) was based on ACR and EORTC/MSG 2008 criteria for SLE and IFD, respectively, excluding patients with confounding comorbidities (HIV, solid organ or hematologic transplant, chemotherapy).

**Results:** 398 cases from 186 studies met criteria for inclusion. Fungal organisms were identified in 369 infections: 231 yeasts (170 *Cryptococcus* spp., 61 *Candida* spp.), 72 *Aspergillus* spp., 35 dimorphic (13 *Coccidioides* spp., 13 *Histoplasma* sp., 8 *Penicillium* sp., 1 *Blastomyces* sp.), and 31 other fungi (20 *Mucormycosis*, 3 *Zygomycosis*, 3 *Pseudoallescheria* sp., 2 *Xylohypha* sp., 2 *Rhodotorula* sp., 1 *Ramichloridium* sp.). IFD was fatal in 164 cases (51% of 321 where outcomes reported). Median SLE duration at the time of IFD was 2.1 years (IQR 0.5-7.0); 39% occurred within 1 year of SLE diagnosis, with 15 cases presenting with IFD and SLE concurrently. Disease activity and corticosteroid dose emerged as risk factors for IFD, as 85% of cases had active SLE (119 of 140 where reported), and 89% were on steroids at presentation (243 of 272 where reported), with a median dose of 30mg (IQR 10-60) prednisone equivalent, and 71 (34%) on  $\geq 60$ mg/day. Half were on other immunosuppressants at presentation (114 of 228 reporting immunosuppressant use). All 43 patients who did not receive antifungal therapy died, and in 44 cases IFD diagnosis was made only on autopsy. Twenty patients were found to have a co-infection with a bacterial pathogen during IFD.

**Conclusion:** Systematic review confirms the severe sequelae of IFD in published cases. IFD occurred in patients with active SLE at early stages of disease, and in patients on significant corticosteroid doses, highlighting the role of poor disease control and a high "net state of immunosuppression". Our study was limited by the uncontrolled retrospective design with bias towards more severe (publishable) cases. In the modern era, with a broader armamentarium of pharmacologic agents (immunosuppressive DMARDs, biologics) for the treatment of SLE, and improved fungal diagnostics and antifungal agents, IFD in SLE should be prospectively examined.

## 185

### **Self Report Dental Symptoms do not Predict Periodontal Status in Patients with Rheumatoid Arthritis**

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**Objective:** Periodontal disease (PD) and inflammatory arthritis (IA) share features of inflammation and bone loss and have been linked in epidemiologic studies. We sought to evaluate the prevalence of periodontal disease in patients with inflammatory arthritis and to determine the validity of self-reported dental symptoms and hygiene habits for PD.

**Methods:** Sixty one patients with inflammatory arthritis (mean age  $50.3 \pm 11.1$  years; rheumatoid arthritis  $n=47$  or undifferentiated arthritis  $n=14$ ) answered questions about their periodontal symptoms and dental habits, functional status (modified health assessment questionnaire mHAQ), co-morbid medical conditions and smoking history. All were examined by a periodontist using the periodontal screening and recording index (PSR) a validated screening tool for periodontal disease. The highest score in each sextant was recorded. Patients were classified as periodontically healthy, gingivitis mild, moderate or severe periodontitis. Associations between rheumatoid factor (RF) and dental symptoms and habits and the validity of the self-reported dental questionnaire were tested. Percentages or means (SD) are reported.

**Results:** No patients were periodontically healthy. (23 gingivitis, 14 mild periodontitis, 16 moderate periodontitis, and 3 severe periodontitis, 5 were edentulous). The mean PSR score was 2 (0.5). Patients were seropositive (RF 67%, CCP2 67%) with moderate disease activity (DAS28CRP(3var) 2.69(1.05) and function (mHAQ 0.4(0.41) despite 95% taking DMARDs, 49% combination DMARDs and 36% biologics. There was no correlation between the PSR score and disease activity (DAS28CRP3var),

functional status (mHAQ) arthritis duration or age at the time of the dental exam. There were no robust associations between PSR and RF, CCP2 or diabetes, a known risk for PD. Increased total pack years of smoking was moderately associated with worse periodontal health. The majority (28/42) rated their overall health as very good or good. The sensitivity for self-reported responses of “sometimes” “often” or “always” for moderate or severe PD based on the PSR score was greatest for reporting bleeding gums (72%), metallic taste (89%), loose teeth (95%) and pain on food impaction (84%). The sensitivity of these questions for moderate or severe PD was poor (32%, 5%, 21%, and 11% respectively).

**Conclusion:** Periodontal disease is common in patients with inflammatory arthritis but does not correlate with arthritis severity or activity. Self-reported dental symptoms have reasonable specificity but poor sensitivity for detecting significant periodontal disease. Formal dental examination should be part of arthritis care. Periodontal disease may play a more important role in the pathogenesis of imminent or very early arthritis.

## 186

### **Do Exercise Interventions for Total Knee Arthroplasty have Therapeutic Validity? A Sensitivity Analysis of Trials included in a Cochrane Systematic Review**

Marie Westby (University of Alberta, Vancouver); Shirin Kazemi (Mary Pack Arthritis Program, Vancouver); Dina Jones (West Virginia University, Morgantown)

**Objective:** To 1) assess the therapeutic validity of post-acute exercise interventions after total knee arthroplasty (TKA) for osteoarthritis; and 2) determine if they meet American College of Sports Medicine (ACSM) exercise guidelines.

**Methods:** This study included trials from an ongoing Cochrane systematic review of post-acute physical therapy after TKA. Two researchers (MW & SK) independently extracted data on therapeutic validity using the 9-item CONsensus on Therapeutic Exercise aNd Training (CONTENT) scale and ACSM exercise guidelines. CONTENT items were rated ‘yes’ or ‘no’ and ACSM guidelines were rated ‘meeting’ or ‘not meeting’ based on frequency, intensity, timing, type and overall training duration (i.e., FITT principle). Disagreements between raters were resolved through discussion. Frequency counts and proportions were calculated to determine the number of CONTENT and ACSM items met. Studies scoring  $\geq 6$  on the CONTENT scale were considered to have high therapeutic validity. We calculated Cohen’s kappa ( $k$ ) coefficient with 95% confidence intervals for individual and overall CONTENT items to determine strength of agreement between raters. Kappa coefficients  $\geq 0.60$  represented good agreement.

**Results:** Of the 17 trials in the Cochrane review, 14 were exercise interventions of strength training alone ( $n=5$ ), neuromotor training ( $n=1$ ) or combined ( $n=8$ ) with/without aerobic training. Overall, there was moderate inter-rater agreement ( $k$  0.59 [CI 0.44, 0.73]) with absolute agreement on 103 of 126 (82%) CONTENT items. Perfect agreement was obtained on CONTENT items addressing exercise intensity and progression and lowest agreement ( $k$  0.21 [CI 0.21, 0.63]) for patient eligibility. Two interventions were judged to be therapeutically valid with CONTENT items related to patient selection and exercise rationale receiving the most positive ratings. No interventions met ACSM exercise guidelines. The exercise parameter most often met (71%) was overall training duration ( $\geq 6$  weeks) whereas exercise intensity was judged adequate in two trials (15%).

**Conclusion:** This is one of the few analyses conducted to address therapeutic validity of rehabilitation exercise interventions. The post-acute TKA exercise interventions included in the Cochrane review have low therapeutic validity and fail to meet ACSM exercise guidelines. Conclusions from individual trials, and ours and other systematic reviews of TKA exercise should be interpreted with caution in light of these limitations. Determining an intervention’s likelihood of providing a training effect would inform interpretation of results. Future trials should be designed to adhere to current exercise prescription

guidelines and provide sufficient details and adherence data to permit examination of possible dose-response relationships.

187

### **Economic Evaluation using Observational Data: A Scoping Review**

Mark Tatangelo (University of Toronto, Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Published economic evaluations and cost analysis of rheumatoid arthritis (RA) drugs are usually performed using Randomized Trial data with few studies conducting economic evaluation using observational or registry data. As a result, most existing evidence surrounding economic analysis do not account for a long-term time horizon, downstream costs to the health-care system and work productivity losses that are needed to capture the true costs of RA treatments. We thus sought to provide a scoping review of the existing literature on economic analysis using observational or administrative data including cost-effectiveness, cost-utility and cost-analysis in RA to identify existing research, gaps in research and future directions.

**Methods:** English language articles from 1964 to October 2013 were searched in Ovid (Medline) and Embase. Exclusion Criteria: Articles not available in electronic form, conference abstracts, meeting summaries, and letters. MeSH terms: Rheumatoid arthritis, compensation and redress, costs and cost analysis, economics, medical economics, pharmaceutical economics, fees and charges, health care sector, health care costs, cohort studies, longitudinal studies, registries, cost-benefit analysis, postmarketing product surveillance, biological agents, anti-inflammatory agents, non-steroidal, antirheumatic agents. Non-MeSH terms: Systematic review, economic evaluation, economic analysis, administrative data, biologics. Individual search terms were then combined strategically using the “and” operator.

**Results:** The original search yielded 3505258 citations without removing duplicates. The search was narrowed using combined search terms to 6024 citations. After removal of duplicates 767 citations remained, which were screened by title down to 167 citations, which were reviewed by abstract. 20 articles were selected for full review.

**Conclusion:** Gaps in full economic evaluation using observational or registry data exist in current literature. Cost-analysis evaluating the downstream costs, health care utilization and productivity losses were more common than full-fledged economic evaluation using observational data. Future research to address the shortcoming of observational or registry based economic evaluation is warranted to address the knowledge gap identified in our scoping review.

188

### **Mapping the Health Assessment Questionnaire on a Preference Based Utility Measure in a Large Canadian Rheumatoid Arthritis**

Mark Tatangelo (University of Toronto, Toronto); George Tomlinson (Toronto General Research Institute, Toronto); Claire Bombardier (University of Toronto, Toronto)

**Objective:** Clinical trials are limited in demonstrating the cost effectiveness of biologic therapies, as these studies often do not collect measures required for economic analysis. Thus we sought to provide a validated algorithm, allowing utility scores to be estimated using mapping (also known as “cross-walking”) of the Health Assessment Questionnaire Disease Index (HAQ-DI) onto a standardized utility measure (EQ-5D).

**Methods:** We studied 5971 patient visits for 1911 patients included in the Ontario Best Practices Research Initiative, a clinical registry of RA patients followed in routine care (2008-2013). Data were collected every 6 months and include patient demographics, socioeconomic status, clinical variables, disease activity measures, and HAQ-DI and EQ-5D. Each patient’s EQ-5D score was converted to a utility value using a Canadian tariff. EQ-5D utility values were then predicted from HAQ-DI scores using a linear random

effects model. HAQ-DI scores were entered as predictors in the model. Random effects for each patient were fitted for intercepts and slopes for the effect of HAQ-DI. Linearity was assessed by fitting non-parametric estimate calculated by mean EQ-5D grouped by HAQ scores.

**Results:** The estimated fixed effect change in EQ-5D for each point of the HAQ-DI scores is -0.15 (SE=0.0027,  $P < 0.001$ ), with a RMSE= 0.099, and  $R^2=0.68$ . Examination of the residual plots suggested mild departures from normality with slightly smaller variance for large EQ-5D values. EQ-5D health utility scores showed a ceiling effect, with 1621 observations achieving a utility value of 1 (perfect health).

**Conclusion:** Preference based utility values like the EQ-5D can be estimated for aggregated data using clinical variables such as the HAQ-DI. These results allow for the prediction of average utility values from functional variables needed for economic analysis in clinical trials. This model will allow for economic analysis of the benefit of biologic rheumatic drugs in Quality Adjusted Life years that are meaningful to payers. Future analysis will use each HAQ item to predict EQ-5D utility score, and external validation of the algorithm.

## 189

### **The Risk of Cerebrovascular Accidents in Systemic Sclerosis: A Population-Based Cohort Study**

Marko Yurkovich (Department of Medicine, University of British Columbia, Vancouver); Hyon Choi (Arthritis Research Centre of Canada, Vancouver); Maurice Agha (Milan Ilich Arthritis Research Centre, Richmond); Iman Hemmati (Department of Medicine, University of British Columbia, Vancouver); Eric Sayre (Arthritis Research Centre of Canada, Richmond); Kamran Shojania (University of British Columbia, Vancouver); Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Richmond)

**Objective:** There is limited data on the risk of cerebrovascular accident (CVA) in patients with systemic sclerosis (SSc). Moreover, the scarce information available has come from selected populations. To fill this knowledge gap, we estimated the risk of newly recorded CVA events among incident SSc cases compared to controls from the general population using physician billing and hospitalization data that covers the entire province of British Columbia.

**Methods:** Our data includes all health professionals and hospital visits covered by the comprehensive provincial medical services plan (1990-2010) and all dispensed medication (1995-2010), for all individuals. We conducted a retrospective matched cohort (1996-2010) study among patients satisfying at least one of the following criteria: a) diagnosis of SSc (> 18 yrs) on at least two visits within a two-year period by a non-rheumatologist physician; b) diagnosis of SSc on at least one visit by a rheumatologist or from hospitalization; c) absence of a prior SSc diagnosis between 1990 and 1995. To increase specificity we excluded cases that were not confirmed by a rheumatologist if they were seen at a later point. Ten controls matched by birth year, sex and calendar year of exposure were randomly selected from the general population for each case. Newly recorded CVA events from hospitals or death certificates were recorded as an outcome. We estimated relative risks (RRs) by comparing SSc cases with age-, sex- and entry-time-matched comparison cohorts, adjusting for confounders.

**Results:** Among 1,236 individuals with incident SSc (83% female, mean age 56.3 yrs), 49 developed CVA. The age-, sex-, and entry-time-matched RRs were significantly increased in the SSc cohort when compared with controls (RR= 2.0, 95% CI 1.4-2.7). The risk was 4 times greater within the first year after diagnosis (incidence rate ratio = 3.7; 95% CI 1.9-6.6) and decreases thereafter. After further adjustment for angina, COPD, obesity, cardiovascular drugs, anti-diabetic drugs, hormone replacement therapy, dyslipidemia, non-steroidal anti-inflammatory drugs, Cox-2 inhibitors, glucocorticoids, oral contraceptives, fibrates, statins, number of hospitalizations and Charlson's comorbidity index at baseline, the results remained statistically significant (RR= 2.0; 95% CI 1.5-2.8).



**Conclusion:** This large population-based study indicates an increased risk of CVA in patients with SSc, especially within the first year of disease onset. The systemic autoimmune inflammatory state in SSc is likely the main driver of this observed increased risk. Furthermore, our results support increased monitoring of CVA complications and risk factors in patients with SSc at the population level.

190

### **Incidence of Cardiovascular Co-Morbidities in Early Rheumatoid Arthritis Patients at 5 Year Post-Diagnosis**

Mathew Pierce (Winnipeg); Mellissa Moyon (Winnipeg); Christine Peschken (University of Manitoba, Winnipeg); Carol Hitchon (University of Manitoba, Winnipeg)

**Objective:** The risk of cardiovascular disease is increased in longstanding rheumatoid arthritis (RA) possibly due to shared risk factors such as smoking, inflammation or adverse effects of treatment. We sought to identify the prevalence of cardiovascular disease in patients with recent onset inflammatory arthritis at presentation and after five years of disease.

**Methods:** Patients presenting with inflammatory arthritis of less than one year symptom duration were followed in a single center. Detailed clinical assessments were recorded at each clinic visit. Comorbid medical conditions were recorded annually by patient self-report and using the Carlson comorbidity index. For this analysis, self-reported cardiovascular co-morbid disease (CVD) included hypertension (HTN), heart problems (defined as angina, myocardial infarction, congestive heart failure, valve problems, or arrhythmias) or circulatory problems (peripheral vascular disease, claudication). We report means (standard deviations). Statistical significance was determined by ANOVA and Chisquared analysis.

**Results:** In this cohort 173 subjects reported comorbidity at baseline and had at least five years of clinical follow-up. At baseline 63 (36 %) reported at least one CVD (HTN 35(20%); heart disease (15(9%); Circ 28(16%)). Patients with cardiovascular disease (CVD) were older (60(14) vs 49(14) yrs  $p < 0.0001$ ) had more functional disability as assessed by the modified health assessment questionnaire (mHAQ) (SD) 0.69(0.61) vs 0.51(0.48)  $p = 0.03$  but similar disease activity (mean DAS28 3.9 vs 4  $p = \text{ns}$ ) than those without CVD. Of patients without baseline CVD ( $n = 97$ ) new cardiovascular conditions after 5 years were reported by 12 (hypertension ( $n = 6$ ), Heart Problems:  $n = 5$ , Circulation Problems:  $n = 5$ ). Of the 3 types of cardiovascular co-morbidities that were reported, 6 were within the first year of diagnosis, 2 in the 2<sup>nd</sup> year, 2 in the 4<sup>th</sup> year and 5 in the 5<sup>th</sup> year. Compared to subjects without new CVD, subjects reporting CVD had higher mean ESR (over 5 years) 23(11) vs 13(10)  $p = 0.03$  and trend to higher maximum ESR (40 (21 vs 29 (21)  $p = 0.08$ ).

**Conclusion:** Cardiovascular disease is increased in early inflammatory arthritis and new cardiovascular disease is associated with greater systemic inflammation. Early disease control aimed at minimizing systemic inflammation may reduce risk of cardiovascular disease in this population.

191

### **Evaluation of BC Rheumatologists' Triage of Early Rheumatoid Arthritis**

Matthew Renwick (Vancouver); John Esdaile (Arthritis Research Center of Canada and Division of Rheumatology, University of British Columbia, Richmond); Jason Kur (Division of Rheumatology, University of British Columbia, Vancouver); Kamran Shojania (University of British Columbia, Vancouver)

**Objective:** Because the new CRA guidelines recommend that DMARDs be administered within three months of rheumatoid arthritis (RA) diagnosis (Bykerk et al., J Rheumatol 2012), we conducted a population-based study of the time from consultation request by a family physician (FP) to booking of the visit with the rheumatologist in British Columbia. We evaluated whether or not the CRA guideline

recommendation was met and contrasted the difference in time to consultation of real referrals for two separate consult requests: one suggesting early RA and the other osteoarthritis (OA).

**Methods:** Two fictitious referrals were developed: one for a patient with likely early RA and one with likely generalized OA. Following ethics approval, one FP from each of the thirteen BC health regions containing a practicing rheumatologist submitted the two referrals to each licensed rheumatologist within their region and collected and forwarded the rheumatologists' responses regarding appointment times. Univariate and bivariate statistical analyses were conducted.

**Results:** Of the 43 licensed BC rheumatologists included in the study, 40 (93%) booked the early RA patient for a consultation within 90 days. The mean, median, standard deviation (SD), and interquartile range (IQR) for the time to consultation for early RA were 36, 33, 24, and 23 days, respectively. In comparison, the corresponding mean, median, SD, and IQR for time to OA consultation were 220, 192, 120, and 183 days, respectively. The consult wait time for RA was significantly shorter than for OA ( $p < 0.001$ ) and wait times varied both across and within regions of BC.

**Conclusion:** BC rheumatologists prioritize early RA patients over OA cases with 93% of rheumatologists booking a likely early RA patient for consultation within 90 days of the FP request, and, thereby, within the maximum time to consultation required to satisfy the 2012 CRA guidelines for RA treatment.

## 192

### **How does Non-Compliance to Prolia® (Denosumab) Affect the Change in Bone Mineral Density (BMD)?**

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**Objective:** The efficacy of Prolia® (denosumab) has proven to be a safe and efficacious therapy for osteoporotic patients in clinical trials. However, few studies have been performed to determine its effectiveness in clinical practice. Currently, best practice guidelines state that Prolia® should be administered every six months. This study explores whether deviation from this recommended subcutaneous injection course would influence BMD.

**Methods:** A retrospective cohort study was conducted from August 2012 to August 2013 for all osteoporotic patients who received a minimum of two subcutaneous injections of Prolia® since May 2010. Patients who have only received their first subcutaneous injection and patients without recent BMD scores were excluded from the study. All patients currently treated with Prolia® for a minimum of twelve months were included in this study. Data obtained included age, sex, injection history, and BMDs. Patients were classified as having a subsequent injection less than five months, between five to seven months, or more than seven months after their initial subcutaneous injection. Changes in BMD from a one-year follow-up were obtained and compared.

**Results:** Of the study population ( $n=212$ ), the baseline characteristics were: mean (SD) age  $68.78 \pm 11.56$  years, 91.9% female, 8.1% male. After one year of treatment, BMD scores increased in all three groups for both lumbar spine (37.79%, 15.16%, 18.09%) and femoral neck (8.77%, 5.55%, 8.77%) for patients receiving a subsequent injection less than five months, between five to seven months and more than seven months after their initial injection, respectively. The relationship between drug administration and change in BMD was found to be statistically insignificant ( $p > 0.05$ ).

**Conclusion:** This study demonstrates that the efficacy of Prolia® (denosumab) is not affected by changes

in injection date. Current best practice is to administer the drug every six months but this preliminary data suggests that there is some flexibility. Clinical guidelines could be adapted based on these findings to improve patient compliance and efficiency of patient management.

## 193

### **Utility of Musculoskeletal Ultrasound in an Outpatient Rheumatology Practise**

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**Objective:** This pilot project seeks to evaluate the role of Musculoskeletal ultrasound (MSUS) in an outpatient rheumatology setting by: 1) describing the cases in which MSUS is used; 2) determining if the use of MSUS in clinic alters referrals, expedites care, or changes treatment; and 3) describing patient satisfaction with outpatient MSUS.

**Methods:** Consecutive patients seen in a Sunnybrook Health Science Centre rheumatology clinic and referred to radiology between May 1- June 30, 2013 (2 months) were recorded as Time 1 (T1). Patients who had MSUS who were referred to radiology or had MSUS in office between July and August 2013 were recorded as Time 2 (T2). Using a standardized case form, information on age, sex, disease diagnosis (if available), reason for referral, anatomical site, and findings were recorded.

**Results:** Twenty-three referrals were made to radiology for MSUS for 30 anatomical sites over T1. These referrals were comprised of 11 (37%) hands, 9 (30%) feet, 4 (13%) shoulders, and other sites. Imaging confirmed the provisional diagnosis in 33% of these patients. During T2, with the implementation of US-guided imaging in the clinic setting, 17 (40%) referrals were made to radiology for ultrasound. 26 (60%) of the patients requiring ultrasound received them in-clinic during their rheumatology appointment. Of those receiving ultrasound in clinic, 16 (57%) had imaging of their hands, 9 (32%) of their feet and the remaining patients had ultrasound of their hips and knees. The diagnosis was confirmed for 83% of the patients with in-clinic MSUS. Of those referred to radiology in T2, 6 (35%) had imaging of their hands, 5 (29%) of their feet, 4 (23%) for shoulders and 2 (12%) for hip. Provisional diagnosis was confirmed for 47% of the patients referred to radiology. 18% of the referrals were for joint injections following the confirmation of the diagnosis. On average, a 29-day time delay existed between rheumatology and radiology appointments. Patient's reacted positively to in-clinic MSUS.

**Conclusion:** The use of MSUS in the outpatient setting aided in the clinical diagnosis of patients, fewer referrals to radiology for MSUS, and improved efficiency in time to diagnosis and amount of patient time invested in clinical care. Overall, more MSUS were completed. This may be because of its ease of use and ready availability. MSUS in an outpatient rheumatology setting has the potential to improve patient care by expediting results and may provide cost savings by decreasing outpatient radiology referrals.

## 194

### **Procedural Pain with Weekly Injections of Subcutaneous Methotrexate in Children with Rheumatic Disorders.**

Melanie Bechard (University of Toronto Mississauga, Mississauga); Julie Lemieux (Children's Hospital of Eastern Ontario, Ottawa); Johannes Roth (Children's Hospital of Eastern Ontario, Ottawa); Karen Watanabe Duffy (Children's Hospital of Eastern Ontario, Ottawa); Ciaran Duffy (Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa); Mary Aglipay (CHEO Research Institute, Ottawa); Nick Barrowman (Ottawa); Roman Jurencak (Children's Hospital of Eastern Ontario and University of Ottawa, Ottawa)

**Objective:** Procedural pain may have long-term negative effects on children. The aim of this study was to evaluate the amount of pain associated with weekly subcutaneous injections of methotrexate.

**Methods:** A prospective observational cohort study was conducted from June 2013 through August 2013. All patients with appointments in rheumatology clinic during this period were screened for eligibility. Patients between the ages of 4-17 years who were currently receiving weekly subcutaneous methotrexate injections for at least 4 weeks were invited to participate in the study. Patients and families underwent a focused interview, conducted by one interviewer, exploring their experience with methotrexate injections. Thereafter, they were trained to use the Faces Pain Scale – Revised (FPS-R) tool to be able rate pain associated with future methotrexate injections. Associations between pain scores and age, duration of therapy, and presence of side effects were tested using simple and multiple linear regression.

**Results:** 41 out of 42 eligible patients consented to the study. Four patients were switched from subcutaneous to oral route of methotrexate at the time of study enrolment. Of the remaining 37 patients, 29 (78%) returned the completed pain scales. The mean age was 11.2 years (SD = 3.9 years) and 68% were female. Most of these patients were diagnosed with JIA (73%). Mean duration of therapy with subcutaneous injections of methotrexate was 2.5 years (SD = 2.1 yrs) and the dosing range was 0.3-1mg/kg/week (maximum 25mg/week). The upper arm was the preferred injection site in 71% of patients. Median amount of pain in the subset of 29 patients was 2/10; 18 (62%) patients reported mild pain (FPS-R score 0-2), 9 (31%) reported moderate pain (FPS-R score 4-6) and 2 participants reported severe pain (FPS-R 8-10). In univariate testing, higher intensity of pain was associated with presence of side effects ( $p=0.004$ ), but not duration of therapy ( $p=0.20$ ) or age ( $p=0.24$ ). Results were largely unchanged in multiple linear regression. Injection pain was successfully alleviated by ice in 10/14 patients (71%), comfort positions in 14/21 patients (67%), rewards in 13/20 patients (65%), reassurance in 11/22 patients (50%), distraction in 10/21 patients (48%), and analgesics in 4/9 patients (44%).

**Conclusion:** While the average amount of pain associated with subcutaneous injections of methotrexate is mild, patients who suffer from methotrexate associated side-effects report significantly higher levels of pain. Patients and families reported using various effective strategies to alleviate injection associated pain.

195

### **Patient-Reported Side Effects with Weekly Injections of Methotrexate in Tertiary Care Rheumatology Clinic**

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**Objective:** Methotrexate is frequently used to treat a variety of paediatric rheumatologic conditions. We explored patient-reported frequency of side effects and coping strategies for weekly injections of subcutaneous methotrexate.

**Methods:** A prospective observational cohort study was conducted from June 2013 through August 2013. All patients with clinic appointments in rheumatology during this period were screened for eligibility. Patients aged 4-17 years who were currently receiving weekly subcutaneous methotrexate injections for at least 4 weeks were invited to participate in the study. A focused interview with the patient and family members, conducted by one interviewer, investigated their experiences with subcutaneous methotrexate. The interview consisted of 18 questions and required approximately 10 minutes to complete.

**Results:** 42 patients met inclusion criteria and 41 consented to participate in the study. The mean age was 11.2 years (SD=3.9yrs) and 68% of participants were female. Most of these patients were diagnosed with juvenile idiopathic arthritis (73%). Mean duration of therapy with subcutaneous injections of methotrexate was 2.5 years (SD=2.1yrs) and the dosing range was 0.3-1mg/kg/week (maximum 25mg/week). Almost all

patients (95%) reported excellent adherence to the treatment regimen, missing less than one dose per month. The two most commonly reported side effects were nausea and vomiting (56% and 34% of patients, respectively). Less frequently reported side effects included fatigue (29%), anorexia (27%), headache (15%), and recurrent oral ulcers (10%). Of patients who experienced nausea, 52% used dimenhydrinate while 26% used ondansetron to manage their symptoms. Similarly, many patients who experienced vomiting tried to alleviate their symptoms with dimenhydrinate (57%) or ondansetron (28%). While dimenhydrinate effectively treated nausea in only 42% of patients, most patients reported good efficacy of ondansetron (83%). A similar effect was observed for treatment of vomiting (efficacy of dimenhydrinate 12% versus ondansetron 75%). None of the patients tried ginger to alleviate nausea/vomiting. Except for oral ulcers, clinical side effects resolved within 24 hours in 92% of patients. Of patients who had used oral methotrexate in the past, only 26% felt that the oral form was better tolerated.

**Conclusion:** More than half of the patients reported at least one side effect that could be attributed to methotrexate injections; the most frequent ones were nausea and vomiting. Importantly, most side effects resolved within 24 hours and patients reported excellent compliance. In general, patients did not have a preference for oral methotrexate.

## 196

### **Economic Impact of Psoriatic Arthritis at a Single Center in Toronto Ontario**

Michal Bohdanowicz (Toronto Western Hospital, Toronto); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Vinod Chandran (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

**Objective:** Psoriatic arthritis (PsA) is heterogeneous, chronic inflammatory condition that most commonly occurs among patients with psoriasis. It can present with swelling and stiffness of affected joints, inflammation of the back (spondylitis), tenderness at the sites of tendon and ligament insertion into bone (enthesitis) and swelling of a whole digit (dactylitis). As these symptoms progress, they limit quality of life and economic output and can ultimately result in joint destruction. Novel therapeutics that target TNF $\alpha$  limit disease progression; however, it is unclear whether these new, expensive drugs make economic sense. In other words, are the direct and indirect costs of PsA significant enough to warrant such expensive interventions?

**Methods:** Patients answered a survey about their direct costs and also filled out the Valuation of Lost Productivity (VOLP) questionnaire to assess their indirect costs. Other data were extracted from the longitudinal, observational database maintained by the University of Toronto Psoriatic Arthritis Program.

**Results:** We recruited 111 patients from the PsA clinic at the Toronto Western Hospital. The participants in the study were demographically similar to the non-participants for all variables except bisphosphonate use, history of myocardial infarction, cigarette smoking history and active joint count. The participants had an average age of 52.5 years, average duration of PsA of 16.2 years, and an average damaged joint count of 10.4 joints. Most participants were on a non-steroidal anti-inflammatory drug (NSAID) or a disease-modifying antirheumatic drug (DMARD) (57.7%) but a significant proportion also used one of the biologics (52.3%). The average annual drug costs per patient in 2012 Canadian dollars were \$61.31 for NSAIDs, \$386.26 for DMARDs and \$10,730.39 for biologics. On top of this, patients spent an average of \$256.54/year for over-the-counter medications and \$549.24/year on complementary or alternative medicine. Their average annual healthcare costs in terms of clinic visits, diagnostic tests, hospital admissions and surgeries were \$1,566.72. Patients lost on average 0.76 days of work per financial quarter.

**Conclusion:** In summary, patients with PsA face a number of economic challenges. Even though the biologics are the most effective treatment for PsA, they are also the most significant economic burden. Further studies need to be done to determine whether the health benefits of the biologics outweighs their

significant cost.

197

### **Safety and Effectiveness of Mycophenolate in Systemic Sclerosis: A Systemic Review**

Mohammed Omair (Toronto Scleroderma Research Program, Division of Rheumatology, Mount Sinai Hospital, Toronto Western Hospital, University Health Network, University of Toronto; Division of Rheumatology, Department of Medicine, King Saud University, Riyadh, Toronto); Abdulaziz Alahmadi (Toronto Scleroderma Research Program, Division of Rheumatology, Mount Sinai Hospital, Toronto Western Hospital, University Health Network, University of Toronto, Toronto); Sindhu Johnson (Division of Rheumatology, Toronto Western Hospital, University Health Network Pulmonary Hypertension Programme, Toronto General Hospital, Mount Sinai Hospital and University of Toronto, Toronto )

**Objective:** Mycophenolate reduces chronic allograft nephropathy and interstitial fibrosis by inhibiting TGF- $\beta$ , which is an important molecule in the pathogenesis of systemic sclerosis (SSc). The main side effects observed are gastrointestinal disturbance, myelosuppression, and increased risk of infection. This maybe a limitation of its use in SSc patients since gastrointestinal involvement is very common. The objective of this study is to evaluate the safety, in particular gastrointestinal adverse events, of mycophenolate in SSc. Secondly we evaluated the effectiveness of mycophenolate in SSc skin and lung disease.

**Methods:** A literature search of Medline, Embase, Cochrane Central Register of Controlled Trials, and CINAHL (inception - September 2012) was performed. Titles and abstracts were screened to identify studies that described the use of mycophenolate in SSc patients. Inclusion criteria included exposure to mycophenolate, and reporting of modified Rodnan skin score (MRSS), forced vital capacity (FVC), diffusing capacity of carbon monoxide (DLCO); or adverse events. The primary outcome was gastrointestinal events occurring after the initiation of mycophenolate. Secondary safety outcomes included myelosuppression, infection, malignancy, and death occurring after the initiation of mycophenolate.

**Results:** 616 citations were identified and 20 were included in the analysis. 477 patients have been exposed to mycophenolate. The mean disease duration ranged between 0.8-14.1 years. There were 89 non-lethal adverse events, of which 43 (48%) were gastrointestinal and 46 (52%) were non-gastrointestinal adverse events. The most commonly reported gastrointestinal events included diarrhea (n=18 (20%)), nausea (n=12 (13%)), and abdominal pain (n=3 (3%)). The most commonly reported non-gastrointestinal adverse events were infections (n=33 (37%)), and 6 cytopenias (n=6, (7%)). The reported rate of discontinuation ranged between 8-40%. Seven observational studies report mycophenolate is effective improvement or stabilization in FVC, and 5 observational studies report stabilization or improvement in MRSS.

**Conclusion:** Observational studies report mycophenolate is effective in improving or stabilizing interstitial lung disease, and may be effective for skin involvement. However, gastrointestinal adverse events are common in SSc patients.

198

### **Relationship between DAS28 and SDAI50 Response in Patients with Early Rheumatoid Arthritis**

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**Objective:** An essential element of treat to target strategy is adjusting therapy in the absence of achieving a target response by 12 wk. A  $\Delta$ DAS28 of 1.2 and Simplified Disease Activity Index of 50% (SDAI50) are used as response measures (RM). Our objective was to assess the relationship between the 2 RM and to

characterize patients failing to respond based on either RM.

**Methods:** Data from the Canadian early Arthritis CoHort (CATCH), an early arthritis cohort of patients with symptoms duration of  $\leq 12$  mo were used. Among patients with RA, we assessed biologic naive patients with available data to calculate DAS28 and SDAI at baseline (BSL) and 12 wk. We included patients on stable DMARD (no  $\Delta$  in therapy) during the first 3 mo of f/u. Response to treatment was evaluated at 12 wk. Correlation and agreement between 2 criteria was assessed by kappa statistics and Spearman correlation. BSL characteristics and median change from BSL were compared in patients with discordant RM. Probability plots of achieving each RM against BSL DAS28 score were evaluated.

**Results:** In total, 419 patients were included. Most were women (75%) with mean age of 52.6 years. Other BSL variables (mean): disease duration 5.7 months, tender joint count (TJC) 9.0, swollen joint count (SJC) 8.2, DAS28 5.2, SDAI 29.7 and CRP 14.4. 198 (47%) patients failed to achieve a DAS28 $\Delta$  and 206 (49%) failed to achieve SDAI50. There was a significant agreement between DAS28 and SDAI50 RM (Kappa 0.66) with a Spearman Correlation of 0.66 ( $p < 0001$ ). Of patients failing SDAI50, 19.2% achieved a DAS28 $\Delta$ , of patients failing a DAS28 $\Delta$ , 16.6% patients achieved SDAI50. In patients with discordant RM, BSL disease activity measures were higher in DAS28 responders (Table). The probability of achieving the DAS28 $\Delta$  was higher in patients in higher disease activity and it was the opposite in the lower activity range. Median change of activity measures was higher in patient who achieved DAS28 $\Delta$ .

**Conclusion:** SDAI50 and DAS28 RM are well correlated although in patients in high disease activity states the likelihood of achieving an SDAI50 is lower than achieving a DAS28 $\Delta$ , while the reverse is true at lower disease activity states.

## 199

### **Drug-Induced Back Pain, Polyarthritis and Uveitis: A Curious Case**

Moiria Rushton (University of Ottawa, Ottawa); Pierre Giguere (Ottawa); Touchie Claire (Ottawa); Douglas Smith (The Ottawa Hosp, Ottawa)

**Case Report:** Rifabutin has been described in the literature to cause side effects such as uveitis and occasionally polyarthritis in immune-compromised patients. Previous cases have been described in the context of treatment for mycobacterium avium complex with both rifabutin and clarithromycin. It is known that protease inhibitors used in human immunodeficiency virus (HIV) treatment inhibit the metabolism of rifabutin and increase its toxic effects. We describe an interesting case of a 33-year-old woman with HIV and pulmonary tuberculosis on antiretroviral therapy, including darunavir/ritonavir and the anti-mycobacterial drug rifabutin. She first developed ankle pain and swelling followed by unilateral uveitis, polyarthralgia, back pain and stiffness suggesting the possibility of a spondyloarthropathy. Extensive work-up for potential causes of reactive arthritis was all negative, including plain X-rays and HLA-B27. With substitution of raltegravir for darunavir/ritonavir and rifampin for rifabutin and short course of naproxen the patient's symptoms completely resolved. This is the first reported case of a clinical syndrome resembling a spondyloarthropathy associated with a drug interaction leading to rifabutin toxicity.

## 200

### **Intra- and Inter-Rater Reliability between a Trainee and Expert in Plain Radiographic Evaluation of Femoroacetabular Impingement**

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Center of Canada and Division of Rheumatology, University of British Columbia, Richmond); Bruce Forster (Department of Radiology - UBC Hospital, Vancouver)

**Objective:** The objective was to determine the intra- and inter-rater reliability of three radiographic signs of femoroacetabular impingement (FAI) and whether an inexperienced reader (medical student) could be trained to read reliably for FAI.

**Methods:** This study was conducted within IMPAKT-HiP\*, a large population based multi-faceted study on the role of FAI and physical activity in cartilage damage and hip pain. An anteroposterior pelvis and bilateral Dunn projection radiographs were acquired. The medical student was trained using a sample set of 25 cases with and without FAI, not from the study cohort. Training results were reviewed with a radiology fellow and an experienced musculoskeletal radiologist to refine reading technique. Following training, 50 subjects were selected, 40 randomly from the study cohort and 10 with clinically confirmed FAI. These were read independently for FAI by the medical student and by a fellowship-trained musculoskeletal radiologist, blinded to subject identity and clinical information. To assess intra-rater reliability, cases were randomized and re-read by the medical student 8 weeks later. Three radiographic signs were evaluated: focal acetabular retroversion (figure 8), lateral center edge angle (LCE angle), and alpha angle. Either a positive figure 8 or a LCE angle of  $>40^\circ$  was considered pincer-type FAI, and an alpha angle of  $>55^\circ$  was considered cam-type FAI. Overall FAI was defined as meeting any of the 3 criteria. Reliability was determined using prevalence adjusted, bias adjusted kappa (PABAK) with corresponding 95% confidence intervals (CI). Weighted analysis was used to account for over-representation of FAI-positive individuals.

**Results:** Intra-rater PABAK for overall FAI was 0.76 (95% CI: 0.57, 0.94). The intra-rater PABAK values were 1.00 (95% CI: 0.85, 1.00) for LCE angle, 0.71 (95% CI: 0.50, 0.91) for alpha angle and 0.72 (95% CI: 0.52, 0.92) for figure 8. Inter-rater PABAK for overall FAI was 0.55 (95% CI: 0.30, 0.80). The inter-rater PABAK values were 0.72 (95% CI: 0.52, 0.93) for LCE angle, 0.74 (95% CI: 0.55, 0.92) for alpha angle and 0.69 (95% CI: 0.48, 0.89) for figure 8.

**Conclusion:** An inexperienced reader can achieve moderate to substantial intra- and inter-rater reliability in the assessment of overall FAI and substantial intra- and inter-rater reliability in the assessment of FAI in respect to individual radiographic signs. Being able to accurately and reproducibly define FAI radiographically is essential to future research to assess prevalence of FAI and its role in causing hip OA.

## 201

### **The Validation of Administrative Osteoarthritis Diagnosis using a Clinical and Radiological Population-Based Cohort from British Columbia, Canada**

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**Objective:** Recently administrative databases have become a popular means of health research for osteoarthritis (OA). We aimed to examine the validity of OA diagnosis in the British Columbia's administrative health records against four gold standards.

**Methods:** Administrative data were linked to a cohort of 171 subjects who had knee pain, aged 40-79 years, and underwent comprehensive clinical assessment, joint examination, x-ray, and magnetic resonance imaging (MRI) to identify knee OA. These subjects did not have inflammatory arthritis, fibromyalgia, or knee arthroplasty/injury. Administrative OA was defined in two ways: 1) at least one visit to a health professional or one hospital admission with the ICD-9 code of 715 or the ICD-10 codes from M15 to M19 (AOA1) and 2) at least two physician diagnoses in two years or one hospital admission with these codes (AOA2). Sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios (LR+ and LR-) were obtained using four gold standards including x-ray (Kellgren-



Lawrence grades), MRI cartilage score, self-report, and American College of Rheumatology clinical criteria.

**Results:** Significant differences were observed among the four knee OA measures ( $p$ -value  $< 0.01$ ), where MRI detected the highest percentages of OA (91.7% and 88.5% in women and men respectively) and x-ray detected the lowest percentages of OA (42.9% and 44.9% in women and men respectively). The sensitivity of AOA1 and AOA2 varied from 47% to 57% and from 21% to 26%, respectively. The highest sensitivity (95% CI) was 57% (48%-66%) for AOA1 when self-reported knee OA was the gold standard. The lowest sensitivity (95% CI) was 21% (15%-29%) for AOA2 when MRI score was the gold standard. The specificity varied from 75% to 87% for AOA1 and from 91% to 100% for AOA2. LR+ was higher than 5 in AOA2 for MRI and self-report gold standards and therefore, AOA2 might be useful in ruling in OA. However, the definitions might not be very useful to ruling out OA since, the values of LR- were between 0.5 and 0.8.

**Conclusion:** The validity of administrative OA diagnosis varied due to case definitions and gold standards. Our data demonstrate that AOA1 might be appropriate in descriptive analysis, as it reduces underestimation due to false negatives, whereas for outcome research, where avoiding false positives is critical, AOA2 should likely be applied. Data from this study provide valuable information to OA researchers using administrative databases.

## 202

### Isolated Aortitis - a Canadian Initiative

Nataliya Milman (University of Ottawa / Ottawa Hospital, Ottawa); Diane Murzin (The Ottawa Hospital, Ottawa)

**Objective:** Isolated aortitis is a single organ vasculitis that is limited to aorta (often ascending) and is not associated with a systemic condition. It is most commonly diagnosed when evidence of vasculitis is found, often unexpectedly, on a pathologic specimen of a resected aortic aneurism or a repaired aortic valve.

**Methods:** A systematic literature review was performed in preparation for a Canada-wide initiative to study isolated aortitis. Medline database (1946 to present) was searched for original studies on “isolated” or “idiopathic” aortitis.

**Results:** Nine relevant studies containing between 11 and 64 patients were identified: 8 retrospective case series and 1 case control study. The oldest of these studies, a retrospective case series of 52 patients from Cleveland clinic, dates to 2000, highlighting the relatively recent recognition of isolated aortitis as a distinct entity. Significant variability was observed in regards to workup, management, and follow-up strategies for patients with isolated aortitis in identified studies, and no disease-specific guidelines exist to facilitate consensus. Although the prognosis of isolated aortitis is felt to be good even with no immunosuppressive treatment, a proportion of patients (24% of untreated patients in the aforementioned study from Cleveland) do develop additional aortic lesions, some with associated complications including death.

**Conclusion:** Systematic studies are needed to better characterize isolated aortitis and to identify the optimal management strategy. Two related studies of isolated aortitis have been launched at The Ottawa Hospital: 1) a retrospective case series, and 2) a prospective (pilot) cohort. The retrospective study will identify patients with aortitis in pathologic specimen from aortic and cardiac surgeries performed over 10 years (2003-2012). Patients' clinical presentation, results of investigations including imaging studies, treatments and outcomes will be described, and pathology specimen will be reviewed to confirm (and further characterize where possible) the diagnosis. The prospective isolated aortitis cohort will include patients diagnosed based on pathologic specimen from cardiac and aortic surgeries or based on aortic imaging. Cardiovascular surgeons, pathologists, and radiologists will refer cases for enrolment. Additional investigations and imaging studies, follow-up, and treatment strategies will be performed according to a

pre-defined protocol. Because of the rarity of isolated aortitis, a large multicentre study is needed to obtain clinically valuable data. Canadian Vasculitis Network (CanVasc) is a network of Canadian investigators interested in studying vasculitis, established in 2010. Other CanVasc constituent centres will be joining Ottawa in effort to study isolated aortitis over the subsequent months to make it a country-wide initiative.

**203**

### **Venous Thromboembolic Events in Patients with Granulomatosis with Polyangiitis: A Population Based Study**

Natasha Dehghan (University of British Columbia, Vancouver); Neda Amiri (Vancouver); Kamran Shojania (University of British Columbia, Vancouver); Eric Sayre (Arthritis Research Centre of Canada, Richmond); Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Richmond)

**Objective:** Limited literature is available on the incidence of venous thromboembolic events (VTE) in patients with Granulomatosis with Polyangiitis (GPA), formerly known as Wegener's granulomatosis. Our objectives were 1) to assess the risk of VTE including pulmonary embolism (PE) and deep vein thrombosis (DVT) and 2) to assess time trends on the risk of VTE in cases with GPA compared to controls from the general population using administrative data.

**Methods:** Our data included all visits to health professionals and hospital admissions (1990-2010) and all dispensed medications (1995-2010) for all individuals. A retrospective matched incident cohort study was assembled (1996-2010) using the following algorithm: a) new diagnosis of GPA by a rheumatologist or from hospitalization or b) two visits for GPA at least two-months and not more than two-years apart by a non-rheumatologist physician; and c) absence of a prior GPA diagnosis between 1990-1995. Ten controls matched by birth year, sex and calendar year of exposure were selected from the general population for each case. Our outcome was new diagnosis of VTE (PE/DVT) from outpatient (DVT only) and hospital visits (VTE) or death certificate (VTE). For nonfatal events, we required the use of anticoagulant medications within six months of the VTE event. We estimated relative risks (RRs) comparing GPA cases with controls before and after adjusting for potential risk factors. Individuals in the respective cohorts with outcomes prior to the index date were excluded.

**Results:** We identified 622 individuals with incident GPA (54 % female, mean age of 59 years). The unadjusted age-, sex- and entry-time matched RRs were significantly increased in the GPA cohort when compared with the controls for VTE, PE and DVT (RRs= 8.3, 95% CI 5.0-13.6; 7.7, 95% CI 4.0-14.5 and 10.6, 95% CI 5.3-21.2, respectively). The multivariable RR for VTE remained statistically significant after adjustment for relevant risk factors at baseline (adjusted-RRs= 8.2, 95% CI 4.6-14.6). Similar results were seen for DVT and PE individually (adjusted-RR= 9.9, 95% CI 4.3-22.8 and 6.5, 95% CI 3.1-13.5, respectively). The risk of developing VTE was highest in the first year of diagnosis (RR= 25.1, 95% CI 10.9-62.6). Similar results were seen for DVT and PE.

**Conclusion:** This large population-based study found an increased risk of VTE (DVT/PE) in patients with GPA. Risk is highest within the first year of diagnosis suggesting that inflammation may be the main driver. Awareness of such associations will help in monitoring for such preventable outcomes in this population.

**204**

### **Depressive Symptoms at Baseline Predict Higher Simple Disease Activity Index (SDAI) Scores and Longer Time to Remission in Patients with Recent-Onset Arthritis**

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de Sherbrooke, Sherbrooke); Pierre Cossette (Université de Sherbrooke, Sherbrooke); Gilles Boire (Université de Sherbrooke, Sherbrooke)

**Objective:** To determine if depressive symptoms at inclusion influence Simple Disease Activity Index (SDAI) scores and time to SDAI remission in patients with recent-onset arthritis (EPA) treated with the objective of 0/66 swollen joint.

**Methods:** Patients were recruited consecutively as part of the EUPA cohort if they presented with immune-mediated arthritis affecting at least 3 joints for 1 to 12 months. Demographics, SDAI, M-HAQ, Sharp-van der Heijde (SHS) radiological scores, Rheumatoid Factor and anti-CCP2 status, tobacco use and treatment data were collected at baseline and at 12, 18, 30 and 42 months after disease onset. Center for Epidemiological Studies Depression Scale (CES-D; 20 items) questionnaires were completed at each visit. Spearman correlations were evaluated between CES-D scores and SDAI. Comparison of CES-D scores during follow-up was evaluated with Friedman test and with generalised estimating equation for dichotomous CES-D scores. Log-transformed SDAI scores were used to compute univariate and multivariate linear regression. Kaplan Meier and Cox regression were used to assess time to remission.

**Results:** 254 EPA patients were eligible (median (IQR) age 60.6 (51.8-69.8) years; median (IQR) symptom duration 3.8 months (2.3-6.4); 62.2% women). CES-D scores decreased from inclusion to the last follow-up ( $p < 0.0001$ ). At inclusion, 18, 30 and 42 months, 46%, 21%, 17% and 19% of patients had a CES-D score  $\geq 19$  (the cut-off score for patients with chronic pain, suggestive of clinical depression), respectively ( $p < 0.0001$ ). Weak but significant correlations ( $r \approx 0.18$ ,  $p < 0.05$  at 18, 30 and 42 months) were found between baseline CES-D scores and follow up SDAI scores; moderate correlations ( $r = 0.34$  at 18 months and 0.40 at 30 months) were found between concomitant CES-D scores and SDAI scores. Kaplan-Meier curves revealed a longer time to SDAI remission in patients with a CES-D  $\geq 19$  at inclusion (median time 22 vs 32 months,  $p = 0.01$ ). In a multivariate linear regression model, baseline CES-D, age and BMI predicted SDAI at 30 and 42 months.

**Conclusion:** Depressive symptoms decreased over time in treated EPA patients. The correlations between CES-D and SDAI scores were highest when assessed concomitantly, although a significant correlation was observed between baseline CES-D and follow-up SDAI at 18, 30 and 42 months, suggesting that patients with higher CES-D scores at baseline took longer to attain remission. Assessment of depressive symptoms at all visits may identify a condition that represents a treatable hurdle to attain remission and to improve patients' outcome.

## 205

### **Risk of Cardiovascular Events in Patients with Granulomatosis with Polyangiitis: A Population Based Study**

Neda Amiri (Vancouver); Natasha Dehghan (University of British Columbia, Vancouver); Eric Sayre (Arthritis Research Centre of Canada, Richmond); Kamran Shojania (University of British Columbia, Vancouver); Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Richmond)

**Objective:** Our objective was to assess the risk of myocardial infarction (MI) and cerebrovascular accidents (CVA) in cases with Granulomatosis with Polyangiitis (GPA) compared to controls from the general population using administrative health data. We also explored time trends for these events since the diagnosis of GPA.

**Methods:** Our data included all visits to health professionals and hospital admissions from 1990 to 2010 and all dispensed medications from 1995 to 2010 for all individuals. A retrospective matched cohort (1996-2010) study was performed among patients satisfying the following criteria: a) new diagnosis of GPA by a rheumatologist or from hospitalization or b) two visits for GPA at least two months and not more than two

years apart by a non-rheumatologist physician; and c) absence of a prior GPA diagnosis between January 1990 and December 1995. Ten controls matched by birth year, sex and calendar year of exposure were selected from the general population for each case. For purposes of matching, the controls were considered "exposed" on a doctor visit date. Our outcome was newly recorded MI and CVA from hospital or death certificate. Individuals in the respective cohorts with outcomes prior to the index date were excluded.

**Results:** We identified 640 individuals with incident GPA (54 % female, mean age of 59 years). Among these patients, 40 developed an MI and 41 developed a CVA. The age-, sex- and entry-time matched RRs were significantly increased in the GPA cohort when compared with the control for both MI and CVA (RR= 2.9, 95% CI 2.0-4.1 and 2.5, 95% CI 1.8-3.6 for MI and CVA, respectively). The multivariable RR remained statistically significant after further adjustment for history of angina, COPD, obesity, hormone replacement therapy, oral contraceptives, glucocorticoids, cardiovascular medications, diabetes, dyslipidemia, NSAIDs, COX-2 inhibitors, fibrates, statins, number of hospitalizations and Charlson's comorbidity index at baseline. The risk of developing an MI or CVA was highest in the first year of diagnosis (RR= 6.6, 95% CI 3.5-12.0 and RR= 4.6, 95% CI 2.5-8.1 for MI and CVA, respectively) and decreased over time.

**Conclusion:** This large population-based study found an increased risk of MI and CVA in patients with GPA in a Canadian setting. Risk is higher within the first year of diagnosis suggesting that inflammation may be the main driver. Awareness of such associations will help in implementation of preventative treatment in decreasing morbidity and mortality in this population.

## 206

### Comparison of Systemic Sclerosis Subsets Based on Skin and Serology

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**Objective:** Anti-centromere antibodies (ACA) are usually associated with limited cutaneous systemic sclerosis (lcSSc) and anti-topoisomerase I antibodies (ATA) with diffuse cutaneous systemic sclerosis (dcSSc). We undertook this study to describe the clinical characteristics of ACA positive dcSSc and ATA positive lcSSc subjects. We hypothesized that subsetting by antibody status would be more accurate than by extent of skin involvement, which is more prone to measurement error.

**Methods:** Data from 1158 subjects in the Canadian Scleroderma Research Group cohort were extracted. Four groups were compared: ATA+ lcSSc, ATA+ dcSSc, ACA+ lcSSc and ACA+ dcSSc. Descriptive statistics were used to summarize the baseline characteristics, including sociodemographic, clinical and serological profiles of the 4 groups. Kaplan Meier curves were generated to investigate survival by group.

**Results:** Of the 1158 patients, 52 (4.5%) had ATA+ lcSSc, 110 (9.5%) ATA+ dcSSc, 297 (25.6%) ACA+ lcSSc and 91 (7.9%) ACA+ dcSSc. Modified Rodnan skin scores (range 0-51) were as follows: ATA+ lcSSc 6.3, ATA+ dcSSc 16.2, ACA+ lcSSc 4.2 and ACA+ dcSSc 12.9. The presence of ATA was associated with younger mean age, higher proportion of males, shorter disease duration, and more finger contractures, polyarthritis and myositis compared to ACA in both lcSSc and dcSSc subjects. The presence of ACA was associated with more gastrointestinal symptoms compared to ATA in both lcSSc and dcSSc subjects. There were striking differences in the 4 groups in the frequency of interstitial lung disease (ATA+ lcSSc 49.0%, ATA+ dcSSc 56.0%, ACA+ lcSSc 13.3% and ACA+ dcSSc 22.1%), pulmonary hypertension (ATA+ lcSSc 4.8%, ATA+ dcSSc 10.0%, ACA+ lcSSc 13.7% and ACA+ dcSSc 16.3%), and scleroderma renal crisis (ATA+ lcSSc 3.8%, ATA+ dcSSc 2.7%, ACA+ lcSSc 0.7% and ACA+ dcSSc 0). Anti-RNA

polymerase III antibodies and/or anti-PM/Scl antibodies were more frequent in ACA+ dcSSc subjects compared to ACA+ lcSSc subjects (11.7% vs 3.1%, respectively). Survival was significantly better in ACA+ dcSSc patients compared to ATA+ dcSSc patients ( $p=0.0046$ ) and similar to ACA+ lcSSc ( $p=0.1982$ ).

**Conclusion:** Clinical features and survival appear to be more strongly associated to serological rather than skin subsets in SSc. In addition to measurement error, overlap with other autoantibodies known to predict more skin involvement (RNA polymerase III and PM/Scl) may contribute to greater skin involvement in ACA+ diffuse subjects. These findings can inform ongoing efforts to define more robust SSc subsets compared to that based on the extent of skin involvement.

## 207

### **Evaluation of a Novel Scoring Tool to Guide Treatment Decisions in Rheumatoid Arthritis: The Gestaltometer**

Stephanie Dizon (Queen's University, Kingston); Henry Aaverns (Queen's University, Kingston)

**Objective:** Rheumatoid Arthritis is a chronic inflammatory joint disease that can lead to irreversible joint destruction and functional limitation. Monitoring disease activity using measurement tools can help guide decision making to achieve disease remission. The gestaltometer has been designed to encompass the many factors that contribute to treatment change decisions including both objective and subjective assessments of disease activity. This tool is intended to be more comprehensive than already established tools and act as a guide to assist with decision making.

**Methods:** Patients with established RA were recruited in Rheumatology clinics at a single centre in Kingston, Ontario. Of the 250 subjects, only 101 of subjects had complete data whereby the clinician completed the assessment, while being blinded to scores. Primary outcomes were the degree of correlation between predicted and actual treatment change. Chi square analyses for correlation were tabulated comparing the actual treatment change to the predicted Gestaltometer, CDAI, and DAS-28 scores.

**Results:** Using the gestaltometer score, the predicted 'no change' score correlated to the actual 'no treatment change' in 100% (40/40) of subjects ( $p < 0.001$ ), whereas a predicted 'yes to change' score matched to an actual treatment change in 83.3% (20/24) of subjects ( $p < 0.001$ ). When comparing these outcomes to the CDAI and DAS-28 tests for correlation, there was greater association with respect to predicting a change in treatment. The CDAI score predicting 'remission' correlated to 'no change' in actual treatment in 100% (14/14) of the subjects ( $p < 0.001$ ), whereas a CDAI score predicting 'moderate-high disease activity' correlated to actual treatment change in 52.1% (21/48) of subjects ( $p < 0.001$ ). With respect to the DAS-28 scores, 94.4% (34/36) of those thought to be in 'remission' did not have an actual treatment change ( $p < 0.001$ ). Only 45% (18/40) of those deemed to have 'moderate-high disease activity' on the DAS-28 index had an actual treatment change at the time of assessment.

**Conclusion:** Based on this RA population, the Gestaltometer scores predicting remission correlate well with "no change" in actual treatment, similar to the CDAI and DAS-28 scores. However, when looking at scores predicting treatment change, the tool has a higher correlation with actual changes in treatment. The proposed scoring system, as a composite of patient's perception of disease activity, clinical assessment, laboratory, and radiographic findings is an excellent tool to predict and guide decisions in changing treatment for rheumatoid arthritis, and may have a role in guiding non-expert clinicians to identify patients needing treatment change.

## 208

### **Wafarin Induced Calciphylaxis**

Norman Madsen (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

**Case Report:** A 65 year old male referred from Renal Insufficiency Clinic, presented with a three week history of progressive left finger pain and paresthesias. He received intermittent hemodialysis for end-stage renal disease due to focal segmental glomerular sclerosis and had a left-sided arterio-venous fistula placed one year previously. The fistula had been ligated 10 days prior to admission as treatment for the pain in his left hand and fingers due to concern for a steal syndrome. On presentation the pain and paresthesias had progressed to involve all extremities and he had ischemic areas on both fingers and toes bilaterally, with small areas of digital necrosis. The patient had a prior history of atrial fibrillation, and had initiated warfarin 8 weeks prior to his presentation following cardioversion for atrial fibrillation. Past medical history was also significant for: hypertension, dyslipidemia, coronary artery disease, idiopathic thrombocytopenic purpura treated with rituximab and splenectomy, benign prostate hypertrophy, gout, ulcerative colitis and prior deep vein thrombosis. The patient denied Raynaud's phenomenon, sicca symptoms, oral ulcers, photosensitivity, skin rash or other symptoms of a rheumatologic disease or vasculitis. Laboratory tests including: anti-phospholipid antibody, complements, serum protein electrophoresis, cold agglutinins, cryoglobulins, ANA, ANCA, and rheumatoid factor were negative. ESR and C-reactive protein were elevated. A thoracic aortogram was performed and showed advanced bilateral peripheral arterial disease with extensive calcification throughout his arterial system. Based on clinical appearance of the ischemic digits and a supratherapeutic INR on admission, the patient was diagnosed with warfarin-induced calciphylaxis. Heparin infusion was initiated and warfarin was discontinued. The patient also received a dose of sodium thiosulfate for his calciphylaxis. The appearance of his digits slowly improved and his pain and parasthesias decreased following initiation of therapy. He was discharged home on acetylsalicylic acid. Given the temporal association of the initiation of warfarin and increased risk secondary to his end-stage renal disease, it is likely that this episode represented warfarin-induced calciphylaxis and skin necrosis. End-stage renal disease, with dialysis in particular, remains the strongest risk factor for calciphylaxis. Warfarin induced skin necrosis usually occurs early into the initiation of warfarin (third to the eighth day), and is caused by extensive thrombosis of the venules and capillaries within the subcutaneous fat. (Hirsh, 1991). There is an 11 fold increase in risk of developing calciphylaxis with warfarin use in patients with chronic kidney disease on dialysis. (Hayashi M, Takamatsu I, Kanno Y, et al, 2012)

## 209

### **Anti-Ro Antibodies and Cancer in Systemic Lupus Erythematosus**

Patrice Chrétien-Raymer (Montreal); Ann Clarke (McGill University, Montreal); Christian Pineau (McGill University Health Centre, Montreal); Jill Buyon (New York); Evelyne Vinet (McGill University Health Centre, Montreal); Emil Nashi (McGill University Health Centre, Montreal); Rosalind Ramsey-Goldman (Northwestern University Feinberg School of Medicine, Chicago); Jennifer Lee (Research Institute of the McGill University Health, Montreal); Sasha Bernatsky (Montreal)

**Objective:** There is a strong association of primary Sjogren's syndrome and lymphoma; anti-Ro antibodies are a characteristic feature of primary Sjogren's, but are also seen in systemic lupus (SLE). Our aim was to assess if positivity for anti-Ro might influence an SLE patient's risk of developing cancer.

**Methods:** We studied subjects from the McGill University Health Centre SLE registry. All patients with at least one visit since the year 2000 were included. Two patients who developed cancer prior to SLE were excluded. Patients were considered 'ever positive' after their first positive test for anti-Ro antibodies. We analyzed the cancer incidence across the entire cohort interval, stratifying person-years according to the antibody test results. Patients were followed from cohort entry up to the time of cancer occurrence, death, loss to follow-up, or end of study. We also ran a Cox proportional hazards regression, including demographics (sex, race, age at SLE diagnosis), SLE duration at cohort entry, smoking, and time-

dependent covariates for other antibody positivity (anti-La, and anti-ds DNA), and key drugs (hydroxychloroquine, ASA, and NSAIDs), modelled as ever-never exposures.

**Results:** In our cohort of 458 patients, 32 developed cancers; 11 breast cancers, 4 lymphomas, 3 uterine, 2 colon, 2 basal cell skin and 2 kidney cancers, as well as one each of bladder, cervix, gallbladder, ovarian, prostate, melanoma, thyroid, and squamous skin cancer. There was a significant difference in the average age at SLE diagnosis between patients that eventually developed cancers (39.4 years, 95% confidence interval, CI 34.3-44.6) versus those that did not (31.8 years 95% CI 30.5-33.0). Across the entire cohort, 46% were ever-positive for anti-Ro antibodies. The cancer incidence ratio was 5.6/1,000 for person-years contributed by patients while anti-Ro negative, versus 3.0/1,000 for subjects after they had tested anti-Ro positive at least once. The differences between these incidence ratios were not statistically significant. The regression model results showed only age at SLE diagnosis (HR 1.07, 95% CI 1.04-1.11) and SLE duration at cohort entry (HR 1.08, 95%CI 1.03-1.14) as a strong predictor of cancer risk.

**Conclusion:** We did not detect a definite effect of anti-RO antibodies on cancer risk in SLE. Our analyses were however limited to a single centre, and we did not consider effect on specific types of cancer. Future analyses will aim to address these limitations.

## 210

### **Development and Usability Testing of the Arthritis Health Journal: An Online Tool to Promote Self-Monitoring with Rheumatoid Arthritis**

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**Objective:** To develop an online patient passport, the Arthritis Health Journal [AHJ], that meets the needs of people with rheumatoid arthritis (RA). To evaluate user satisfaction and identify usability issues for tool refinement.

**Methods:** Structured interviews were held with adults with RA and rheumatologists to identify desired components and attributes of the tool. Patients were asked how it could assist self-management and rheumatologists how information could be incorporated into clinical practice. Interviews were taped, transcribed and analyzed using a thematic approach. Following development, two iterative cycles of usability tests were conducted with people with RA, using the concurrent think-aloud protocol, where thoughts are verbalized while performing tasks. Sessions were audio-taped and field notes taken. The System Usability Scale (SUS) was used to evaluate usability of the tool (0-100; higher=more user friendly), and simple content analysis was performed to identify issues and refine the tool.

**Results:** Pre-development interviews with 9 adults with RA and 5 rheumatologists revealed that people with RA desired a tool that would increase self-awareness, improve self-management and cue the need for rheumatologist visits. Rheumatologists identified that a tool such as the AHJ could improve RA patients' involvement in their own care and that succinct patient data and concerns could focus care. However, they feared it could heighten patient anxiety and might not adequately discern poor disease control. Based on these results, the AHJ was developed. The tool consists of six sections: symptom and exercise log; disease activity assessment; mood assessment; medical information; goals and action plans; and health reports. Usability testing was conducted with 9 adults with RA, 5 in the first iteration and 4 in the second (mean (SD) RA duration: 11(12.6) yrs; age: 51.6(10.2) yrs; all female; 89% had college or university education). Overall usability was good, with a mean (SD) SUS score of 84.7(7.7). Participants liked the

content and design, specifically the ability to view trends over time, and relationships between symptoms and other aspects of their disease or management. Modifications after the first iteration led to improved satisfaction. Long text was not read and was replaced with simple, succinct instructions, and key points were emphasized to ensure comprehension.

**Conclusion:** We developed a patient passport to promote patient self-monitoring and involvement in their care. Usability testing provided valuable insight into how people with RA use online tools. While general satisfaction was high, important issues were revealed leading to refinement of the prototype. Supported by a CIORA grant.

## 211

### **Long-Term Safety and Tolerability of Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients with Psoriatic Arthritis: Pooled Safety Analysis of Three Phase 3, Randomized, Controlled Trials**

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**Objective:** Apremilast (APR) safety/tolerability was assessed in a pooled analysis of PALACE 1, 2, and 3, which evaluated the efficacy/safety of APR in patients with active PsA despite prior conventional DMARDs and/or biologics.

**Methods:** Patients were randomized 1:1:1 to placebo, APR 20 mg BID (APR20), or APR 30 mg BID (APR30) stratified by baseline DMARD use (yes/no). At week 16, patients with < 20% reduction from baseline in SJC or TJC qualified for protocol-defined early escape; placebo patients were re-randomized to APR20 or APR30 and APR patients remained on their initial APR dose. At week 24, all remaining placebo patients were re-randomized to APR20 or APR30 through week 52. Patients taking concurrent DMARDs could continue stable doses (methotrexate, sulfasalazine, leflunomide, or combination).

**Results:** The APR-exposure periods (weeks 0- $\geq$ 24 and 0- $\geq$ 52) included 720 (APR20) and 721 (APR30) patients. No new safety findings were identified; previously identified adverse events (AEs) were reported at lower rates for the  $\geq$ 0-52- vs 0- $\geq$ 24-week exposure. The most common AEs (weeks 0- $\geq$ 52) were diarrhea (14.3%), nausea (12.6%), URTI (10.3%), headache (10.1%), and nasopharyngitis (7.4%). Diarrhea, nausea, and headache appeared to increase in a dose-dependent manner. Most AEs were mild/moderate in severity. Discontinuations due to AEs (APR20=7.5%; APR30=8.3%) were low (weeks 0- $\geq$ 52), occurring primarily in the first 24 weeks. Nausea and diarrhea were predominantly mild, occurring at a reduced incidence after the first month, with the highest incidence reported in the first 2 weeks. Most cases resolved within 30 days despite continued therapy. Severe nausea (APR20=0.3%; APR30=0.4%) and diarrhea (APR20=0.6%; APR30=0.3%) rates were low (weeks 0- $\geq$ 52). Gastrointestinal AEs leading to APR discontinuation were 4% over 52 weeks, with nausea (1.7%) and diarrhea (1.5%) being the most common. No new severe AEs of diarrhea, nausea, URTI, or nasopharyngitis were reported after the 0- $\geq$ 24-week APR-exposure period to the 0- $\geq$ 52-week APR-exposure cutoff. Serious AEs occurred in 6.8% (APR20) and 7.2% (APR30) of patients (weeks 0- $\geq$ 52). One death occurred (APR20) due to multiorgan failure not suspected to be treatment-related. No imbalance between placebo and APR, or dose effect, with MACE, malignancies, or serious or



systemic opportunistic infection (including tuberculosis) was observed. Individual, marked laboratory abnormalities were infrequent and returned to baseline or were associated with a concurrent medical condition.

**Conclusion:** APR demonstrated an acceptable safety profile and was generally well-tolerated with no new safety concerns identified with long-term exposure for  $\geq 52$  weeks. These data do not indicate a need for laboratory monitoring.

## 212

### **Factors Affecting the Discrepancy between Physician and Patient Global Assessment of Disease Activity in Early and Established Rheumatoid Arthritis Patients- Results from the Ontario Best Practices Initiative**

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**Objective:** Discrepancy between patient (PGA) and physician (MDGA) global assessments in Rheumatoid Arthritis (RA) can adversely affect therapeutic decisions. The objective of this study was to assess the pattern of PGA-MDGA discrepancy in early and established RA and to identify predictors of each global measure and their discrepancy in both populations.

**Methods:** Patients with RA were recruited from the Ontario Best Practice Initiative (OBRI), a clinical registry of RA patients followed in routine care. PGA and MDGA were scored from 0-100. PGA-MDGA discrepancy was calculated by subtracting MDGA from PGA at baseline. A clinically meaningful discrepancy was considered a difference of  $\geq 30$  (PGA-MDGA  $> 30$ : Positive (Pos) and PGA-MDGA  $< -30$ : Negative (Neg)). The rate of discrepancy was determined in patients with disease duration of less than or equal to 12 months (early RA) and disease duration of greater than 5 years (established RA) at baseline. Linear regression analysis was used to evaluate factors associated with MDGA, PGA and the PGA-MDGA discrepancy when adjusted for potential confounders including patient demographics, ESR, swollen joint count (SJC), tender joint count (TJC), pain, RF and anti-CCP and joint damage in both early and established disease.

**Results:** 439 early and 737 established RA patients were analyzed with the mean age of 57.0 and 59.0 years and DAS28 of 4.7 and 4.5 respectively. Mean PGA was 50.0 and 53.0 and MDGA was 48.0 and 43.0 in early and established groups respectively. A meaningful PGA-MDG discrepancy was found in 182 (41%) early (101 positive and 81 negative) and 309 (42%) established (229 positive and 80 negative) RA.

Regression analysis showed that there was a significant association between MDGA and pain, TJC, SJC and ESR at baseline in both groups and pain score was the only predictor of PGA. PGA-MDGA discrepancy was associated with pain ( $p < .0001$ ), TJC ( $p = 0.0014$ ), SJC ( $p = 0.004$ ) and ESR ( $p = 0.01$ ) in early RA and was associated with pain ( $p < .0001$ ), TJC ( $p = 0.002$ ), SJC ( $p < .0001$ ) and age ( $p = 0.05$ ) in patients with established disease (Table). In both groups higher pain score, SJC or TJC would increase the discrepancy. Higher pain score would increase the positive discrepancy (PGA > MDGA) whereas SJC, TJC and ESR (only in early RA) would increase the negative discrepancy (MDGA > PGA).

**Conclusion:** PGA-MDGA discrepancy exists in a significant portion of RA patients irrespective of their disease duration. Pain score and active joints are the main clinical factors affecting this discrepancy in patients with either early or established disease.

## 213

### **Disease Activity does not Improve Significantly in One System and Worsen in Another System**

Zahi Touma (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objective:** To determine whether SLEDAI-2K identifies patients who have a clinically important overall improvement but with no worsening in any systems.

**Methods:** This is an analysis of prospectively collected data on all active lupus patients who attended the Lupus Clinic from 2000-2012. Patients were included if at baseline visit: 1) SLEDAI-2K  $\geq 6$ , 2) at least 1 of the 6 SLEDAI-2K clinical organ systems was active and for the renal system the presence of proteinuria was mandatory and 3) start or increase in the dose of prednisone. All patients had at least one follow-up at 9-12 months. Based on the change in the total SLEDAI-2K scores on follow up visits, patients were grouped as: 1) improved (SLEDAI-2K decreased by  $\geq 4$ ), 2) flared/worsened (SLEDAI-2K increased by  $\geq 4$ ) and 3) unchanged. Focusing on patients who improve, each organ system was defined as 1) New Organ: organ system inactive at start but active at study end 2) Same: no change in activity between start and end 3) Improved: lower activity in organ system at the end and 4) worse: higher activity in organ system at study end.

**Results:** 158 patients were analyzed. SLEDAI-2K was  $12.25 \pm 5.27$  at baseline and  $6.65 \pm 4.88$  at follow-up visits. Of the 158 patients studied 109 patients had improved on SLEDAI-2K scoring on follow-up visit, 38 stayed the same and 11 worsened. 109 patients improved with a mean SLEDAI-2K score at baseline visit of  $13.1 \pm 5.7$  and at follow-up visit of  $4.8 \pm 4.4$ . In this group, no one had a new system at study end. Worsening was identified in 5 patients at study end and this resulted from abnormal laboratory results: 1) one patient developed pyuria at follow up visit in addition to existing proteinuria and hematuria that were persistent from study start and 2) 4 patients had worsening in the immunological system (either a new anti-DNA positivity or low complements). In all 5 patients, this laboratory worsening was not clinically significant and did not require a change in the management.

**Conclusion:** Overall clinical improvement detected by SLEDAI-2K is not associated with clinically important deterioration in specific organ systems recorded in SLEDAI-2K. SLEDAI-2K can be used as a single measure in the assessment of disease activity.

## 214

### **Do we know how and when to Taper and Stop in Immunosuppressants in Lupus Patients?**

Zahi Touma (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

**Objective:** To determine if: 1) tapering of immunosuppressant in patients in remission is possible and 2) if successful tapering of immunosuppressant triggers flares.

**Methods:** Analysis on all patients seen in The Lupus Clinic from 1987-2012 who met the inclusion criteria was conducted: 1) patients in clinical remission (no activity in the clinical SLEDAI-2K descriptors and absence of proteinuria or lupus related thrombocytopenia and leukopenia), 2)  $\geq 25\%$  taper of the immunosuppressant and 3) prednisone  $\leq 7.5\text{mg/day}$ . The study outcomes were partial and complete tapering of immunosuppressant and clinical flare. Flare was defined as: Start or any increase in either immunosuppressant or prednisone. Success was defined as no flare at last clinic visit if still on immunosuppressant or no flare after stopping immunosuppressant to last clinic visit or at 2 years Descriptive analysis was performed and generalized estimating equations were used to model success in patients with complete tapering

of immunosuppressant.

**Results:** Of the 1678 lupus patients registered at the Lupus Clinic, 204 tapering episodes in 179 (11%) patients were identified (123 azathioprine, 42 methotrexate and 39 mycophenolate mofetil). 162 were female with age  $39.0 \pm 13.3$  and lupus duration  $11.2 \pm 8.5$  years at tapering. Of the 204 tapering episodes 124 were successful. Immunosuppressant was partially tapered in 103 episodes. 53% of the episodes flared with a mean time from tapering of  $1.5 \pm 1.2$  years. 47% of the patients were still on immunosuppressant at last clinic visit (mean time  $2.1 \pm 2.5$  years). Immunosuppressant was completely tapered and stopped in 101 episodes. 25% stopped immunosuppressant at  $0.9 \pm 0.9$  years and flared with a mean time from tapering of  $0.8 \pm 0.5$  year. 75% stopped immunosuppressant at  $1.7 \pm 1.8$  years and did not flare with a mean time from tapering to last clinic visit at  $1.6 \pm 0.6$  years. As time to discontinue immunosuppressant increases, chance of flare decreases [OR 1.61, 95% CI 1.09 to 2.44)  $p=0.02$ ].

**Conclusion:** Of the patients who were clinically inactive but on immunosuppressants therapy, at least 1/2 were able to completely discontinue immunosuppressants. In 3/4 of those who were able to completely discontinue immunosuppressants, there was no flare in up to a mean of 1.6 years. Successful tapering and discontinuation of immunosuppressants in lupus patients is possible. A longer tapering period of immunosuppressants is associated with a higher likelihood of success.

## 215

### A Delphi Exercise for Treatment Algorithms for Systemic Lupus Erythematosus

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**Objective:** Some SLE organ-based treatment lacks guidelines. The purpose of this study was to gain consensus on treatment of complications of SLE especially when first-line treatment fails.

**Methods:** We invited authors of SLE papers over 10 years ( $n=69$ ) to participate in three surveys; 19% answered all surveys. Respondents were asked to write therapies for SLE organ complications assuming inadequate response to each choice. Management algorithms were constructed; agreement with the algorithm was obtained (0-100%). The median agreement for each recommendation is given.

**Results:** Consensus was reached for some algorithms. For widespread DLE, first-line: topical steroids or tacrolimus+hydroxychloroquine(HCQ)±systemic glucocorticoids, then adding azathioprine(AZA) and then switching to mycophenolate mofetil(MMF) [70% median agreement]. For cutaneous vasculitis, first-line was GC±HCQ±methotrexate(MTX), followed by adding either AZA or MMF and then IV cyclophosphamide(CYC) [80%]. For gangrenous vasculitis, first-line induction was glucocorticoids+CYC, then rituximab(RTX) or plasmapheresis [90%] and maintenance with MMF or AZA. For arthritis, first-line therapy was HCQ±glucocorticoids; adding MTX and then RTX [80%]. For pericarditis refractory to NSAIDs, first-line was glucocorticoids±HCQ, then adding MMF, AZA, or MTX and then belimumab or RTX; and a pericardial window and/or aspiration if needed [75%]. For myocarditis, first-line was glucocorticoids+CYC±HCQ, then MMF and then RTX, Belimumab or IVIG [90%]. For interstitial lung disease, induction therapy was glucocorticoids+MMF or CYC and then RTX or IVIG [90%]; maintenance with AZA or MMF. For pulmonary arterial hypertension, first-line was glucocorticoids+CYC or MMF+endothelin receptor antagonist, then

adding phosphodiesterase-5 inhibitor and then add a prostanoid. RTX then added if failing CYC [80%]. For lupus associated antiphospholipid antibody syndrome, venous [60%] and arterial [70%] thrombosis, first-line therapy was anticoagulation±HCQ. Changing to a direct thrombin inhibitor was second-line therapy for venous thrombosis, vs. adding low dose aspirin or another platelet aggregation inhibitor for arterial thrombosis. For mononeuritis multiplex [75%], and CNS vasculitis [60%], first-line induction was glucocorticoids+CYC followed by maintenance with MMF or AZA, and then RTX, IVIG or plasmapheresis. For LN type III/IV and V first-line was glucocorticoids+MMF, then adding RTX for LN type III/IV or switching to AZA, CYC or RTX for LN type V [80%].

**Conclusion:** Although variable SLE treatment agreement was found, there are many organ-based complications in SLE that gained consensus.

## 216

### **Low Socioeconomic Status at Diagnosis Predicts High Health Resource Utilization and Direct Medical Costs in Systemic Lupus Erythematosus**

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**Objective:** Low socioeconomic status (SES) negatively impacts health outcomes and access to care in systemic lupus erythematosus (SLE), but the impact of patients' SES on direct medical costs has not been evaluated. We examined the relationship between SES at diagnosis, and health resource utilization and costs, in a population-based cohort of SLE.

**Methods:** Data: We used British Columbia administrative data capturing all provincially-funded outpatient encounters and hospitalizations (1990 through 2010), and all dispensed prescriptions regardless of funding source (1996-2010). Sample: A population-based cohort of incident SLE (cases with no SLE diagnosis from 1990 to 1998) was identified using a previously-validated algorithm for the period 1998-2008: a) two ICD codes for SLE at least two-months apart and within a two-year period by non-rheumatologist physician; or b) one ICD code for SLE by a rheumatologist or hospitalization. Analysis: Costs for outpatient services and prescriptions were summed from paid claims. Case-mix methodology was used for hospitalization costs. Statistics Canada neighbourhood income quintile data, for the year of SLE diagnosis, served as a proxy for SES. Cases in the bottom-two income quintiles were classified as lower-SES and the top-two quintiles as higher-SES. Linear and logistic regression models were used to evaluate the relationship between SES at baseline, and health resource utilization and costs after adjusting for sex, age, and Charlson's co-morbidity index at baseline. All costs are reported in 2010 Canadian dollars.

**Results:** We identified 4,526 incident SLE cases (86% female, mean age of 49.2 years (±15.9)) contributing 18,754 person-years (PY). Cumulative direct medical costs for 1998-2010 totalled \$144,180,359 (2010 Canadian), with 46%, 28%, and 25% from hospitalizations, outpatient, and prescription medications, respectively. Overall, cases, averaged \$15,503/PY. Unadjusted mean costs for the lower-SES cases were \$18,856/PY, 38% greater than costs for the highest-SES cases (\$13,459/PY). Lower SES remained a significant predictor of direct medical costs after

adjusting for sex, age, and baseline Charlson comorbidity with per-PY costs for the lower-SES cases being 43% more than the higher-SES ( $p=0.0003$ ). Lower SES was also predictive of hospitalization at any point during follow-up ( $OR=1.31$ , 95% CI 1.14-1.50), and of averaging more hospital admissions/PY (1.4 for lower-SES vs. 1.0 for higher-SES,  $p=0.0048$ ), more outpatient encounters/PY (38.0 vs. 32.6,  $p < 0.001$ ), and more prescriptions/PY (35.5 vs. 20.6,  $p < 0.001$ ) than higher-SES cases.

**Conclusion:** Even in a universally-funded healthcare system, lower SES is an independent predictor of high health resource utilization in SLE, especially hospitalization.

## 217

### **The Risk of Myocardial Infarction in Systemic Sclerosis: A Population-Based Study**

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**Objective:** An increased risk of premature atherosclerosis has been well described in patients with rheumatoid arthritis and systemic lupus erythematosus. However, there is limited population-based data on the risk of myocardial infarction (MI) in patients with systemic sclerosis (SSc). The objectives of our study were: 1) to estimate the risk of MI in patients with SSc and 2) to assess time trends on the risk of MI in patients with SSc.

**Methods:** Our data included all visits to health professionals and hospital admissions covered by the provincial medical services plan (1990 -2010) and all dispensed medication (1995-2010) for all individuals  $\geq 18$  years of age. Matched cohort analysis was performed among patients satisfying one of the following criteria: a) diagnosis of SSc on at least two visits within a two-year period by a non-rheumatologist; b) diagnosis of SSc on at least one visit by a rheumatologist or hospital records. Ten controls matched by birth year, sex and calendar year of exposure were selected randomly from the general population for each case. Newly recorded MI events from hospital or death certificate were recorded as an outcome. We estimated relative risks (RRs) comparing SSc with age-, sex- and entry time-matched comparison cohorts, adjusting for potential cardiovascular risk factors. Sensitivity analysis was performed to assess the potential role of unmeasured confounders with low (10%) and high (20%) prevalence and with low ( $OR=1.3$ ) and high ( $OR=3.0$ ) association between the confounder and the outcome.

**Results:** Among 1,207 individuals with incident SSc and no prior record of MI at baseline (83% female, mean age of 53 yrs [SD 12.8]), 89 developed a first new MI (incidence rate= 20.2 per 1000 person years), compared with non-SSc individuals ( $N=12,080$ ; incident rate = 5.3 per 1000 person years). The age-, sex-, and entry-time-matched RR for MI was 3.8 (95% CI, 2.8- 4.8). The risk was 8 times greater within the first year after the disease onset and progressively decreases over time. After further adjustment for potential cardiovascular risk factors, the RR remained similar (4.1, 95% CI, 3.1 to 5.4). Our results remained statistically significant in our sensitivity analyses of simulated confounders.

**Conclusion:** This large population-based study indicates an increased risk of MI in patients with SSc, especially within the first year of disease diagnosis. These findings support increased monitoring of MI complication and risk factors in those with SSc, particularly during the early phase of SSc diagnosis.

## 218

### **Survival after Lung Transplantation in Systemic Sclerosis. A Systematic Review**

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**Objective:** Lung transplantation is a life-saving option for systemic sclerosis (SSc)-associated pulmonary arterial hypertension (PAH) and interstitial lung disease (SSc-ILD) patients. Yet, there is risk of post-transplantation mortality. The objective of this study was to evaluate survival of SSc patients post-lung transplantation. We secondarily evaluated SSc lung transplant recipient characteristics, and compared post-lung transplantation survival of SSc patients to non-SSc patients (idiopathic PAH, and ILD).

**Methods:** A systematic review of MEDLINE, EMBASE, Cochrane Central Registry of Controlled Trials and CINAHL (all inception to 2012) was performed to identify studies evaluating post-lung transplant survival in SSc compared to non-SSc patients. Two reviewers independently abstracted study and survival data using a standardized form.

**Results:** 226 citations were screened to identify 7 observational studies reporting SSc patients who underwent single lung, double lung, or heart-lung transplantation. Mean age at transplantations ranged 46-53 years. SSc post-transplantation survival ranged 69%-91% at 30-days, 69%-85% at 6-months, 59%-93% at 1-year, 49%-80% at 2-years, and 46%-79% at 3-years. ILD post-transplant survival was 80% at 30-days, 80%-90% at 6-months, 59%-83% at 2-years, and 69% at 3-years. IPAH post transplant survival was 79% at 30-days, 79%-90% at 6-months, and 74%-90% at 1-year. The reporting of overlapping cohorts potentially including the same patients precluded meta-analysis. Causes of death in SSc patients, when reported, included graft failure (n=6), infection (n=8), cardiac events (n=3), hemorrhagic stroke (n=1), respiratory failure (n=3), malignancy (n=2), pulmonary hypertension (n=1), complications of bronchiolitis obliterans syndrome (BOS) (n=1), anesthetic complication (n=1), and scleroderma renal crisis (n=1). There were no reports of recurrence of SSc in the lung allograft.

**Conclusion:** SSc survival post-lung transplantation is very good, and improving with time. The short-term and intermediate-term survival post-lung transplantation are similar to IPAH and ILD patients requiring lung transplantation. Future researchers should delineate the access process for lung transplantation and report the occurrence of acute rejection, infection, bronchiolitis obliterans syndrome, renal dysfunction and dialysis, gastroparesis, and need for tube feeding.

## **219**

### **Lower Socioeconomic Status Associates with Increased Symptom Severity and Functional Impairment in Fibromyalgia**

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**Objective:** Lower socioeconomic status (SES) associates with poorer health status for many medical conditions. Reasons may include limited access to care, health related behaviours and variable adherence. Symptom expression in fibromyalgia (FM), a clinical construct with psychosocial implications, may be influenced by SES. We have examined the effects of SES for disease severity in a cohort of FM patients.

**Methods:** FM patients in a prospective cohort were stratified according to SES by education level: high school or less (Group 1; N=99), college (Group 2; N=84), and university (Group 3; N=63). Demographic and disease severity measures included pain VAS, patient global assessment disease activity (PGA), Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire (HAQ), McGill Pain Questionnaire (MPQ), Pain Disability Index (PDI), Pain Catastrophizing Scale (PCS), anxiety and depression by Arthritis Impact Measurement Scale (AIMS). Between-group differences in discrete and continuous variables were assessed for statistical significance, with linear regression to assess differences in disease activity while adjusting for confounders.

**Results:** The cohort comprised 246 patients, mean  $\pm$  SD age  $47.8 \pm 10.4$  years, disease duration  $10.8 \pm 9.8$  years, and 91.1% female. Baseline values were: pain VAS  $6.5 \pm 2.3$ , PGA  $6.7 \pm 2.1$ , FIQ  $67 \pm 17$ , HAQ  $1.19 \pm .59$ , MPQ  $41 \pm 15$ , PDI  $38 \pm 14$ , PCS  $29 \pm 12$ , AIMS anxiety  $6.3 \pm 1.8$ , AIMS depression  $4.9 \pm 1.8$ , with mean medication count of  $2.6 \pm 1.3$  per patient. There were no significant differences between groups for the following parameters: disease duration, marital status, cigarette smoking, previous eating disorder or alcohol abuse, current medication categories, and total number of medications used per patient. Higher education associated with greater use of alternative medicines ( $P < 0.001$ ) and chiropractic, massage or osteopathic treatments ( $P = 0.021$ ). Lower education level was significantly associated with older age ( $P = 0.039$ ), previous drug abuse ( $P = 0.016$ ), current unemployment ( $P < 0.001$ ) and lower score for: PGA ( $P = 0.019$ ), FIQ ( $P = 0.002$ ), HAQ ( $P = 0.001$ ), MPQ ( $P = 0.026$ ), PDI ( $P = 0.031$ ), and PCS ( $P = 0.015$ ). These associations remained significant when adjusting for age and gender differences. No significant differences in pain severity, anxiety, and depression were observed between groups.

**Conclusion:** Similar to other health conditions, FM patients with lower SES reported greater symptom severity, functional impairment and unemployment, but not mood disorder. Although FM spans all socioeconomic groups, societal factors, rather than specific disease characteristics or mental status, appear to play an important role in patients' perception of illness..