Introduction

Canadian Rheumatology Association Meeting

The 64th Annual Meeting and the 17th Winter Workshop of The Canadian Rheumatology Association (CRA) was held at the Delta Lodge, Kananaskis, Alberta, February 18–21, 2009.

The Program consisted of presentations covering original research, symposia, workshops, poster sessions, the Royal College debate, the Dunlop-Dottridge Lecture, and special awards and presentations, including the CRA Distinguished Rheumatologist, Distinguished Investigator, and the Teacher-Educator Award.

A practical course and update for Fellows that included a special luncheon was held prior to the meeting. The national Annual Update, chaired by Shahin Jamal, covered a Mexican update by Javier Cabiedes, corticosteroid usage in rheumatoid arthritis by Mala Joneja, and new tumor necrosis factor (TNF) inhibitors for juvenile arthritis by Nicole Johnson. President John Thomson delivered his opening remarks, followed by podium presentations chaired by Proton Rahman, and by a state of the art lecture "Vitamin D Deficiency: a Silent Epidemic," by David Hanley of Calgary, whose insightful presentation aroused considerable discussion.

Workshop sessions were followed by a timely thieves' market session on the new face of tuberculosis complicating anti-TNF therapies, a topic that was elucidated by crossfire presentations by Bob Offer and Wojciech Olszynski, chaired by Vivian Bykerk. A state of the art lecture by Dan Kastner, Chief and Clinic Director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), Bethesda, MD, USA, provided comprehensive coverage of the periodic fever syndromes, with emphasis on some Canadian connections.

The 2009 Royal College debate, entitled "Industrial Relations: Good For You or Not?", pitted Easterners Brian Feldman and Paul Haraoui against Westerners Paul Davis and Liam Martin. Moderator Stephanie Ensworth was kept on her toes by the intensity of their heated presentations.

Contributions to Canadian Rheumatology were acknowledged with a number of awards. The Basic Science Award went to Dr. Nigil Haroon, University of Toronto, for his family-based association analysis study that confirmed the role for ARTS1 in ankylosing spondylitis. The P.S. Rosen Award went to Dr. Barry O'Shea, University of Toronto, for his study showing discordance between patient-reported subjective measures and physician-determined objective measures of spinal disease in ankylosing spondylitis. The Ian Watson Award went to Dr. Karen Adams, University of

Toronto, for her study on cytokine screening for potential biomarkers to monitor disease activity in patients with SLE; her studies indicated that fluctuations in plasma inducible protein 10 (IP-10) may function best as a flare-specific biomarker in lupus. The Best Overall Paper award went to Dr. Julie Kim, University of Toronto, for her study of altered activation of newly-emergent bone marrow-derived B cells in lupus. The Best Paper by an Undergraduate Student went to Kim Baker, Queen's University, for a multicenter multi-ethnic study of work disability in lupus that was predicted by sociodemographic and disease-related factors.

Dr. Manfred Harth of London, Ontario, was presented with the Distinguished Rheumatologist Award. Manfred's career has included his role as Division Head of Rheumatology at the University of Western Ontario from 1966 to 1987, where he pursued research interests in rheumatoid arthritis and fibromyalgia. He also served as President and Vice President of the CRA in the 1980s as well as Chair of the Rheumatology Specialty Committee of the Royal College from 1982 to 1986. He has also received many teaching awards and contributed locally and nationally to the work of The Arthritis Society.

Dr. Claire Bombardier was awarded The Distinguished Investigator Award. Claire is the Director of the Division of Rheumatology at the University of Toronto and holds the recently established Pfizer Research Chair in Rheumatology. In 2003 she was the Founding Director of the clinical epidemiology program at the University of Toronto. As an international ambassador for rheumatology she has pioneered the establishment of OMERACT and the development of guidelines for the diagnosis and treatment of rheumatic diseases. As such she currently leads the Ontario Biologics Research initiative, bringing together researchers, government, and patients in one of the most comprehensive postmarketing initiatives for biologic therapies. She also continues to be the recipient of federal funding as the co-scientific director of the Canadian Arthritis Network. Claire also contributes to the Ontario Institute for Work and Health, The Toronto General Hospital Research Institute, and serves as a clinical rheumatologist at Mount Sinai Hospital.

The Teacher-Educator Award went to Dr. Heather McDonald-Blumer. Heather is the current Program Director for postgraduate rheumatology training at the University of Toronto and the Chair of the Specialty Committee and Examination Board for Rheumatology of the Royal College of Physicians and Surgeons of Canada. Her early medical

career involved full-time practice as a community rheumatologist that evolved into a part-time faculty appointment at Women's College Hospital, where she was the Medical Director of the Multidisciplinary Osteoporosis Program from 1996 to 2004. She is currently Associate Director of the Osteoporosis Program of the University Health Network and a member of the Scientific Advisory Council of Osteoporosis in Canada. Throughout, her strong interest in medical education led to her completion of a Master of Science degree in health professional education at the University of Toronto.

The meeting concluded with the Dunlop-Dottridge Lecture, given by Dr. Cornelia Weyand, the David Lowance Professor of Medicine at Emory University School of Medicine, Atlanta, GA, USA. Her presentation focused on the immunopathogenesis of vascular inflammation, with emphasis on how human macrovessels from different vascular beds specialize in immune-monitoring functions.

Last but not least, an important milestone in the life of the CRA and *The Journal* was proudly acknowledged at the Annual Meeting. The membership's unanimous approval of the CRA's acquisition of The Journal of Rheumatology at the previous year's meeting in Mt. Tremblant had now been made official. This unique transition will ensure continuity of *The Journal*'s mission as a Canadian-based international voice of Rheumatology under the continued ownership and operation by rheumatologists like you. It is my pleasure, on behalf of our editorial team, to express our optimism for this new and renewed relationship with all the members of the CRA — our colleague-shareholders. As in the past, members of the CRA will continue to contribute to *The Journal* as readers, reviewers, and authors as we strive to disseminate new information that benefits all our patients.

DUNCAN A. GORDON, MD,
Editor

PODIUM PRESENTATIONS

1

Circulating Levels of SVCAM, IP-10 and MCP-1 Correlate with Changes in Disease Activity in Systemic Lupus Erythematosus

Karen Adams (University of Toronto); Carolina Landolt-Marticorena (University of Toronto); Thulasi Unnithan (University of Toronto); Dafna Gladman (University of Toronto); Murray Urowitz (University of Toronto); Paul R. Fortin (University of Toronto); Joan E. Wither (University of Toronto)

Objective: Lupus patients have elevated plasma levels of a number of cytokines/chemokines and it has been proposed that fluctuations in the concentration of these soluble mediators may mirror changes in SLE disease activity. The plasma concentration of 20 cytokines/chemokines was determined in an initial cross-sectional study with promising proteins further evaluated in a longitudinal analysis to examine their potential as SLE biomarkers.

Methods: Patients (n = 53) satisfying 4 or more ACR criteria were recruited from the University of Toronto Lupus Clinic. 21 healthy controls were also recruited. All patients underwent 2 assessments over the study period with 7 patients having 3 or more encounters. Disease activity was measured by the SLEDAI-2K. The plasma concentration of 20 analytes was determined by a Luminex assay. The statistical significance of correlations was determined by linear regression and differences between groups where analyzed by the Mann-Whitney test.

Results: Of the analytes assayed, sVCAM, MCP-1, IP-10, and adiponectin were found to be significantly elevated (p = 0.001, 0.005 < 0.0001, < 0.0001 respectively) in SLE patients when compared to controls. Patients were stratified into a high disease activity (SLEDAI > 7) group (n = 30) and a low/moderate activity group (n = 23). All four proteins were found to be significantly elevated (sVCAM, p = 0.0001; MCP-1, p = 0.005; IP-10, p = 0.0006; and adiponectin, p = 0.002) in patients with high disease activity versus patients with low/moderate disease activity. To examine the relationship between disease activity and cytokines/chemokine plasma concentration, 41 patients underwent assessment at recruitment and a year subsequent. The change in disease activity (SLEDAI-2K) and in the concentration of each of the four analytes was calculated by subtracting the values obtained at the second assessment from those at the initial visit. Linear regression analysis between the change in disease activity and cytokine concentration showed a moderate positive correlation for sVCAM (r = 0.64, p < 0.0001), IP-10 (r = 0.6, p < 0.0001) and MCP-1 (r = 56, p = 0.0002). In a longitudinal study of 7 SLE patients changes in disease activity where closely mirrored by contemporaneous fluctuations in the IP-10 plasma concentration in 6 of the patients surveyed.

Conclusion: From our initial cytokine screen sVCAM, IP-10, MCP-1 have emerged as potential biomarkers to monitor disease activity in SLE patients. Preliminary results suggest that fluctuations in plasma IP-10 may function best as a flare-specific biomarker in SLE.

2

Evidence for Altered Activation of Newly-emergent Bone Marrow-derived B Cells in Systemic Lupus Erythematosus (SLE)

Julie Kim (Department of Immunology, University of Toronto; Toronto Western Research Institute, University Health Network); Ellie Aghdassi (Toronto Western Research Institute, University Health Network); Dafna Gladman (Department of Medicine, University of Toronto; Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, University Health Network); Murray Urowitz (Department of Medicine, University of Toronto; Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, University Health Network); Paul Fortin (Department of Medicine, University of Toronto; Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, University Health Network); Joan Wither (Departments of Immunology and Medicine, University of Toronto; Centre for Prognosis Studies in the Rheumatic Diseases, Toronto Western Hospital, University Health Network)

Objective: The presence of autoantibodies in SLE suggests that B cell tolerance mechanisms are defective in lupus patients. We have previously shown that lupus patients have an expanded proportion of activated naïve B cells with properties suggesting self-antigen engagement. In this study we examined whether these abnormalities are also present in the newly-emergent bone marrow-derived B cell population.

Methods: Patients satisfying ≥ 4 ACR criteria, taking less than 20 mg of prednisone and between the ages of 18-43 years were recruited from the University of Toronto Lupus Clinic. Healthy controls with no family history of systemic autoimmune disease were also recruited. PBMCs were isolated over a Ficoll gradient, stained with various combinations of fluorescently labelled antibodies and analyzed by flow cytometry.

Results: As in our previous study there was an increased proportion of immature transitional cells (CD20$^+$CD27$^-$CD24^{++}CD38^{++}) within the B cell population of lupus patients. Using mean forward scatter as a measure of cellular activation, both the transitional 1 and transitional 2 B cell populations were significantly more activated in lupus patients than controls (p = 0.017 and 0.0005, respectively). To further characterize the activation within these populations, 7-color flow cytometry was used. We previously found an increased expression of co-stimulatory molecules on the naive (CD20$^+$CD27$^-$CD23$^+$) B cell population of lupus patients. Here we show that these increases occur within both the naïve mature (CD19$^+$CD27$^-$IgD$^+$CD38$^{-/+}$CD10$^{-/+}$) and transitional (CD19$^+$CD27$^-$IgD$^+$CD38^{++}CD10^{++}) B cell populations (CD80: p = 0.0043 and 0.068, CD86: p = 0.0001 and 0.012, for mature and transitional B cells, respectively). B cells that have engaged antigens or that have a reduced threshold for activation demonstrate lower levels of cell surface IgM, while retaining IgD expression. As in the mature B cell population, there was a trend to lower levels of IgM cell surface expression in the transitional B cells of lupus patients.

Conclusion: The B cell abnormalities seen in lupus patients are already present in the newly-emergent transitional B cell population, suggesting that they may arise from intrinsic B cell signalling differences that alter B cell selection. Ongoing experiments are seeking to address this possibility.

3

Work Disability in Systemic Lupus Erythematosus Is Prevalent and Predicted by Socio-demographic and Disease Related Factors: Results from a Multi-ethnic Cohort

Kim Baker (Queen's University); Janet Pope (University of Western Ontario); Earl Silverman (University of Toronto); Glinda Cooper (NIH-NIEHS); Paul Fortin (University of Toronto); Michel Zummer (Hôpital Maisonneuve-Rosemont); C. Douglas Smith (Ottawa General Hospital); Ross Petty (University of British Columbia); Lori Tucker (University of British Columbia); Lori Albert (University of Toronto); Adam Huber (Dalhousie University); Suzanne Ramsey (Dalhousie University); Hector Arbillaga (University of Calgary); Gaëlle Chedeville (McGill University); Marie Hudson (McGill University); Christine Peschken (University of Manitoba); Investigators of 1000 Faces of Lupus/CaNIOS

Objective: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder that often affects women during their working decades. Increased work disability (WD) leads to increased indirect costs of SLE, which represents a significant proportion of the overall costs of the illness. WD is common in SLE, but there is a large amount of variety in results generated by previous studies (range of 5-58% SLE patients are WD), and there are relatively few studies on employment and SLE in multi-centered multi-ethnic cohorts. The objectives of this study were to examine the prevalence of WD and factors associated with job loss in SLE in a large multi-centered Canadian sample to determine the current prevalence of WD and identify the contribution of disease activity, damage, and co-morbidities (fatigue, depression, arthralgias and fibromyalgia) with respect to WD.

Methods: Cross-sectional data on WD status from the 1000 Canadian Faces of Lupus database (multi-center multi-ethnic cohort of SLE patients) along with clinical measures (number of ACR criteria ever, SLICC, SLAM, SLEDAI, SF-36 and Charlson Co-morbidity Index scores), demographic features (age, sex, high school education, household income, marital status, disease duration) and comorbidities (fibromyalgia, arthralgias, depression and fatigue) were used in bivariate and logistic regression analyses.

Results: Of 1137 SLE patients, mean age 50 years (SE 0.75) and mean dis-

ease duration of 18 years (SE 0.70), 19.09% were work disabled and 49.78% were employed. Those with WD were more likely than non-WD SLE to have: a higher number of ACR criteria for SLE; not completed high school; older age; single marital status; a lower household income; longer disease duration; higher SLICC and SLAM scores; lower SF-36 PCS and MCS scores; less vigorous activity per week; and fibromyalgia, arthralgias, fatigue and depression (p<0.05).

Conclusion: This contemporary rate of WD is lower than in many past reports. Socio-demographic factors, comorbidities (fibromyalgia and fatigue) and disease related factors were strongly associated with WD. We cannot determine cause and effect as the study was cross-sectional.

4

Family Based Association Analysis Confirms a Role for ARTS1 in Ankylosing Spondylitis But the Candidate Exonic Variant K528R Is Not Related to Cytokine Receptor Shedding Profiles

Nigil Haroon; Florence Tsui; John Reveille; Basil Chiu; Hing Wo Tsui; Proton Rahman; Robert Inman, Arthritis Center of Excellence, Toronto Western Hospital.

Background: A recent genome-wide association scan reported that ARTS1 is a major non-MHC locus associated with ankylosing spondylitis (AS). The ARTS1 K528R variant has previously been shown to be associated with hypertension, and transient transfection experiments demonstrated that the 528R variant had decreased aminopeptidase activity. ARTS1 has two known functions: (i) promoting shedding of cytokine receptors such as TNFRI, IL-1RII and IL-6R; (ii) trimming peptides for MHC class I-mediated antigen presentation.

Objective: 1. To assess whether there is excess transmission of ARTS1 alleles in multiplex families with AS. 2. To assess whether the 528R variant correlates with cytokine receptor shedding profiles.

Methods: We genotyped 231 multiplex AS families with two ARTS1 exonic SNPs (rs30187 and rs27044), and performed family-based association analyses. Sera from 80 AS patients (not on biologic treatments) were assayed for sTNFRI, sIL-1RII and sIL-6R by ELISA. The soluble receptor levels were correlated by Spearman's rank correlation, after controlling for ESR and CRP.

Results: FBAT analysis on our cohort of AS families revealed that the exonic variant (rs30187[G]) is associated with AS (dominant model; p-value = 0.012). There was no significant association of the other exonic variant (rs27044) with AS. The AS cohort for the functional analysis (n=80) had a mean age of 42.31 ± 10.6 years. In this cohort, the ESR (mean 18 ± 15.6 mm/hr); CRP (mean 14.8 ± 18. 8 g/dL); BASDAI (mean 5.3 ± 2.4) had no correlation with the major or minor alleles of rs30187 and rs27044. In terms of serum levels of sTNFRI, sIL1R, and sIL6R, there was no relationship to the respective ARTS1 alleles. There was a significant correlation of sIL-6R with sIL-1RII (R=0.49; p<0.0001) and with sTNFRI (R=0.31; p=0.007) but there was no correlation between sTNFRI and sIL-1RII.

Conclusion: This is the first report showing excess transmission of rs30187[G] in multiplex AS families, and thus confirms previous population studies on the association of rs30187 with AS. However, we observed no relationship between the AS-associated ARTS1 K528R variant and cytokine receptor shedding profiles. Our results suggest that the functional relevance of the ARTS1 K528R variant might relate more to peptide trimming for antigen presentation.

5

Discordance Between Patient-reported Subjective Measures and Physician-determined Objective Measures of Spinal Disease in Ankylosing Spondylitis

FD O'Shea (Toronto Western Hospital); R Riarh (Toronto Western Hospital); RD Inman (Toronto Western Hospital)

Objective: Patient self-reported "subjective" indices such as BASDAI and BASFI are used routinely to define therapeutic targets in the treatment of Ankylosing Spondylitis (AS). Clinicians utilize "objective" measures such as BASMI and mSASSS in the management of AS. Whether or not these domains of outcomes correlate or capture the same aspects of AS has not been rigorously examined. We addressed this issue in the current study.

Methods: The patients were drawn from the spondylitis clinic in a large teaching hospital. Patients are evaluated according to a standard protocol in which demographic, clinical, radiographic and laboratory variables are recorded at regular intervals. Part of the assessment involves a number of self reported instruments such as the BASDAI, BASFI and AS quality of life (ASQoL) questionnaire. Patients have a full set of back measurements performed which allows calculation of the BASMI. Radiographic severity is determined by calculation of the mSASSS score. Mean and standard deviation (SD) were calculated for the various clinical variables. The mSASSS and BASFI were correlated with the clinical variables of interest using Pearson's correlation coefficients.

Results: 220 AS patients were extracted from the database. 80.9% were male. 81.5% were HLA-B27 positive. Mean (±SD) current age was 39.8 (±13.4) years. Mean disease duration was 16.4 (±11.4) years. 26% of the cohort had juvenile onset symptoms (≤ 16 years). 26.4% were on an anti-TNF agent at time of assessment. 21.4% had evidence of radiographic hip disease. Mean (±SD) BASDAI was 4.7 (±2.5), mean BASMI was 3.2 (±2.6), and mean mSASSS was 19.5 (±24.2). Mean ASQoL was 8.2 (±5.8), and mean BASFI was 3.9 (±2.8). The strongest correlation with BASFI was seen with ASQoL (r = 0.754, p<0.001) and BASDAI (r = 0.689, p<0.001). BASFI correlated modestly with BASMI (r = 0.561, p<0.001) but poorly with mSASSS (r = 0.227, p=0.001). On the other hand, mSASSS correlated very well with BASMI (r = 0.708, p<0.001), but only poorly with BASFI. ASQoL had a poor correlation with BASMI (r = 0.327, p<0.001) and did not significantly correlate with mSASSS. ASQoL had a better correlation with BASDAI than BASFI (r = 0.710, p<0.001).There was no correlation between mSASSS and BASDAI, ASQoL, ESR or CRP.

Conclusion: Although the spine is the primary therapeutic target in the treatment of AS, current "objective" measures of the severity of spinal disease have little bearing on patient self-reported assessments. BASDAI, BASFI and ASQoL bore little relationship to radiographic severity of disease in AS.

6

The Minimally Important Difference (MID) For Patient Centered Outcomes Including Health Assessment Questionnaire (HAQ), Fatigue, Pain, Sleep, Global VAS and SF-36 in Scleroderma (SSc)

Suneet Sekhon (University of Western Ontario); Janet Pope (University of Western Ontario); Investigators of the Canadian Scleroderma Research Group; Murray Baron (McGill University)

Objective: Patient reported outcomes are important to gauge impact of disease in scleroderma (SSc). We studied a large clinical practice and a multi-center database to estimate the MID in SSc using global rating of change anchors for HAQ-DI, and VAS in pain, fatigue, sleep and global status and the SF-36.

Methods: Longitudinal data were collected on scleroderma patients (N=109) from a scleroderma clinic who had completed questionnaires at two consecutive visits less than 18 months apart; subjects completed HAQ-DI and pain/fatigue/sleep/global status VAS (0 to 100mm) at each visit and rated their change in overall status since the last visit as *much better, better, same, worse* or *much worse*. Data were also extracted from the CSRG database (N=341) for two consecutive yearly visits in which the patients had completed HAQ-DI and SF-36, and SF-36 change in health item.

Results: For the single site: The mean (SD) baseline HAQ-DI was 0.895 (0.672) and 0.911 (0.654) at follow up with a mean change of 0.016 (0.277). The MID estimates for improvement and worsening respectively were -0.0125 (0.224)/ 0.042 (0.314) for HAQ-DI, -8.00 (32.48)/3.61 (24.52) for pain, -10.00 (10.63)/ 3.79 (25.32) for fatigue, -18.50 (33.91)/ 5.92 (28.83) for sleep, and -6.70 (26.58)/ 4.05 (22.35) for global VAS. In the CSRG database, baseline scores were 0.787 (0.683) for HAQ-DI, 37.20 (11.12) for PCS and 37.53 (10.75) for MCS. The MID estimates for improvement and worsening were -0.037 (0.402)/ 0.140 (0.387) for HAQ-DI, 2.18 (6.58)/ -1.74 (7.72) for PCS, 1.33 (7.78)/ -2.61 (10.91) for MCS.

Conclusion: This study provides MID estimates in SSc from two large databases at variable time points for commonly used patient-reported outcomes.

POSTERS 1

The Rheumatology Multidisciplinary Assessment Clinic

L Beker; C Johns; and L Martin, (Division of Rheumatology, University of Calgary)

Objective: To develop and assess the utility and acceptability of a Rheumatology Multidisciplinary Assessment Clinic (MDA) to address the needs of patients referred to a rheumatology service for the management of presumed NIM complaints.

Methods: We have initiated a pilot project whereby NIM patients are scheduled into a MDA clinic where they are assessed by an experienced rheumatology nurse practitioner (NP) and physiotherapist. A rheumatologist acts as a resource person for the clinic. A history and physical examination is completed on each patient. A diagnosis is made and a care plan, which includes education and an exercise prescription, is developed. If there is any uncertainty about the patient's diagnosis further assessment occurs with the rheumatologist. The patient may also request an assessment by the rheumatologist. The NP completes all documentation and dictates the consultation letter to the referring physicians. These letters are reviewed by the rheumatologist before being mailed.

Results: To date 21 patients have been evaluated by the MDA clinic. The average wait time was 10 weeks. Female to male ratio was 19:2. The average age was 46 yrs. Thirteen patients were employed, 3 retired, 2 on disability and 3 had other employment status. Eight patients we referred with a diagnosis of fibromyalgia (FM). In seven the post assessment diagnosis remained unchanged but the eighth patient had a possible sleep disorder and was referred to the Sleep Clinic. Five patients were referred with a diagnosis of OA. This diagnosis was confirmed in four patients but the fifth patient had psoriatic arthritis. Four patients were referred for assessment of polyarthralgia and abnormal serology. One patient had Raynaud's phenomenon, 1 had an allergic skin disorder and was referred to a dermatologist, and the remaining 2 had no rheumatic disease. Four patients were referred with polyarthralgia. One patient had AS, 1 had DISH, 1 had OA in the hands with an ulnar neuropathy and 1 had FM and hypermobility. Twenty of the 21patients were satisfied with their care. One patient, although satisfied with the care, requested further assessment of her OA by a rheumatologist.

Conclusion: Patients with musculoskeletal complaints require skilled assessment. The assessment can be undertaken by skilled allied health professionals in a collaborative environment with rheumatologists. The multidisciplinary approach to patients with probable NIM complaints can improve the timeliness of access for patients.

2

Evidence-based Clinical Decision-making in the Treatment of Hand Arthritis

Ilene Cohen-Ackerman (The Arthritis Society); Marie Eason Klatt (St. Joseph's Health Centre); Susan Ellis (St. Joseph's Health Centre); Antoinette Krakovsky (St. Joseph's Health Centre); Susan Hannah (University Health Network); Maureen Riley (St. Michael's Hospital)

Objective: To examine current best practice in the treatment of clients with a variety of rheumatoid and osteoarthritis hand conditions and to present evidence-based clinical "pearls" to apply to the treatment of clients with hand arthritis.

Methods: Through a series of focus groups with therapists involved in the treatment of clients with hand arthritis, recommendations for treatment or "pearls" were developed. Focus group participants represented clinicians with academic, hospital-based and community-based practices. After synthesizing their recommendations for treatment, an extensive literature review was conducted to determine available evidence for each clinical pearl. Sackett's criteria for levels of evidence were used to determine the strength of evidence for each "pearl".

Results: Through the focus groups and literature review, a comprehensive list of sixty evidence-based "pearls" was developed for application in a variety of clinical settings. "Pearls" were organized around the themes of orthotic fabrication and design, appropriate exercise, recommendations for post-operative care, and, enhancing occupational performance through assistive devices and patient education.

Conclusion: Optimizing occupational performance when treating clients with hand arthritis poses multiple challenges for the therapist. As clinicians we must learn to base our treatment decisions on a critical examination of the relevant literature and shape our practice around integration of this evidence with each clinical challenge. This evidence-based process resulted in sixty "pearls" to assist therapists in the management of these complex arthritis hand problems.

3

Inter-professional Learning and the Use of Arthritis Best Practices in Primary Care

Sydney Lineker (The Arthritis Society); Elizabeth Badley (University Health Network); Mary Bell (Sunnybrook Health Sciences Centre)

Objective: This study evaluated an inter-professional community-based educational program to improve the management of rheumatoid arthritis (RA) and osteoarthritis (OA) in primary health care (PHC).

Methods: A taskforce of PHC providers, adults with arthritis, health services researchers and government representatives designed and pilot tested this evidence-based program. The program was based on social cognitive theory and published arthritis clinical practice guidelines (CPGs) adapted for the primary care environment (best practices). Nation-wide implementation of the program consisted of 27 accredited workshops, educational materials for providers and their patients and six months of activities to reinforce the learning and support the delivery of arthritis care in the community. Workshop content focused on the pharmacological and non-pharmacological management of OA and RA and was delivered by local arthritis specialists and community partners. Primary outcome analysis compared provider self-reported use of best practices in response to three standardized case scenarios (early and late RA; moderate knee OA) at baseline and six months post workshop using the ACREU Primary Care Survey, used previously in the assessment of physicians in primary care. One point was given for each recorded best practice and totalled for each case (late RA and moderate knee OA = 8 points; early RA = 7 points). Satisfaction and confidence with ability to manage arthritis were assessed using 10 point visual analogue scales (1=not at all confident/not satisfied; 10=extremely confident/satisfied). Changes from baseline were assessed using non-parametric statistics.

Results: 553 primary care providers from rural and urban PHC facilities attended one of 27 workshops across Canada; 275 (50%) completed six-month follow-up surveys. At follow-up, providers reported increased use of arthritis best practices for all three case scenarios, increased satisfaction with their ability to deliver arthritis care and increased confidence in their ability to manage patients with arthritis (Wilcoxon Signed Ranks Test; P<.01).

Conclusion: This national evidence-based educational intervention increased PHC providers' self-reported use of arthritis best practices and their confidence and satisfaction in arthritis care delivery. Results suggest that this inter-professional learning program is an effective method for the dissemination of CPGs and can improve the delivery of arthritis care at the primary care level.

4

"Prescription for Education": A Pilot Study of the Effectiveness of an Education Program for Adults with Inflammatory Arthritis

Carol A Kennedy (St. Michael's Hospital, Institute for Work & Health, University of Toronto); Dorcas E Beaton (St. Michael's Hospital, Institute for Work & Health, University of Toronto); Rachel Shupak (St. Michael's Hospital, University of Toronto); Kelly Warmington (St Michael's Hospital)

Objective: To examine the effect of a single day, interdisciplinary, inflammatory arthritis education program (RxEd) on arthritis self-efficacy and other secondary outcomes (arthritis knowledge and coping efficacy). This new program integrates self-management and didactic education. This pilot study was designed to: 1) Assess the feasibility of performing this study; 2) Explore secondary outcomes; and 3) Estimate sample sizes needed for a study.

Methods: Non-randomized, wait-listed control (with cross-over) trial of RxEd program (I) among patients with inflammatory arthritis recruited from tertiary level arthritis care clinics. Data were collected at the beginning of the study (T1), immediately following I (T2) and at 6 months (T3). Self-report

questionnaires served as the data collection tool. Measures included demographics, disorder-related, Arthritis Self-Efficacy Scale (SE), arthritis knowledge [ACRUE RA knowledge questionnaire (PK) and RxEd Content knowledge questionnaire (CK)] and coping efficacy (CE). Analysis included: Univariate comparisons by group (I vs C), Relative Standardized Response Means [RSRM (T3-T1) = mean I-C/PSD (Pooled Standard Deviation of mean I-C)], direct between-group statistical comparison (unpaired t-test) and mean scores plotted over time.

Results: 42 persons participated in the study (I n=23; C n=19). No significant baseline differences were found for: demographics, disorder-related, SE, PK, CK and CE measures. For the primary outcome (SE): RSRM = 0.6 and t-test of borderline significance (p = 0.06). I group showed immediate effect (improved SE) after the intervention and sustained the effect at 6 months while C group had no effect. For the secondary outcomes: PK RSRM = 0.6, t-test p = 0.07; CK RSRM = 0.5, t-test p = 0.12; CE RSRM = 0.7, t-test p < 0.05. I group showed an immediate effect in uptake of arthritis knowledge (PK and CK) after the intervention that diminished slightly over the 6 months while C group had no effect. I group showed an increase in CE that was sustained at 6 months while C group had no effect.

Conclusion: Despite small sample sizes and thus being underpowered, we found RSRM ranging from 0.5 to 0.7 and significant or borderline significant between-group comparisons. This pilot study provides evidence that the "Prescription for Education" program is feasible and likely to improve arthritis self-efficacy, arthritis knowledge and coping efficacy among persons with inflammatory arthritis. Data from this pilot study will help guide in estimating sample sizes and choosing appropriate primary and secondary outcomes for a study.

5

Factors Influencing Inpatient Rehabilitation Length of Stay after Revision Hip and Knee Arthroplasty
SM Teresa Yeung (West Park Healthcare Centre; HPME, University of Toronto); Dr. Rajka Soric (West Park Healthcare Centre; Division of Physiatry, Department of Medicine, University of Toronto); Dr. Aileen Davis (Division of Health Care and Outcomes Research and Arthritis Community Research & Evaluation Unit, Toronto Western Research Institute; Department of Health Policy, Management and Evaluation and Rehabilitation Science, University of Toronto)

Objective: To determine factors associated with inpatient rehabilitation length of stay (LOS) after revision hip or knee arthroplasty.
Methods: The study included patients admitted to an inpatient rehabilitation program between 2002 and 2006 who had revision hip (group H) or knee (group K) arthroplasty. Exclusion criteria included infection, use of skin/muscle flaps during surgery, wound dehiscence, unicondylar knee revisions and knee extensors reconstruction. Functional discharge criterion was safe independent or supervised mobility in patient's planned discharge destination. Patient and clinical data including LOS were collected retrospectively from the National Reporting System with supplementation by chart abstraction. Multiple regression was used separately in group H and K to identify variables predicting LOS at p<.05.
Results: The mean age of group H (n=275) was 69 years, 62% were female and the mean LOS was 29.6 days (sd=16.4, range=87). Factors that predicted longer LOS were low admission FIM score (p<.01), female gender (p<.05), multiple revisions (2 or more revisions, p<.05), limited support at home (p=.06), non-/touch-weight-bearing restriction (p<.08) and prior lower extremity surgeries in other joints (p<.05). Acetabular revision predicted shorter LOS (p<.05). The mean age of group K (n=92) was 69 years, 76% were female and their mean LOS was 28.8 days (sd=18, range=93). Similar to group H, low admission FIM score, female gender, multiple revisions (2 or more revisions), limited support at home and non-/touch-weight-bearing restriction predicted longer LOS in group K (all p-values <.01). Longer duration from surgery to rehabilitation admission (p<.01) and the presence of complications (p=.09) were other predictors of longer LOS in group K. Predictors corresponding to group H and K explained respectively 29% and 57% of variance in the mean LOS in each group; admission FIM score was the strongest predictor of LOS in both groups of patients.
Conclusion: Resource allocated to optimize modifiable predictors may shorten inpatient LOS. Strategies such as early intensive functional training for patients at risk of longer LOS and pre-arrangement of support before surgery should be considered. Further studies are needed to validate the predictors of inpatient LOS.

6

Assessment of Fracture Risk and Treatment of Osteoporosis in Postmenopausal Women: Bone Density vs. BONE DESTINY©
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Objective: To assess the proportion of women recommended for osteoporosis treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines, were compared in all female patients who visited the bone density clinic within a given time period.
Methods: All females ≥60 years of age who underwent a DEXA scan between January 2007 and October 2008 were included in the analyses. Treatment recommendations were made based on:
• BMD alone where those with a BMD ≤-2.5 are considered to be at risk for fracture;
• Bone DESTINY where five colour codes represent fracture risk and those who are at high or very high risk for fracture (red or purple) are recommended;
• Osteoporosis Canada (OC) guidelines which categorize patients at low, moderate or high fracture risk and those at high risk are recommended for treatment.
Bone DESTINY's estimation of fracture risk combines BMD, age, steroid use, propensity to fall, previous history of falls, previous history of fracture and BMI <20 kg/m^2 while OC guidelines included sex, BMD, age, previous history of fragility fracture and steroid use. The proportion of women recommended for treatment was compared between the three groups.
Results: Of 14,812 females included in the analyses, 7,049 were 60-69 years old, 5,252 were 70-79 years. In the youngest group, 19% would be recommended for treatment according to BMD alone, 28% according to bone DESTINY and 20% according to OC guidelines. In the 70-79 year old group, 29% would be recommended for treatment based on BMD alone, 43% according to bone DESTINY and 51% according to OC guidelines. In the eldest group, 47%, 77% and 72% would be recommended for treatment according to BMD alone, bone DESTINY and OC guidelines, respectively.
Conclusion: Given that bone DESTINY and OC guidelines account for fracture risk factors in addition to BMD alone, it is not surprising that there is a large discrepancy in the proportion of women who would be recommended for treatment between these groups. Differences between bone DESTINY and OC guidelines are likely a result of differences in the weightings of risk factors such as steroid use and previous fragility fracture and the impact of additional risk factors. Based on the agreement in results between DESTINY and OC guidelines, the visual ease of interpretation make DESTINY an attractive option for reporting fracture risk.

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Patients with Fragility Fracture Assessed by BMD, BONE DESTINY© and Osteoporosis Canada Guidelines
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Objective: To assess the proportion of males and females with ≥ 1 previous

fragility fracture recommended for treatment based on three different assessment methods, bone mineral density (BMD), Bone DESTINY and Osteoporosis Canada (OC) guidelines.

Methods: Individuals ≥50 years of age with a history of fragility fracture who underwent a DEXA scan between January 2007 and October 2008 were included in the analyses. Fracture risk and treatment recommendations were made based on:
• BMD alone
• Bone DESTINY (fracture risk estimation combining BMD, age, steroid use, propensity to fall, previous history of falls, previous fragility fractures and BMI <20 kg/m^2), and
• Osteoporosis Canada (OC) guidelines (included sex, BMD, age, history of fragility fracture and steroid use).

Those with a BMD ≤-2.5, a DESTINY fracture risk in the red or the purple categories or those at high risk for fracture according to Osteoporosis Canada guidelines are those recommended for treatment. The proportion of males and females recommended for treatment was compared between groups.

Results: Included in the analyses were 3914 females and 572 males with each sex divided into age groups. Of all females in the 50-59 years old group (N=763), 19% would be recommended for treatment according to BMD alone, 39% according to bone DESTINY and 36% according to OC guidelines. In the 60-69 year old group (N=1118), 27% would be recommended for treatment based on BMD alone, 79% according to bone DESTINY and 81% according to OC guidelines. In the 70-79 year old group (N=1225), 37% would be recommended for treatment based on BMD alone, 89% according to bone DESTINY and 96% according to OC guidelines. In the 80-89 year old group (N=810), 56%, 96% and 98% would be recommended for treatment according to BMD alone, bone DESTINY and OC guidelines, respectively. Of all males in the 50-59 year old group (N=111), 24% would be recommended for treatment according to BMD alone, 39% according to bone DESTINY and 12% according to OC guidelines. In the 60-69 year old group (N=175), 22% would be recommended for treatment based on BMD alone, 79% according to bone DESTINY and 15% according to OC guidelines. In the 70-79 year old group (N=185), 30% would be recommended for treatment based on BMD alone, 77% according to bone DESTINY and 57% according to OC guidelines. In the eldest group (N=101), 30%, 95% and 85% would be recommended for treatment according to BMD alone, bone DESTINY and OC guidelines, respectively.

Conclusion: Overall, Bone DESTINY suggests treatment in a much higher number of fragility fracture patients than BMD alone with an overall treatment recommendation in 78% of women assessed by bone DESTINY compared to 35% assessed by BMD alone and 73% of males assessed by bone DESTINY compared to 26% assessed by BMD alone and 41% by OC guidelines. Like DESTINY, 80% of women would be recommended for treatment based on OC guidelines. However, in males, results suggest that both BMD and OC guidelines under-indentify males with a fragility fracture who require treatment. This may be explained by the addition of the history of falls and propensity to falls in the DESTINY software which is not used in OC risk-stratification. These results warrant further investigation.

8

Quality Of Life In Lupus Patients With And Without Renal Involvement

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Objective: To determine:1.Whether the quality of life (QOL) is different between patients with highly active (H-SLE) & less active systemic lupus erythematosus (L-SLE) with & without renal involvement, 2.Whether there is an association between the QOL mental & physical scores and SLE disease activity index (SLEDAI).

Methods: Patients were enrolled in the CIHR Lupus Nephritis New Emerging Team (LuNNET) study in Canada. Disease activity was done by SLEDAI and scores≥7 considered significant clinical activity. Subjects were classified into those with & without renal involvement (LN, NLN) and further to those with active (ALN & ANLN) and inactive disease (ILN & INLN). The Medical Outcomes Study 36-item Short Form (SF-36) was used to calculate mental (SF-MCS) and physical (SF-PCS) component scores. Scores<48 were considered impaired.

Results: 116 patients (98 female,18 male), age 38.5±1.3 yr, disease duration 12.3±0.9 yr, 71 L-SLE & 45 H-SLE, 62 with LN (30 ALN, 32 ILN) and 54 NLN (14 ANLN, 40 INLN) were enrolled. Disease duration was shorter in all H-SLE subjects with or without LN than L-SLE (9.6±1.4 vs 14.1±1.2, p=0.02). H-SLE subjects were also younger than L-SLE (34.6±2.0 vs 41.0±1.7, p=0.02) and, ALN subjects tended to be younger (35.0±2.4 vs 41.2±2.4, p=0.08) than ILN. Average scores for SF-MCS or SF-PCS between H-SLE & L-SLE; LN & NLN; ALN & ILN were similar, but were much lower than the mean for the general population. However, SF-MCS was significantly higher in INLN than ANLN (49.9±1.6 vs 41.6±2.9, p=0.02). Impaired SF-MCS was significantly more prevalent in H-SLE than L-SLE (57.8% vs 38%, p=0.04) and in ANLN than INLN (69.2% vs: 35%, p=0.03). Impaired SF-MCS and SF-PCS were similarly prevalent between ALN and ILN. However, impaired SF-PCS was significantly more prevalent in LN than NLN (83.9% vs 66%, p=0.03). There was no association between SLEDAI and SF-PCS or SF-MCS. But, there was a weak and significant correlation between disease duration and SF-PCS (r=-0.288, p=0.002).

Conclusion: Patients with SLE have poor physical health regardless of renal status. Mental health is also worse in active SLE and NLN. Thus, renal involvement did not significantly impact on health status in this cross-sectional study. The difference in age and disease duration between groups may partly explain these results.

9

Is There Relevant Information about Scleroderma Renal Crisis on Most Frequently Visited Internet Search Engines?

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Objective: To determine if there is accurate information regarding the risk of developing Scleroderma Renal Crisis (SRC) with the use of corticosteroids (CS) on the most frequently visited internet Search Engines (SE). Almost 50% of patients with diffuse Systemic Sclerosis (SSc) show some evidence of renal involvement. SRC develops in approximately 10 to 20 % of patients with diffuse SSc and less frequently in limited SSc. SRC is an early complication of diffuse SSc usually seen within first five years of the disease onset. Moderate dose CS (prednisone ≥15 mg/ day) use six months prior to SRC onset has been shown to be a major risk factor in inducing SRC.

Methods: We surveyed 8 people including medical students and non-professional lay people about their favourite SE. The following six SE including Google, Yahoo, Dogpile, AltaVista, Metacrawlers and Ask were most commonly used. We reviewed these SE specifically for SRC to see if they mentioned potential risk of developing SRC with the use of moderate dose CS in SSc patients.

Results: There were five common websites on the SE. Websites: Emedicine and Medscape were available on all six SE, whereas Scleroderma Foundation and Sclero.org were available on five SE and Wikipedia was available on four of the SE. Emedicine and Sclero.org were the only two websites which mentioned the risk of inducing SRC with the use of CS. Emedicine was available on the entire above mentioned SE, whereas Sclero.org was available on all SE except Yahoo.

Conclusion: All of the six most frequently visited SE do have accurate information on SRC, but only limited websites including Emedicine and Sclero.org

mentioned the potential risk of precipitating SRC with the use of steroids to the general public. There is limited public information on viewed websites, so it is important that patients understand the possible risk of using CS when diagnosed with SSc. Appropriate disease information must be provided to the patient, as it does not exist on most of the websites patients would access.

10

Creation of a Bedside Teaching Atlas

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Objective: To describe the development of The Bedside Teaching Atlas ©, a pilot bedside teaching tool for promoting recognition of physical findings in the rheumatic diseases.

Methods: Photographs were obtained of key physical findings that can be observed in the rheumatic diseases such as joint effusions, nailfold changes and skin findings. Pictures were chosen based on 1) findings typically missed by medical students and residents or those cited as "never been seen" 2) physical findings that Patient Partners® wish to demonstrate but may not possess themselves. Photos were organized according to the GALS (Gait Arms Legs Spine) scheme, often used for teaching physical examination. Pages were spiral bound for "flip chart" style use. Descriptive information for each photo was placed on the back of the preceding page to face the instructor. This was done to encourage thoughtful "inspection" of the photo by the student, while permitting non-expert teachers to have information regarding the picture. The number of photos was limited to ensure portability and ease of use.

Results: Implementation of the pilot Bedside Teaching Atlas is currently underway. The Atlas is being used for medical student and resident physical exam teaching. The Atlas is also being introduced into use by Patient Partners®. Informal assessments indicate high level of student satisfaction with use of the Atlas during teaching sessions. Feedback comments indicate enthusiasm over observing and understanding rheumatologic findings "for the first time". Many students indicate that this has promoted more careful and informed examination of their patients. This pilot Atlas will initially be circulated to Rheumatologist clinician teachers at all teaching hospitals at University of Toronto and evaluated for student and teacher satisfaction. A similar evaluation will be done for use of the Atlas in Patient Partner® teaching sessions.

Conclusion: It is predicted that demonstration of key physical findings using the Bedside Teaching Atlas, in the context of teaching rheumatology physical exam with a "normal" patient, will enhance recognition of these findings in "real" patients and improve the diagnostic acumen of trainees. It is also predicted that use of the Atlas will enhance the effectiveness of Patient Partners® teaching. It is anticipated that this pilot project will stimulate submissions of excellent photographs from other rheumatologists across Canada to build a comprehensive collection for bedside use.

11

Use of Rituximab or Abatacept after Anti-TNF Discontinuation in Patients with Severe Rheumatoid Arthritis

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Objective: At the present time, patients with rheumatoid arthritis (RA) who discontinue anti-TNF therapy are limited to B-cell depletion therapy (Rituximab, RIT) or T-cell costimulation inhibition (Abatacept, ABAT). Our objective is to characterize the clinical experience with these two agents in patients who have discontinued anti-TNF therapy.

Methods: A prospective, longitudinal database of all patients who have received RIT or ABAT for RA in our centre was reviewed. Demographic information and therapeutic history was obtained. The clinical response was determined using DAS28 scores, EULAR response, and HAQ scores. Adverse events were documented.

Results: As of November 2008, a total of 24 patients have been treated with RIT, and 16 patients with ABAT. These patients have severe RA, with long disease duration (17.3 (SD 10.3) years), a high seropositivity rate, and multiple previous DMARDs. All patients had previous anti-TNF exposure, with 71% of the RIT patients and 63% of the ABAT patients receiving all 3

anti-TNF therapies available. Of note, 5 of the ABAT patients had received RIT. The average baseline DAS28 scores were 6.3 (SD 1.1) for RIT patients and 6.1 (SD 1.2) for ABAT patients. The average baseline HAQ scores were 2.0 (SD 0.4) for RIT patients and 1.7 (SD 0.6) for ABAT patients. Average follow-up duration is 15.5 months (sum 310.3 months) and 11.2 months (sum 179.7 months) for RIT and ABAT respectively. Nine patients have required a 2nd course of RIT after an average of 11.5 (SD 3.6) months (range 7.1 to 19.8 months), and 2 patients have required a 3rd course. After treatment, the DAS28 declined significantly to 3.9 (SD 1.3) in the RIT group and 3.5 (SD 1.6) in the ABAT group (p<0.0001). HAQ scores also improved in both groups (to 1.2 in the RIT patients and 1.0 in the ABAT patients). EULAR responses were good or moderate in 82% of RIT patients and 78% of ABAT patients. For RIT, adverse events included 5 serious infections and 5 non-serious infections, 5 infusion reactions, and 2 elective hospitalizations for orthopaedic procedures. For ABAT, adverse events have included 6 non-serious infections, 1 allergic reaction during infusion and general malaise after infusion in 5 patients. No deaths or malignancies have occurred with either agent, with excellent continuation rates.

Conclusion: RA patients who have discontinued anti-TNF therapy obtain equal efficacy when switching to either RIT or ABAT, with acceptable safety profiles.

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Cross-Cultural Adaptation And Validation Study Design For An Early Inflammatory Arthritis Detection Tool In The Canadian Francophone Population

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Objective: To develop a questionnaire to identify French Canadian inflammatory arthritis patients that is equivalent to one that exists in English.

Methods: This study will be done in two parts. Part One: The questionnaire will be translated and adapted using the following steps: 1) The questionnaire will be professionally translated and then reviewed by French-speaking laypersons to determine if they understand the translation. 2) The French translation will be professionally translated back into English and reviewed by English-speaking laypersons. 3) In steps 1) and 2), comments from laypersons will be used by the translators to change the translation into better-understood language. 4) Steps 1) and 2) will each be done twice to make sure that at least one appropriate translation is created. 5) A committee will review the two sets of translations and determine which is best. The following persons will be included in the committee: translators, laypersons, family doctors, arthritis specialists, language experts, and scientists. Part Two: The French questionnaire will be proven to work as well as the English version. This will be done by showing that different groups of arthritis patients answer the questionnaire differently. The answers of 402 patients from three groups will be studied: 134 with new inflammatory arthritis symptoms, 134 who have had inflammatory arthritis for a long time, and 134 without inflammatory arthritis. All study patients will be selected from the offices of arthritis specialists. The study will be conducted at the offices of arthritis specialists where there is the greatest density of French-Canadians: 6 in Quebec, 2 in Ontario, 1 in Manitoba, and 1 in New Brunswick. Each arthritis specialist will be asked to include 13-14 patients from each group in the study.

Results: Scientists have previously used similar studies to translate and adapt other health questionnaires and prove that they continue to work in the new language. We are using these scientifically accepted methods in this study.

Conclusion: A working, translated and adapted early inflammatory arthritis questionnaire for French-Canadians may help them receive appropriate treatment sooner.

13

Neuropsychological Outcome of Childhood Primary CNS Vasculitis (cPACNS)

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Objective: To evaluate the neuropsychological outcome of children with cPACNS and to explore differences between the distinct clinical subgroups.

Methods: A single center cohort study of cPACNS patients aged < 18 years diagnosed between 1992 and 2008 was performed. Patients were included if they 1) met Calabrese criteria and 2) were diagnosed at ≥ 2 years of age and 3) had neurocognitive testing performed. Patients were classified as medium-large vessel (MLVcPACNS) or small vessel (SVcPACNS) vasculitis based on cerebral angiography ± brain biopsy results. All patients received a standardized battery of validated neuropsychological tests to assess verbal and non-verbal reasoning, mental speed, mental manipulation, learning and memory. Tests were scored against validated norms and expressed as standardized scores. The medical charts were reviewed for: sex, age at diagnosis, age at time of 1st testing, language spoken at home, parental education level and family history of learning disability.

Results: A total of 58 (33 M; 25 F) patients completed neuropsychological testing after diagnosis. Mean age at diagnosis was 8.0 ± 3.7 years (2.6-16.5). Average time between diagnosis and 1st testing was 1.6 ± 1.8 years. Forty-five children had medium-large vessel vasculitis and 13 children had small vessel vasculitis. Forty-nine children spoke english as a first language. Children with SVcPACNS had significantly lower full scale IQ scores as compared to children with MLVcPACNS (97.9 ± 18.2 vs. 80.8 ± 18.4; t=2.97,df=56,p=0.004). 8/13 children were > -1 SD (62%) and 3/13 > -2 SD (23%) in the SVcPACNS group compared with 9/45 (20%) and 3/45 (6.6%) in the MLVcPACNS group. On tests of verbal reasoning, processing speed, working memory and perceptual reasoning the children with SVcPACNS scored significantly lower.

Conclusion: SVcPACNS may to be more detrimental to overall intellectual ability and affect cognitive function in a more diffuse way than medium-large vessel disease. Children with small vessel CNS vasculitis were more consistently impaired over multiple cognitive domains. Significantly lower scores were noted on tests of working memory, processing speed, verbal and non-verbal memory and visual-motor integration. Follow up assessments are mandatory to determine the long-term impact of cPACNS.

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SDAI and CDAI for Predicting Outcome of a Second Course of Rituximab for Patients with Rheumatoid Arthritis (RA)

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Objective: To explore whether the Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI) are predictors of disease activity after a second course of Rituximab (RTX) treatment.

Methods: In the 24-week phase III REFLEX trial (A&R, 2006;54), RA patients with past inadequate response (IR) to one or more TNF inhibitors were randomized to RTX or placebo + methotrexate. During open-label extension, physicians chose patients who had achieved ≥20% improvement in SJC, TJC to receive further courses of RTX. This study includes patients who received a first course (C1) of RTX and a second course (C2) during extension, with SDAI and CDAI calculated ~every 4 weeks. Using a generalized linear mixed model fit to all visits after C2, the effects of the following variables were evaluated at weeks 12-24 after C2: pre-trial characteristics, SDAI/CDAI scores, HAQ- DI at various times, and time between courses.

Results: 207 of the 298 patients who received RTX entered the extension. C2 was received by 173 patients, with 168 evaluable. These patients (82% female, 86% RF+, age 53±11) began C2 a median 43 weeks after C1. At data cut-off, their 24-week follow-ups after C2 were labeled as complete (n=138), not yet complete (n=5), or completed by imputation after patient withdrawal (n=25). The lowest mean SDAI and CDAI scores occurred at week 20 after both courses. The factors that independently increased SDAI and CDAI after C2 were 4-fold: baseline age, scores just prior to C2, SDAI/CDAI at week 20, and HAQ-DI at 16 weeks post-C1. For every 1.0 point that SDAI worsened before C2, there was a 0.21 point higher SDAI score post-C2. For CDAI, the same 1.0-point worsening resulted in a 0.24 point higher CDAI score. Non-significant predictors in the pre-trial characteristics (except age) included HAQ-DI immediately before C2, and time between courses.

Conclusion: For RA patients who respond to RTX after IR to ≥1 TNF inhibitors, these data suggest that SDAI or CDAI are predictors of the outcome of a second course of RTX; the less that disease activity, as measured by these two indexes, is allowed to worsen before repeating treatment, the better.

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Serious Infections in a Population-based Cohort of Older Individuals with Rheumatoid Arthritis

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Objective: To study serious infections in a population-based cohort of older individuals with rheumatoid arthritis (RA).

Methods: We assembled an RA cohort using physician billing and hospitalization data for the province of Ontario (April 1st 1992 to March 31, 2007); we limited our analyses to persons aged >65. A diagnosis of RA was based on 2 or more billing code diagnoses of RA, at least 60 days apart but within 5 years. Cohort members were further required to have at least one prescription for an oral glucocorticoid, disease-modifying agent or biological response modifier in the 90 days preceding, or any time following, the cohort entry date. Cohort entry was defined by the date of the first RA billing code; subjects were followed until death, outmigration, or March 31, 2007. Baseline co-morbidity and history of joint-replacement were determined using hospitalization, billing and procedure code data. The primary outcome of interest was any infection associated with a hospitalization.

Results: We identified 36,789 individuals aged >65 with RA; 69.8% of the subjects were female, and the average age was 74.0 years (standard deviation 5.8 years).Co-morbidity included chronic lung disease in 39.8%, diabetes in 25.5%, and renal disease in 14.8%. About one-fifth (19.4%) had a history of joint replacement. The subjects were followed for a total of 267,227 person-years (average of 7.3 years each). The most common infections included skin/soft tissue infection (2,414 events; 9.0 cases/1,000 person-years), pneumonia (1,189 events; 4.5 cases/1,000 person-years), and bacteremia (1,183 events; 4.4 cases/1,000 person-years). Our multivariate models indicated age, male sex, increasing co-morbidity, and history of joint replacement as independent risk factors for over-all infection, as well as for specific infections (skin/soft tissue, pneumonia, and bacteremia). Chronic lung disease (hazard ratio, HR 1.98, 95% CI 1.91, 2.05), diabetes (HR 1.23, 95% CI 1.18, 1.28), and renal disease (HR 1.80 95% CI 1.73, 1.88) were each independent predictors of over-all infection as well as specific infections. A history of joint replacement was associated with a HR of 1.05 (95% CI 1.01, 1.09) for infections overall, and a HR of 1.28 (95% CI 1.16, 1.43) for skin/soft-tissue infection.

Conclusion: We found a high burden of infection in this population-based cohort of older persons with RA. Increasing age, male sex, co-morbidity, and history of joint replacement were independent predictors of infection in our sample.

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Baseline Characteristics of Patients Receiving Biologic and DMARD Therapy in Ontario: Results from the Ontario Biologics Research Initiative

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The Ontario Biologics Research Initiative (OBRI) is performing real world surveillance of Rheumatoid Arthritis (RA) using clinical and patient self-

reported data with administrative database linkages. Patients are enrolled and prospectively followed to assess their response to treatment and to capture detailed information about adverse events.

Objective: To describe baseline characteristics of the first 233 patients enrolled

Methods: Patients were enrolled when prescribed new treatment (DMARD or Biologic) from 14 rheumatology clinics in Ontario.189 (81%) patient baseline information were obtained from the treating rheumatologist through standard questionnaires. Information included disease characteristics, clinical and laboratory data and current antirheumatic therapies. 233 (100%) patients have completed telephone questionnaires including standardized informed consent, demographic and work productivity variables, the Rheumatoid Arthritis Disease Active Index (RADAI) and the Health Assessment Questionnaire (HAQ). Comorbidity was assessed at the time treatment was prescribed, using a prespecified list of coexisting conditions. We compared physician and patient-reported comorbidities as the presence of any comorbidity and the number of comorbidities.

Results: Patient characteristics included: Mean (SD) age 56.5(13.7), RA duration 8.5(11.8) years, 73% female; 74% RF positive; 30% early RA (≤1year). 21% of entire cohort was prescribed new biologic therapy. Concomitant MTX was reported in 92% in biologic group compared to 70% DMARD group. From time biologic prescribed, mean time to treatment start was 26.1(SD25.6) days; ranging from 0 to 101 days. Biologic patients had a longer mean disease duration compared to DMARD patients [11.2(10.3) vs. 7.8(12.1)years P=0.15]. Biologics patients also had higher mean DAS28 at baseline than DMARD patients [5.7(SD1.2) vs. 5.1(SD1.3)P=0.026]. Patients reported higher mean disease activity at baseline in the biologic group [RADAI: 5.6(SD1.9) vs. 4.7(SD2.1)]. Both patients and rheumatologists reported mild (6%,11%), moderate (41%,37%) and severe (53%,53%) disease activity, respectively. Biologic patients also reported more disability: [HAQ scores: 2.0(SD0.8) vs. 1.7(SD0.8)].Comorbidity was common, and reported more frequently by patients than by rheumatologists (84% vs. 71% reporting at least 1 comorbid condition). According to patients, the most frequent comorbidities were back pain (49%), hypertension (34%), depression (28%) and other forms of osteo or degenerative arthritis (27%). Rheumatologists reported more patients having ≥1 comorbidities in the biologic cohort compared to DMARD group (81%vs69%).

Conclusion: In routine practice, biologics are being prescribed to patients with longer mean disease duration who have more severe disease activity and disability compared to DMARD patients in this sample. High levels of baseline comorbidity strengthen the need for real-world data and will influence future analysis on the effectiveness and safety of RA therapies in routine rheumatologic care.

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Efficacy of Bazedoxifene in Reducing the Incidence of Nonvertebral Fractures in Postmenopausal Osteoporotic Women at Higher Fracture Risk

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Objective: In a recent phase 3 trial, treatment with bazedoxifene for 3 years effectively reduced the risk of new vertebral fracture relative to placebo in postmenopausal women with osteoporosis. Here we report the results of post hoc analyses of nonvertebral fracture (NVF) incidence among women at higher risk for fracture in that study.

Methods: Generally healthy postmenopausal women (N = 7,492; mean age, 66.4 y) with osteoporosis were randomized to daily therapy with bazedoxifene 20 or 40 mg, raloxifene 60 mg, or placebo; all subjects received supplemental elemental calcium (1,000-1,200 mg/d) and vitamin D (400-800 IU/d). Kaplan-Meier estimates of the incidence of NVFs at 36 months were evaluated for the overall population and for subgroups of women at higher fracture risk, based on known skeletal risk factors (low femoral neck [FN] T-score and/or prevalent vertebral fracture).

Results: The overall incidence of NVFs was similar among groups. In a subgroup of women at higher risk for fracture (FN T-score ≤-3.0 and/or ≥1 moderate or ≥2 mild vertebral fractures; n = 1,772), NVF rates were 4.9%, 6.5%, 8.4%, and 9.1% with bazedoxifene 20 and 40 mg, raloxifene 60 mg, and placebo, respectively. Bazedoxifene 20 mg significantly reduced NVF incidence relative to placebo and raloxifene 60 mg (50% and 44%, respectively; P<0.05); a similar reduction was observed when NVF data for bazedoxifene 20 and 40 mg were combined (40% relative to placebo; P = 0.03). Conversely, there were no significant between-group differences in NVF rates in the lower-risk subgroup (n = 5,710). Further evaluation of NVF incidence in subjects with FN T-scores ≤-2.5 or ≤-2.0 and/or ≥1 moderate or ≥2 mild vertebral fractures showed a trend toward NVF risk reduction with bazedoxifene treatment, supporting the robustness of the results. The selection of subjects at higher fracture risk was also supported by Cox regression analyses, which showed that the treatment by risk category interaction was significant with bazedoxifene 20 mg (P = 0.025) and was of borderline significance with bazedoxifene 20 and 40 mg combined (P = 0.052).

Conclusion: Treatment with bazedoxifene significantly reduced the risk of NVF in postmenopausal osteoporotic women at higher risk for fracture.

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Effects of Denosumab in Postmenopausal Women Transitioning from Alendronate Therapy in Comparison with Continued Alendronate

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Objective: Previous studies showed the RANKL inhibitor denosumab increased bone mineral density (BMD) and decreased bone turnover in postmenopausal women with low BMD. Many patients with osteoporosis are currently treated with bisphosphonates, but may want or need to switch therapy in their lifetime, thus it is important to understand the safety and efficacy of transitioning patients from bisphosphonates to denosumab.

Methods: In this phase 3, double-blind, double-dummy study, postmenopausal women ≥55 years old with a lumbar spine or total hip T-score of ≤-2.0 and ≥-4.0 and who had received alendronate therapy equivalent to 70 mg/week for ≥6 months were eligible. After enrollment, all subjects received open-label branded alendronate 70 mg once weekly for 1 month, then were randomized to continue receiving alendronate or to receive subcutaneous denosumab 60 mg Q6M. All subjects received daily supplements of calcium and vitamin D. The primary endpoint was the percent change in total hip BMD at 12 months.

Results: A total of 504 subjects (253 denosumab; 251 alendronate) with a mean age of 67.6 years and mean lumbar spine T-score of -2.63 were enrolled. The mean (sd) length of prior bisphosphonate therapy was 44 (33) months. Denosumab increased total hip BMD by 1.90% at 12 months compared with a 1.05% increase in subjects continuing on alendronate (P<0.0001). Significantly greater BMD gains with denosumab compared with alendronate were also achieved at 12 months at the lumbar spine (3.03% vs 1.85%), femoral neck (1.40% vs 0.41%), trochanter (2.95% vs 1.90%), and 1/3 radius (0.87% vs 0.15%) (P<0.05 for all). Serum CTX levels remained near baseline in the alendronate group and were significantly decreased vs alendronate at

all time points in the denosumab group. Subject incidence of adverse events (AEs) (197 denosumab; 196 alendronate) and serious AEs (15 denosumab; 16 alendronate) was balanced between the two treatment groups. No AEs of hypocalcemia were reported.

Conclusion: Denosumab increased BMD at all measured skeletal sites and had a greater reduction of BTMs compared to continued alendronate with a similar safety profile in both groups.

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Improvements in Physical Function and Pain Relief Were Sustained in Rheumatoid Arthritis Patients Treated for 2 Years with Certolizumab Pegol
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Background: Rheumatoid arthritis (RA) is a chronic disease characterized by significant pain. In the RAPID 1 trial, certolizumab pegol (CZP), the first PEGylated, Fc-free TNF inhibitor, provided rapid, sustained and meaningful improvements in both physical function and pain, when administered at 200 mg or 400 mg every 2 wks as add-on therapy to methotrexate (MTX). A phase III, open-label extension (OLE) study to RAPID 1 is currently assessing the long-term safety and efficacy of CZP (400 mg every 2 weeks) as add-on therapy to MTX. The objective of this analysis was to evaluate physical function and pain with continued administration of CZP + MTX over a 2-year period.
Methods: Patients who successfully completed the RAPID 1 trial at 52 weeks (completers) and enrolled in the OLE received CZP 400 mg + MTX every 2 weeks. This analysis evaluated completers who received continuous treatment with CZP for at least 2 years as of August 31, 2007. Physical function was assessed by the HAQ-DI and pain was assessed by the Patient's Assessment of Arthritis Pain (PAAP) Visual Analog Scale (0-100 mm). Score changes from baseline for all outcomes and proportions of patients achieving Minimum Clinically Important Differences (MCID) in HAQ-DI (≥0.22) were reported. Missing scores were imputed using the last observation carried forward method.
Results: Sustained improvements in physical function were maintained throughout 100 weeks of treatment in patients originally treated with CZP 200 mg + MTX (N=168) or with CZP 400 mg + MTX (N=177). The percentage of HAQ-DI MCID responders at Week 100 was 72.4% or 70.1% for patients originally treated with CZP 200 mg or CZP 400 mg, with MTX, respectively. Patients' pain was relieved on average by 39.1 or 38.1 points for patients originally treated with CZP 200 mg or CZP 400 mg, with MTX, respectively, while the threshold of meaningful improvement is 10 points. No additional benefit was observed when the dose of CZP was increased from 200 mg at Wk 52 to 400 mg in the OLE in completers.
Conclusion: CZP as add-on therapy to MTX provided sustained, long-term, clinically meaningful improvements in physical function and pain in RA patients. In addition, increasing the dose from 200 mg to 400 mg every 2 weeks did not appear to result in additional benefit in completers.

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Experience of Office-based Use of Abatacept for RA Patients
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Objective: to describe Abatacept use for RA patients who failed anti-TNF and/or DMARDs in a community-based practice in Calgary
Methods: 39 RA patients (29F:10M) were treated with Abatacept. The treating Rheumatologist administered and supervised every treatment on site for infusion related reaction, serious adverse effects, joint count, patient global self assessment and HAQ. Average/follow up HAQ/DAS-28 and Prednisone/methotrexate dose were tabulated.
Results: 39 (18 anti-TNF/21 DMARDs failures) patients underwent >500 (2-28) Abatacept infusions (25 received >8 infusions) over two years. Infusion reactions were noted for one episode of hand swelling due to the IV catheter misplacement and one patient experiencing dizziness. 9/39 discontinued infusions (one each for urinary tract infection, possible epidural infection, pulmonary fibrosis and non-compliance; two for primary failure; three for loss of insurance). 3 held Abatacept temporarily (transient deterioration of renal function and urinary tract infection, soft tissue infection and diverticuli-

tis). Average initial/follow up daily prednisone was 6.5mg/1 mg. 20/39 patients were on steroids initially. 9 stopped prednisone and one started prednisone. Average initial/follow-up weekly methotrexate doses were 20/15mg. Initial/follow-up DAS score (5/3.6) and HAQ (1.12/.25) were noted.
Discussions: Abatacept infusions have virtually no infusion related reaction. Noted were four serious infections and one pulmonary fibrosis. There were two primary failures. Several drop outs were related to insurance/compliance issues. There was 77% retention of the treatment. Not counting insurance and compliance, the retention rate would be 85%. There was also improvement of DAS and HAQ accompanied by reduced use of prednisone. Delta DAS was modest (1.4), but this was likely related to aggressive reduction of prednisone use. There seemed to be no escalation of average methotrexate dose in the whole group.
Conclusion: use of Abatacept in a solo practice in a community setting is associated with rare infusion reactions, predictable adverse side effects profile, favourable change of objective measures of efficacy and reduced reliance on prednisone. Retention rate of treatment was high. While the study is not intended to give vigorous statistical analysis of treatment outcomes, this experience may serve as a model for Abatacept use for Rheumatologist in community practice.

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High Unmet Need for Arthritis Pain Management among EU and US Rheumatoid Arthritis Patients Despite Effective Therapies
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Background: A previous survey conducted in Europe (EU) has indicated many patients still experience various levels of pain despite effective rheumatoid arthritis (RA) therapies (1). The objectives of this analysis were to examine pain associated RA and to determine if pain management is an unmet need in both the EU and US.
Methods: A survey was conducted in the US (via the Internet) and the EU (via structured face-to-face interviews in the UK, France, Germany, Spain and Italy) with adult RA patients. Eligible patients were >18 years of age, formally diagnosed with RA, and under the care of a rheumatologist. Questions covered disease-specific topics including severity and satisfaction/dissatisfaction of RA pain. An ANOVA was used and p-values for the Pearson correlation coefficient calculated by independent t-test.
Results: 756 (EU) and 2039 (US) RA patients completed the surveys. Patients in the EU (34%) and US (37%) reported similar dissatisfaction in levels of arthritis pain experienced in the past 30 days and the majority (75% EU; 82% US) of patients reported moderate to severe pain in the past 2 months. In the US, 44% of patients rated pain relief as the top benefit wanted from their RA medication, and among the 700 biologic users, 45% rated reduction of pain as the top reason for satisfaction with a biologic. Of the 179 biologic users in the EU, the majority were somewhat to extremely satisfied with their biologic therapy. However, 57% of the patients who were satisfied with their biologic did not rank pain relief as the number one reason for satisfaction. Both the EU and US patients agreed/strongly agreed that they worried one day their medicine would not be sufficient to control their pain. In the EU, severe RA patients who were either current or previous biologic users appeared to be more satisfied with their arthritis pain than severe RA patients who had never been on a biologic. The % of patients reporting high satisfaction with pain was low in both groups.
Conclusion: This survey indicates that, despite treatment, RA patients' levels of arthritis pain remain high in both the EU and the US and effective pain management remains an extensive unmet need for patients in the treatment of RA. (1) JM Alvaro-Gracia, et al. [abstract] In: EULAR 2008: Abs 1930.

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First Rituximab Course Efficacy Profile in Clinical Practice
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Background: Phase II-III trials have shown efficacy of rituximab in controlled set-up. Patients from clinical practice present different characteristics from those of clinical trial. Efficacy and safety data can thus differ from those trial. Observational prospective cohorts such as the one from the Institute of Rhumatology of Montreal, Rhumadataâ, provides us with the possibility to extend this knowledge to standard clinical practice.

Methods : Data from the Rhumadataâ electronic database was used. Data collected from the first 30 rheumatoid arthritis(RA) patients exposed to rituximab is shown. All patients underwent clinical evaluation at baseline, 3, 6, 9 and 12 month by one of the investigators. Data collected include demographics, disease duration, rheumatoid factor and anti-CCP assessment, erosive status, prior medication use, 28 tender and swollen joint count, ESR and CRP, HAQ, patient and physician global evaluation (VAS10cm), morning stiffness (Minutes) , fatigue scale (VAS), pain global scale (VAS). Rituximab was administered according to the canadian product monograph.

Results: Mean age is 52.4 years . 76 % of the group is of female gender. Average duration of disease is 15.7 years. 82 % are RF + and 62 % anti-CCP +. 82 % have erosive disease. Mean previous DMARDS failure is 3.1. 75% of patients have failed at least one biologic agent. Average dose of methotrexate for those who are taking it at initiation of rituximab is 17.5 mgs. Mean baseline tender joint count (TJC) is 14 and swollen joint count (SJC) 14. Mean TJC at 6 month is 6.7 and SJC 5.4 . Mean TJC at 9 month is 8.9 and SJC 11.1. Mean baseline DAS 28esr is 6.11 Mean DAS 28esr improvement at 6 month is 2.86.

Conclusion: In a population of RA patients with several markers of severity and resistance to treatment, rituximab was able to induce a clinically significant improvement in several measured parameters. On average patient show relapse of their disease between 6 and 9 months after the first course.

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Patients with Rheumatoid Arthritis Achieve a Rapid Response When Treated with Certolizumab Pegol Irrespective of Background Treatment

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Background: Certolizumab pegol (CZP), the first PEGylated, Fc-free TNF inhibitor, has been shown to effectively reduce the signs and symptoms of rheumatoid arthritis (RA) as both monotherapy and when combined with methotrexate (MTX). The purpose of this analysis was to investigate the rapidity of response to CZP as monotherapy and in combination with MTX.

Methods: Study 011 and RAPID 1 were phase III, placebo-controlled trials investigating the safety and efficacy of CZP as monotherapy (study 011) or in combination with MTX (RAPID 1) in patients with active RA. In 011, patients who had previously failed ≥1 DMARD were randomized 1:1 to subcutaneous (SC) CZP 400 mg or placebo every 4 weeks. In RAPID 1, patients with an inadequate response to MTX (previously treated for ≥6 months with MTX) were randomized 2:2:1 to SC CZP (400 mg at Weeks 0, 2 and 4 followed by 200 or 400 mg every 2 weeks) + MTX or placebo + MTX. Assessment of ACR responses at Weeks 1, 2, and 4 was analyzed using the Cochran-Mantel-Haenszel (CMH) test controlling for country in 011 and logistic regression with treatment and region as factors in RAPID 1. In both studies, baseline demographics and disease status were similar across all treatment arms.

Results: In both studies, the onset of ACR20 response was rapid with significant differences from placebo reported at Week 1. At Weeks 1, 2, and 4, 36.7%, 43.0%, and 44.5% of patients receiving CZP 400 mg monotherapy achieved ACR20 responses, respectively (P≤0.05 vs placebo). Similarly, 22.9%, 33.5%, and 43.6% of patients in the CZP 200 mg + MTX group achieved ACR20 responses at Weeks 1, 2 and 4 (P≤0.05 vs placebo + MTX). Results were similar for CZP 400 mg + MTX. ACR50 responses were significantly higher than control by Week 1 with CZP monotherapy (P≤0.05) and by Week 2 with CZP + MTX (P≤0.05). ACR70 responses were significantly higher than control by Week 8 (P≤0.05) and Weeks 4-6 (P≤0.05), respective-

ly. Significant improvements in all ACR core components were also observed by Week 1 in both trials.

Conclusion: Certolizumab pegol provides rapid relief of the signs and symptoms of RA, as measured by significant improvement of ACR scores, when administered as monotherapy or add-on therapy to MTX.

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Comparative Analysis of MR, VEGFR2 and HIF1α Gene Expression Profiles in Systemic Sclerosis Patient Biopsies from Affected Versus Non-affected Skin

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Objective: Vasculopathy, inflammation and hypoxia have been observed in Systemic Sclerosis (SSc). The etiology of SSc is still unknown but we hypothesize that the expression patterns of certain genes in vascular cells may provide clues to the etiology of the vascular abnormalities typical of SSc. As a first step, we have focused our investigation on changes in expression patterns in vascular cells of three candidate genes; vascular endothelial growth factor receptor (VEGFR2), mineralocorticoid receptor (MR) and hypoxia inducible factor 1α (HIF1α). We will compare gene expression analysis between pathological and normal skin within patients.

Methods: 6mm punch biopsies were taken from the forearm and the abdomen of SSc patients. Biopsies were fixed in optimal cutting temperature embedding medium. 8μm slides were prepared and endothelial cells were visualized with anti-CD31 immunostaining and extracted using Laser Capture Microdissection (LCM). Total RNA was extracted and used to synthesise cDNA. Quantitative PCR was performed to measure VEGFR2, MR and HIF1α expression from arm versus abdomen samples.

Results: We have been successful in being able to isolate, with LCM, vascular cells from XX patients. Gene expression analysis has been completed on one patient, with four more patients to be screened. Preliminary data show that in this patient, VEGFR2 and MR gene expression are three to five times higher in arm derived endothelial cells compared to those from abdomen skin. HIF1α expression, however, has not shown any statistically significant changes.

Conclusion: VEGFR2, MR and HIF1α expression has not been adequately studied in the endothelium of scleroderma patients. Preliminary results show differences in gene expression between affected and normal skin. Specimens from further SSc patients are currently being analyzed and gene expression arrays will also be performed to determine the precise extent of transcription level changes with vascular disease pathology. These results will help to explain how signalling pathways in the vasculature may influence scleroderma pathology.

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Hospitalized Infections in the Abatacept Rheumatoid Arthritis Clinical Development Program: An Epidemiological Assessment with >10,000 Person-years of Exposure

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Objective: To assess the risk of infections in the cumulative abatacept program

Methods: Data from the abatacept rheumatoid arthritis (RA) clinical development program were included through December 2007. The incidence rate (IR) of hospitalized infection was calculated. Standardized incidence ratios (SIRs), adjusted for age and sex, were computed comparing the observed number of hospitalized infections in the abatacept cumulative (double-blind [DB] and open-label) experience to that expected based on 4 cohorts of RA patients treated with non-biologic disease-modifying anti-rheumatic drugs (DMARDs; the predominant background therapy in the abatacept clinical

development program) from 2 administrative data sources (British Columbia RA Cohort [BC], PharMetrics) and 2 early RA registries (Norfolk Arthritis Register [NOAR], Sweden Early Rheumatoid Arthritis Register [ERA]).

Results: A total of 4150 patients in 8 clinical trials were treated with abatacept for a total of 10,365 patient-years (p-y). The median exposure was 26.2 months. In the DB period, the IRs of hospitalized infections were 3.05/100 p-y and 2.15/100 p-y in the abatacept and placebo groups, respectively. There were 272 hospitalized infections in the cumulative abatacept experience for an IR of 2.73/100 p-y. The most common hospitalized infections were pneumonia, bronchitis, cellulitis, and urinary tract infection. The SIRs (95% CI) of hospitalized infection in the cumulative abatacept program compared with non-biologic DMARD-treated RA patients were 0.88 (0.8, 1.0), 0.75 (0.7, 0.8), 1.88 (1.7, 2.1) and 1.44 (1.3, 1.6) for BC, PharMetrics, NOAR, and ERA, respectively.

Conclusion: The IR of hospitalized infection was stable over time. There was considerable variation in the SIRs depending on the comparator cohort; differences may be related to demographic and RA-related factors as well as comorbid conditions and concomitant treatments, including glucocorticoids. The safety of abatacept with respect to hospitalized infections will continue to be monitored as part of a post-marketing surveillance program and in RA patient registries.

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Abatacept Provides an Increasing Degree of Inhibition of Structural Damage Progression Through 3 Years in Patients with Rheumatoid Arthritis and an Inadequate Response to Methotrexate Who Remain on Treatment

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Objective: To assess the effect of abatacept in reducing structural damage progression, through 3 years of treatment in the AIM trial.

Methods: This was a long-term extension (LTE) of a 1-year, Phase III, randomized, double-blind (DB), placebo-controlled trial. During the DB period, patients received abatacept (~10 mg/kg) or placebo + MTX, on Days 1, 15, 29, and every 4 weeks thereafter. Patients completing the DB phase entered the LTE (abatacept ~10 mg/kg + MTX). Radiographs of hands and feet were performed at baseline, 1, 2 and 3 years, or upon early termination. Results of early study terminators were linearly extrapolated for up to 1 year; data presented are based on all patients who entered the LTE. Paired radiographs were scored for erosion (ES), joint-space narrowing (JSN) and total score (TS) using the Genant-modified Sharp score.

Results: Of the patients initially randomized to abatacept (N=433), 328 (76%), 324 (75%) and 295 (68%) were evaluated at baseline and at the end of Years 1, 2 and 3, respectively. The mean changes in ES were 0.53, 0.25, and 0.14 from baseline to Year 1, from Year 1 to 2, and from Year 2 to 3, respectively. The mean changes in JSN were 0.35, 0.18, and 0.12 from baseline to Year 1, from Year 1 to 2, and from Year 2 to 3, respectively. The mean changes in TS were 0.89, 0.43, and 0.25 from baseline to Year 1, from Year 1 to 2, and from Year 2 to 3, respectively. An approximately 50% reduction in all scores was observed in the second year relative to the first year. Further decreases were seen in the third year of treatment and the rate of change observed in Year 3 versus Year 2 was significantly lower (p= 0.02 for TS). 79% of the non-progressors at Year 1 remained non-progressors in the second year (TS ≤ 0). 73% of the non-progressors during Year 2 remained non-progressors during Year 3.

Conclusion: Over 3 years abatacept provided an increasing and significant degree of inhibition of structural damage progression in the approximately two-thirds of patients who remained on treatment. This suggests that abatacept may have an increasing disease-modifying effect on structural damage over time in patients who have responded to the drug, a unique observation among biologics.

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Malignancies in the Abatacept Rheumatoid Arthritis Clinical Development Program: An Updated Epidemiological Assessment with >10,000 Person-years of Exposure

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Objective: To present the cumulative malignancy in the rheumatoid arthritis (RA) abatacept clinical trials after >10,000 person-years (p-y) of exposure.

Methods: Incidence rates (IRs) of pre-specified malignancies in the double-blind (DB) period and in the cumulative abatacept clinical development program through December 2007 were calculated. IRs of malignancies were computed using US general population (USGP) data from SEER and 41,529 RA patients ever exposed to non-biologic disease-modifying anti-rheumatic drugs (DMARDs) in 5 data sources: the British Columbia RA Cohort (Canada), Norfolk Arthritis Register (UK), National Data Bank for Rheumatic Diseases (US), Early Arthritis Register (Sweden), and General Practice Research Database (UK). Standardized incidence ratios (SIRs), adjusted for age and sex were used to compare the numbers of events in the cumulative abatacept periods with the numbers expected based on the rates in the RA cohorts and the USGP.

Results: The cumulative abatacept experience included 4,150 abatacept-treated RA patients from 8 trials representing 10,365 p-y of exposure. Observed IRs (incidence/100 p-y) during the DB period in the placebo vs. abatacept-treated patients were 0.63 : 0.59 for overall malignancies*, 0.25 : 0.06 for breast, 0 : 0 for colorectal, 0 : 0.24 for lung, and 0 : 0.06 for lymphoma. Abatacept cumulative IRs were 0.71, 0.09, 0.02, 0.16, and 0.07 for overall malignancies*, breast, colorectal, lung, and lymphoma, respectively. The ranges of SIRs for the RA cohort comparisons were 0.40-1.06, 0.25-0.81, 0.14-0.41, 0.65-1.84, and 0.60-1.23 for overall malignancies*, breast, colorectal, lung, and lymphoma, respectively. The SIRs for the USGP comparison were 0.95, 0.45, 0.27, 1.69, and 2.25 for overall malignancies*, breast, colorectal, lung, and lymphoma, respectively.

Conclusion: After >10,000 p-y of exposure in the abatacept clinical development program, the IRs of pre-specified malignancies are not greater than those observed during the DB period or those expected based on comparisons with external RA cohorts. The SIRs compared to the USGP were consistent with those reported in the literature comparing RA populations to general populations. These results reflect the lack of a safety signal.

*excluding non-melanoma skin

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Predictors of Response to Intra-Articular Steroid Injection In Psoriatic Arthritis

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Objective: To assess the effectiveness of intra-articular corticosteroid (IAS) injections in psoriatic arthritis (PsA) and to determine factors that predict clinical response.

Methods: A cohort analysis of PsA patients who were followed prospectively was performed. Only injections performed in the clinic for which there was a post-injection follow-up visit within 6 months were included. Remission was defined as no stress pain or effusion in the injected joint at the first

post-injection assessment. Relapse was defined as re-occurrence of joint pain or effusion.

Results: 220 patients with 579 IAS injections were included in the study. The probability of remission at 3 months was 40.8% and increased to 51.5% at 6 months. Of the injected joints that achieved remission, 35.3% relapsed within 12 months. On multivariate analysis factors that increased the probability of remission included duration of psoriasis (Odds Ratio (OR) 1.028 for each year with psoriasis) and the use of methotrexate or anti-Tumour Necrosis Factor agents at the time of injection (OR 2.69). Factors that increased risk of relapse included injection into large joints (OR 4.6) and elevated sedimentation rate (OR 15.0), whereas absence of clinical and/or radiographic damage (OR 0.23) and duration of PsA (OR 0.91) reduced risk of relapse.

Conclusion: IAS injections are effective in PsA and result in remission in 40.8% of the patients at 3 months. Factors associated with high inflammatory burden reduce the chance of achieving remission.

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Biologics Use in Patients with Active JIA Transitioning to Adult Clinic Improves Disability Even after Prolonged Disease Course

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Objective: To describe the effect of biologics on disability in juvenile idiopathic arthritis (JIA) patients after age 18 years

Methods: A retrospective chart review of all consecutive JIA patients transitioned to adult care between years 2006 and 2008 was performed. Data was collected on 1) demographics; 2) biologic treatment and 3) functional outcome at age < 18 years and at final follow-up, as measured by Childhood Health Assessment Questionnaire (CHAQ)/Health Assessment Questionnaire (HAQ) in patients < 18 and > 18 years, respectively. Disease activity score 28 (DAS28) in the biologic group was documented at final follow-up. DAS28 < 2.6 was defined as disease remission.

Result(s): A total of 70 JIA (48F, 22M) patients were transitioned (6 systemic, 9 rheumatoid factor (RF) positive, 20 RF negative, 6 oligoarticular, 24 enthesitis related, and 5 psoriatic JIA patients). 11 patients did not require DMARDs, and 15 (21.4%) required biologics (11F: 4M) (4 systemic, 4 RF positive, 4 RF negative, 1 enthesitis related, 1 psoriatic and 1 patient with persisting uveitis). Biologics were initiated in 10/15 patients at age ≤ 18 years and in 5/15 at age > 18 years. The mean (range) duration of treatment with biologics was 26 (4-60) months. Mean age at disease onset in the biologic group was 10 (standard deviation (SD) 5.94) years, compared to 13.2 (SD 3.45) years in the non-biologic group (p: 0.013). The mean disease duration in the biologics group was 9.2 (SD 5.00) years compared to 6 (SD 4.48) years in the non-biologic group (p:0.031). The mean CHAQ/HAQ immediately before treatment in biologic patients was 1.052 compared to 0.45 in the non-biologic group (p:0.01). At final follow-up, the mean HAQ in the biologic group was 0.297, compared to 0.089 (NS) in the non-biologic group. DAS28 was available for 11/15 biologic patients; 7/11 had DAS28 <2.6, with mean DAS28 score at 1.73 (SD 1.9). 2/15 patients were able to discontinue biologics. No serious adverse events were noted.

Conclusion(s): Despite earlier onset of disease, longer duration of disease and more disability at baseline the patients on biologics improved their disability to the level of patients on DMARDs alone. 21% of JIA patients required biologic therapy after age 18 years. Majority of these patients required ongoing biologics for disease control. One third of JIA patients treated with biologics required initiation of biologics when > 18 years of age, emphasizing the need for ongoing follow-up in this population.

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Anxiety and Depression Subselects Fibromyalgia Patients: a Cluster Analysis with Treatment Implications

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Objective: Successful management of fibromyalgia (FM) remains a challenge. Identification of parameters that could direct treatment approaches would be advantageous. We have previously identified 2 patient subgroups, without or with comorbid depression and anxiety, by hierarchical cluster analysis using the fibromyalgia impact questionnaire (FIQ), a well validated quality of life (QOL) assessment for FM. In the present study we report the validation of these subgroupings on a large population of FM patients in a tertiary care setting.

Methods: The FIQs for 132 FM patients attending a tertiary care multidisciplinary pain clinic were analysed as follows: (A) patients were assigned to the respective cluster, FM-Type I (without depression and anxiety) and FM-Type II (with depression and anxiety), using the classification coefficient previously published (Souza et al., Rheum. Int. 2008) and; (B) the cluster analysis was reapplied with this new sample. To confirm the number of clusters with this new cluster analysis (B), we analysed progressive changes in the agglomeration coefficient. Positive and negative predictive values for clustering according to mood disorder, as well as specificity and sensitivity for both models were calculated (A and B). Additional measures of pain and QOL included the McGill Pain Questionnaire (MPQ), Health Assessment Questionnaire (HAQ), Pain Catastrophizing Scale (PCS) and Pain Disability Index (PDI)

Results: Tertiary care FM patients were grouped into Type-I (n=28) and Type-II (n=104) groups with Type-II patients demonstrating higher values for pain, fatigue, stiffness, morning tiredness, anxiety, depression on the FIQ. Repeat analysis (B), identified 2 clusters dependent on mood. The intermodel analysis showed a sensitivity of 0.96, and specificity of 0.71; with positive predictive value of 0.41 and negative predictive value of 0.99. Type-I vs Type-II did not differ regarding duration of pain (p=0.90) or tender point count (p=0.11), but Type II were younger (47 vs 53 yrs p<0.01), and reported higher values for MPQ, HAQ, PCS and PDI (all p<0.01).

Conclusion: We have shown that the clustering of FM patients remained valid in a tertiary care setting, often considered to represent patients with more severe symptoms. There is therefore little doubt that different FM profiles exist, and may be identified by a single, comprehensive instrument, the FIQ. These clusters groups have implications regarding treatment approaches. Future studies should take these different patient groups into consideration in order to focus treatment interventions applicable to distinct patient groups.

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WCWL Rheumatology Priority Referral Score Testing with Rheumatologists

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Objective: Improved patient access to rheumatologists is needed due to increased rheumatology referrals but limited numbers of rheumatologists and primary care providers (PCPs). The Western Canada Waiting List project (WCWL), working with clinicians, developed the Rheumatology Priority Referral Score (PRS) to assess relative urgency of referrals. The PRS is a weighted score of 8 criteria and sublevels. This paper reports testing of the PRS with rheumatologists.

Methods: A sample of rheumatologists reviewed 16 paper-based descriptions of actual referrals. These included 3 Red Flag cases, meant to be identified for expedited referrals and not usually scored by PRS. Rheumatologists ranked the relative urgency of cases initially using clinical judgment. Following instruction on the PRS rationale, criteria and levels, they scored each of the cases. Relative ranking of urgency was compared using both methods. Testing was repeated 6 weeks later.

Results: Fourteen rheumatologists from 3 Provinces ranked cases by clinical and PRS-derived means. Six weeks later, uninformed by initial results, they ranked all cases using both methods. The average correlation between clinical ranking and the PRS was 0.71. Inter-rater reliability for the PRS was 0.80 on both occasions. Reliability coefficients for individual criteria ranged from 0.56-0.91, with the least reliable criteria being pain, complexity of

management and evidence of disease progression. Average intra-rater reliability was 0.83. The Red Flag cases were, on average, given high rankings. Initially, these three cases were correctly identified as Red Flags by 10, 12 and 14 of the evaluators respectively, and 13, 13 and 14 evaluators on retest. One case of early Rheumatoid Arthritis was not ranked consistently high and requires further scrutiny. Pilot implementation and PCP-testing is in-progress.

Conclusion: The WCWL Rheumatology PRS ranks relative urgency across the full spectrum of referrals and is not dependent on diagnosis. The PRS has face validity for rheumatologists and has acceptable reliability between raters and over time.

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Adalimumab for Psoriatic Arthritis: Improvement in Psoriasis Is Associated with Long-term Inhibition of Radiographic Progression

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Objective: The ADalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT), a 24-week, double-blind, randomized clinical trial, demonstrated that adalimumab 40 mg every other week (eow) significantly improved both arthritis and skin disease and inhibited radiographic progression in patients with psoriatic arthritis (PsA).[1] Improvement in skin disease, as measured by the Psoriasis Area and Severity Index (PASI), appeared to be associated with inhibition of radiographic progression after 24 weeks of ADA treatment.[2] Here, we further evaluate the relationship between PASI scores and radiographic progression after 144 weeks of adalimumab treatment.

Methods: PsA patients randomized to receive adalimumab in ADEPT who completed the 24-week trial could enrol in an open-label extension period and receive 40 mg eow for up to 144 weeks. Patients with ≥3% body surface area affected by psoriasis and radiographs at Week 144 (N=43) were included in this analysis. The mean changes in the modified total Sharp score (mTSS) from baseline to Week 144 were determined for patient subgroups of <PASI 50, PASI 50, PASI 75, and PASI 90 responses at Week 144. These *post-hoc* analyses were based on observed data.

Results: At Week 144, the mean changes in mTSS by PASI responses were 8.1 (<PASI 50; n=8), -0.1 (PASI 50; n=35), 0 (PASI 75; n=29), and -0.2 (PASI 90; n=20).

Conclusion: After 144 weeks of treatment, adalimumab-treated patients with PsA who had PASI 50, PASI 75, and PASI 90 responses also had inhibition of radiographic progression. In addition, patients with less than a PASI 50 response demonstrated more radiographic progression than patients with at least a PASI 50 response. These results demonstrate that patients with PsA whose psoriasis responds well to adalimumab have less radiographic progression.

1. Mease PJ, et al. *Arthritis Rheum*. 2005;52:3279-89.
2. Choy EHS, et al. *Ann Rheum Dis*. 2008;67(Suppl II):524.

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Evaluation of Response Using the Psoriatic Arthritis Joint Activity Index Scoring Tool in Patients Treated with Adalimumab: Post-hoc Analysis of the Acclaim Study

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Objective: To apply the Psoriatic Arthritis Joint Activity Index (PsAJAI) scoring tool and assess the response rate in patients (pts) with active PsA who have failed prior PsA treatment included in the ACCLAIM trial cohort and treated with adalimumab.

Methods: The ACCLAIM trial was an open-label, multicenter, Phase IIIb study conducted in Canada. Pts with active PsA and insufficient response to prior DMARD therapy received adalimumab 40 mg every other week for 12 weeks. The PsAJAI is a weighted sum measuring change from baseline in tender joint count (TJC), C-reactive protein (CRP) concentration, Physician's Global Assessment of disease activity, Pt's Global Assessment of disease activity, pt assessment of pain, and the Health Assessment Questionnaire (HAQ). A reduction of 30% or more in each contributes 1 point, with the exception of TJC, CRP, and Physician's Global Assessment of disease activity, which are assigned 2 points. The PsAJAI score ranges between 0 and 9; a score of ≥5 indicates response.

Results: Data at 12 weeks were available for all 127 pts enrolled in the study. Mean (SD) age was 49 (11), and 54.3% were male. Mean (SD) duration of PsA disease was 11 (9) years. There were 37 pts (29.1%) who reported prior exposure to biologic therapies. For all pts, the mean (SD) PsAJAI score was 6.0 (2.5), including 96 responders (PsAJAI≥5, 75.6%). Results stratified by age (<50 years [n=67]; ≥50 years [n=60]) yielded mean (SD) scores of 6.2 (2.5) and 5.8 (2.6), respectively. There were 52 (77.6%) and 44 (77.3%) responders of those <50 and ≥50 years of age, respectively. For concomitant DMARD users (n=83) vs. nonusers (n=44), the mean PsAJAI (SD) scores were 6.2 (2.6) and 5.8 (2.3), with 61 (73.5%) and 35 (79.5%) responders, respectively. Results stratified by disease duration (≤3 years vs. >3 years) yielded PsAJAI mean (SD) scores of 5.7 (2.9) vs. 6.1 (2.5), with 13/19 (68.4%) and 83/108 (76.9%) responders, respectively.

Conclusion: The PsAJAI is an easy-to-use scoring tool responsive to the effects of treatment in pts with active PsA. In this trial, 75.6% of the PsA pts treated with adalimumab for 12 weeks experienced therapeutic response as measured by the PsAJAI. We observed responses for all subgroups evaluated (age, sex, DMARD use, and disease duration).

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Prior Use of Leflunomide Increases the Hazard Ratio of Discontinuation of Infliximab in a Canadian Open Label Prospective Study with Overall Drop-out Rates Similar to Other Biologic Therapies for the Treatment of Rheumatoid Arthritis

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Objective: To assess the drop-out rate of infliximab in a real world setting and identify predictors of discontinuation.

Methods: This is an ongoing multi-centre, prospective, observational, non-interventional study conducted at Canadian sites. Patients enrolled in the study have rheumatoid arthritis (RA) and started infliximab (IFX) at the time of registration or had started IFX for a period of less than 6 months prior to baseline. Patients were treated with IFX according to the approved dosing guidelines in Canada; 3 mg/kg IV 0,2,6 weeks then q8weeks thereafter to be given with methotrexate (MTX). The dose could be increased as per the product monograph. A survival analysis was conducted in two parts: a Kaplan-Meier curve (not reported here) and a Cox regression model to identify predictors for discontinuation, with the following baseline factors: age, sex, disease duration, CRP, ESR, weight, morning stiffness, swollen joints, HAQ, physician global assessment, number of DMARDs using backward stepwise covariate selection. This is an interim analysis as 143 patients are still enrolled and continuing in the study with recruitment ongoing. Drop out rate is based on 408 patients (551-143).

Results: The results presented here are as of February 2008, for 551 recruited patients representing 785 patient-years with a mean exposure time of 1.8 years. The mean (SD) age was 57.0 (13.6) years, 418 (75.9%) were female, with a mean (SD) disease duration of 10.9 (10.3) years. The Cox regression model used to identify predictors for discontinuation showed that current use of methotrexate gave a lower hazard rate while previous use of leflunomide, current use of NSAIDS, of hydrocortisone, and a higher HAQ score gave a higher hazard rate. The drop-out rate was 36% (148/408) after 12 months. This is comparable to other biologic registries such as the RABBIT registry from Germany reporting a 35% drop-out rate after 12 months for IFX treated patients. There were 442 adverse events (AEs) reported by 171 patients

(31%). Most frequently reported AEs were headache (2.7%) and nausea (1.9%). There were 81 serious AEs reported by 51 patients.

Conclusion: This analysis demonstrates that the drop-out rate is consistent with the reported literature that approximately 1/3 anti-TNF treated patients will discontinue or switch due to primary/secondary failure or adverse events. Further this analysis establishes that prior use of leflunomide, concurrent use of NSAIDs, hydrocortisone and higher HAQ predispose patients to early withdrawal from treatment.

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Safety of Rituximab in Patients Failing with an Inadequate Response to One Anti-TNF Agent: Data from a Joint Canadian and Swedish Cohort

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Objective: To evaluate the safety of rituximab (RTX) in combination with methotrexate in patients with active rheumatoid arthritis (RA) who had a previous or current inadequate response (IR) or were intolerant to treatment with only one other anti-TNF therapy.

Methods: This open-label, multi-centre study was conducted in Canada and Sweden; results are from an interim analysis of 50 patients who had 24 weeks of follow-up. Patients with an IR to one TNF inhibitor received RTX 1000 mg on Days 1 and 15 (as per approved labeling). Primary safety endpoints were evaluated at Days 1 and 15 (RTX infusions), and at 4, 8, 12 and 24 weeks after Day 1. Adverse events (AEs) were graded by intensity according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0. Acute infusion reactions were defined as those linked to cytokine release, and occurring within 24 hours of infusion.

Results: The patients, 34 females and 16 males, had a mean age of 55.6 years and mean disease duration of 13.6 years. All received at least 2 infusions (Day 1 and Day 15). Forty-six patients (92%) experienced a total of 225 AEs, with 36% deemed drug related. The majority were mild (46%, Grade 1) to moderate (34%, Grade 2), with six patients (12%) experiencing a severe AE (Grade 3). Only 3 patients (6%) experienced a serious AE, with none reported as life threatening (Grade 4), and no patients withdrawing from the primary treatment period due to an AE. Acute infusion reactions were observed in 7 patients (14%) on Day 1, and in 8 patients (16%) on Day 15. All AEs were either Grade 1 or 2, with the exception of 1 severe headache associated with Day 1 infusion. Infection occurred in 27 patients (54%) during the 24-week observation period, the most common being nasopharyngitis (26%), urinary tract infection (UTI; 22%), and onychomycosis (15%). With the exception of one serious Grade 3 UTI, all infections were classified as mild to moderate.

Conclusion: Given the low incidence of acute infusion reactions, drug-related AEs and serious AEs, RTX was generally well tolerated in this patient population.

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Combination Therapy with Certolizumab Pegol Plus Methotrexate Maintains Long-term Efficacy in the Treatment of Rheumatoid Arthritis: A 2-year Analysis

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Background: The RAPID 1 trial showed that certolizumab pegol (CZP), a PEGylated, Fc-free TNF inhibitor, was effective in the treatment of RA when administered at 200 mg or 400 mg every 2 weeks as add-on therapy to methotrexate (MTX) in MTX-inadequate responders. A phase III, open-label extension (OLE) to RAPID 1 is ongoing and will assess the long-term safety and efficacy of SC CZP (400mg every 2 weeks+MTX). This analysis assesses whether efficacy was sustained over 2 years of exposure.

Methods: Two populations from RAPID 1 entered the OL study: patients who completed RAPID 1 through 52 weeks and patients who failed to achieve an ACR20 response at Week 12 (confirmed at Week 14) and were withdrawn from study at Week 16. In RAPID 1, 255 and 274 patients completed treatment through 52 weeks in the 200 mg and 400 mg arms, respectively. Of these, 95.3% and 96.7% re-consented and entered into the OL phase. Out of these, 87.7% and 89.4% were still in the study at the cut off date (08.31.07), with a mean drug exposure of 113.5 and 112.6 wks. An ACR efficacy analysis was carried out for completers who had been exposed to CZP + MTX for at least 2 years on 08.31.07 (n=168 and 177 for 200 mg and 400 mg, respectively). Treatment-emergent adverse events (TEAEs) were assessed at regular intervals over the 2-year period and are reported for all patients.

Results: ACR responses in patients from the CZP 200 mg + MTX and 400 mg + MTX arms were sustained through 100 weeks. At Week 100, ACR20 response rates were 77.2% and 79.0% in patients originally receiving CZP 200 mg or 400 mg plus MTX, respectively (all receiving CZP 400 mg plus MTX in the OLE). ACR50 responses were 59.9% and 54.5% and ACR70 responses were 35.9% and 35.2% at Week 100 in those originally receiving CZP 200 mg and 400 mg, respectively. Improvements in all ACR core component scores were maintained over 2 years. No additional efficacy benefit was apparent when the dose of CZP was increased. Within the patient population achieving at least 2 years of exposure, SAEs were observed in 21.1% of the patients. Four patients discontinued due to TEAEs.

Conclusion: CZP as add-on therapy to MTX provided sustained long-term benefit in improving the signs and symptoms of RA. CZP demonstrated a favourable risk/benefit profile among patients who had 2 years of study drug exposure.

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Antibodies to *Porphyromonas Gingivalis* Are Associated with Anti-citrullinated Protein Antibodies (ACPA) in RA Patients and Their Relatives

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Objective: ACPA are specific for RA and precede the onset of clinical disease. Porphyromonas gingivalis (PG), a common etiologic agent of periodontitis, has been proposed to be involved in breaking tolerance to citrullinated antigens. We studied a high risk cohort of First Nations RA patients and their first degree relatives (FDR), looking for associations between anti-PG antibodies, RA autoantibodies, predisposing HLA-DRB1 alleles, and oral and articular symptoms.

Methods: RA patients (n=82) and their relatives (n=205, 75% FDR) were evaluated with questionnaires including oral hygiene and joint symptoms and joint examination. Serum samples were tested for anti-CCP2 antibodies (IgM, IgA, IgG1-4 isotypes) by ELISA, IgM and IgA RF by nephelometry and ELISA, respectively. IgG antibodies to PG lipopolysaccharide (anti-PG) were tested by ELISA. HLA-DRB1 testing was performed by sequencing.

Results: Demographics of RA vs. FDR: age = 47 vs. 37, p<0.01; females = 90% vs. 72%, p<0.01. Autoantibodies in RA vs. FDR: ACPA (any isotype) = 91% vs. 19%; IgM RF = 82% vs.17%; IgA RF = 48% vs. 22%, all p<0.001. Of ACPA and/or RF seropositive individuals, mean autoantibodies titres were significantly higher in RA compared to FDR. Anti-PG antibodies titres were also higher in RA vs. FDR (p=0.002), and were higher in ACPA+ vs. ACPA- RA (p=0.02) and FDR (p=0.002). Anti-PG titers were similar in RF+ and RF- patients and FDR. There was no association between self-reported symptoms of poor oral hygiene and ACPA, RF, or anti-PG. ACPA+ FDR tended to see a dentist less frequently than ACPA- FDR. Hand symptoms potentially suggestive of early RA were present in 54% of FDR; there was no correlation with autoantibodies or oral hygiene symptoms. HLA-DRB1 analysis indicated that 81% and 73% of RA and FDR respectively were shared epitope (SE) positive (p=NS). FDR with 2 SE alle-

les were much more likely to have ACPA (OR 10.6, p=0.001); there was no association between SE status and anti-PG immune response.

Conclusion: In a high risk population of relatives of RA patients with a predisposing genetic background, anti-PG antibodies were associated with ACPA but not with RF or SE alleles. ACPA and immune responses to PG antigens may develop in parallel, although the role of PG in breaking tolerance to citrullinated antigens needs further study.

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Aplastic Anemia and Large-Vessel CNS Vasculitis: Report of a Novel Clinical Association

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Objective: To report a new clinical association of severe aplastic anemia with extensive medium and large vessel CNS vasculitis and to consider the treatment dilemma this case presents.

Case: A previously healthy 10 year old boy presented to the emergency room with several months of fatigue and easy bruising. On routine lab work he was found to have severe pancytopenia. Bone marrow aspiration and biopsy demonstrated marked hypocellularity without the presence of blasts, and a diagnosis of severe aplastic anemia was made. Due to mild headaches in the context of critical thrombocytopenia, a CT scan of the head was performed, which was normal. Following several weeks of investigations including negative autoantibodies, no definitive etiology was found, and treatment with anti-thymocyte globulin, corticsteroids and cyclosporin A was instituted. The patient presented to hospital shortly thereafter with headaches, ataxia and subtle left-sided weakness. MRA revealed extensive beading, stenosis and irregularity in large and medium vessels of the anterior and posterior circulation, with multiple foci of ischemia in the subcortical white matter demonstrated on MRI. Investigations to determine a unifying underling diagnosis were pursued, however clinical exam was otherwise normal, full body MRA was normal, and again autoantibodies were negative. As a result of fluctuating platelet levels conventional angiography and anticoagulation were determined to be unsafe. The neurological abnormalities found on exam resolved within days, at which point the child received 3 days of 1 g/kg of IVIG and pulse methylprednisolone (30 mg/kg iv). Repeat MRI one week later demonstrated new areas of ischemia in the bilateral occipital lobes. The patient remained asymptomatic, with normal ophthalmological exam including visual field testing. Given the high risk for stroke and development of new neurological deficits the decision was made to treat with high dose prednisone (2 mg/kg/day) and pulse IV cyclophosphamide.

Conclusion: This is the first reported case of aplastic anemia and CNS vasculitis presenting in a child without an underlying identifiable autoimmune disease. Response to treatment and further clinical characterization of this condition remain to be seen.

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Pediatric Lupus Nephritis: Impact of Ethnicity on Histological Subtype and Initial Presentation

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Objective: 1) determine the association between ethnicity and lupus nephritis (LN) subtype, 2) To compare clinical and laboratory characteristics of LN subtypes.

Methods: A single-center cohort study of all consecutive patients <18 years of age with biopsy proven LN diagnosed in 1980-2006 was performed. Self-designated ethnicity, clinical and laboratory features including renal function, urinalysis and overall activity (SLEDAI) were recorded. Associations of ethnicities, LN subtypes, clinical and laboratory variables were tested using chi-squared analysis and analysis of variance; Bonferroni and Tukey correction were used for all multiple comparisons.

Results: 150 LN patients were included in the study; 81% females, mean age 12.9 years (SD=3.1). 44 children were Caucasian, 45 Asian, 22 South Asian,

30 Black and 9 of other ethnic origin. Diffuse proliferative LN (DPGN) was seen in 38%, focal proliferative LN (FPGN) in 31%, membranous LN in 17% and mesangial LN in 14%. All ethnic groups had similar proportions of all LN subtypes. Disease activity (SLEDAI) at the time of LN diagnosis was highest in patients with DPGN. Nephrotic range proteinuria was significantly more common in DPGN than in FPGN or mesangial LN, but not membranous LN. Patients with DPGN presented more frequently in renal failure as compared to mesangial or membranous LN, but not FPGN.

Conclusion: Ethnicity does not influence the LN subtype. Renal failure is present in 1/3 of patients with DPGN and FPGN at diagnosis. Of all LN subtypes, DPGN at presentation was associated with the highest disease activity, nephrotic range proteinuria and renal failure.

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Dermatomyositis Presenting as Cryptogenic Organizing Pneumonia: a Case Report

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Objective: We describe an unusual initial presentation of Dermatomyositis (DM), an inflammatory muscle disease which typically presents as proximal muscle weakness, elevated creatine kinase (CK), & rash.

Case: A previously well 44 year old female presented to hospital with a 3 month history of fevers, hoarse voice, 10kg weight loss & arthralgias. She became increasingly hypoxic requiring mechanical ventilation with a 6 week admission to the ICU. A routine CK was normal at 45 (N<200). An open lung biopsy was performed, demonstrating Cryptogenic Organizing Pneumonia (COP). Treatment followed with daily high dose prednisone & monthly cyclophosphamide (CYC) for 6 months with good results. She required a walker for presumed deconditioning. By December 2007, CYC was discontinued & a prednisone taper was initiated. In March 2008, she presented to the hospital with dyspnea, cough & fever. She had a 4 month history of a progressive diffuse erythematous maculopapular rash which was biopsied demonstrating a superficial neutrophil rich dermatosis. She denied a history of muscle weakness, although complained of mild proximal muscle pain. Upon examination, the rash was predominantly over the metacarpophalangeal & proximal interphalangeal joints, with evidence of a heliotropic rash. Quadriceps strength was reduced to 4/5 bilaterally, with a normal CK (192). ANA & anti-Jo1 antibodies were both negative. A muscle biopsy was completed & was diagnostic for DM. The patient was restarted on both high dose prednisone & CYC with positive results. A malignancy screen was negative.

Discussion: This case demonstrates COP as the initial manifestation of DM, associated with a normal CK. Pulmonary involvement in DM is not uncommon, with nearly 50% of patients exhibiting asymptomatic pulmonary manifestations at some point in their illness; however only 10% have symptoms. COP is a rare initial presentation of DM, infrequently reported in the literature.

Conclusion: This is a unique initial manifestation of DM, presenting as COP. In the future, clinicians should consider DM in their differential diagnosis as a cause for COP.

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Better Long-term Inhibition of Radiographic Progression in Early RA with Adalimumab and Methotrexate Initial Combination Therapy: 5-Year Results of The PREMIER Trial

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Objective: Previously reported results from the PREMIER study showed that the combination of adalimumab (ADA) and methotrexate (MTX) was significantly better at inhibiting radiographic progression at 2 years (yrs) than either monotherapy in patients (pts) with early rheumatoid arthritis (RA).[1] In a long-term, open-label extension of PREMIER, we evaluated the effects of ADA,

with and without MTX, on sustained inhibition of radiographic progression through 5 yrs.

Methods: 799 pts with early RA (<3 yrs) received blinded treatment with ADA+MTX, ADA alone, or MTX alone for 2 yrs.[1] All pts who had remained on blinded therapy at Yr 2 were permitted to enrol in an open-label extension and receive monotherapy ADA 40 mg every other week. Blinded MTX/placebo were discontinued. MTX could be restarted at any time during the open-label extension at investigator's discretion. For pts who had reached 5 yrs in the study, 5-yr radiographs were evaluated by the van der Heijde modified total Sharp score (mTSS) method by 2 readers, blinded to pts and sequence. The readers also reassessed radiographs taken at baseline and 2 yrs. We assessed mean changes in mTSS based on pts' original randomization arms.

Results: 354 pts had available American College of Rheumatology responses and radiographic scores at 5 yrs of therapy (124 originally randomized to ADA+MTX; 115, to ADA monotherapy; 115, to MTX monotherapy). Pts from the original combination-therapy arm had a smaller mean change from baseline in mTSS at 5 yrs (2.9) vs. ADA alone (8.7) and MTX alone (9.7). Percentages of pts with no radiographic progression at 5 yrs were 53% of those originally randomized to ADA+MTX and 34% and 33%, respectively, of those originally randomized to ADA or MTX monotherapy.

Conclusion: For pts with early RA, initial ADA+MTX therapy for 2 yrs led to the best long-term inhibition of radiographic progression at 5 yrs. More than half of these pts had no radiographic progression at 5 yrs. Despite receiving open-label ADA for 3 yrs, pts originally randomized to MTX experienced more radiographic progression from Yrs 3 to 5 than pts in either of the other 2 groups.
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Impact of Joint Damage Inhibition on Work Performance in Patients with Early Rheumatoid Arthritis: Results from a PREMIER Companion Study

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Objective: To identify factors associated with work performance and assess whether baseline (BL) radiographic scores had an impact on work performance in patients (pts) with RA.

Methods: Study data were derived from a companion health-outcomes study to PREMIER, a 2-year, Phase III trial of adalimumab and methotrexate (MTX) in MTX-naïve pts with early RA (<3 years). Patient-reported work outcomes assessed at BL and over 2 years were missing work because of RA, degree of work performance affected by RA based on a visual analog scale (VAS-work), and change in employment status (retain/gain employment or not). Radiographic progression was based on joint space narrowing (JSN), joint erosion (JE), and total Sharp scores (TSS). Pearson's correlation analysis and logistic analysis and multivariate logistic regression were used to assess associations of work outcomes with BL radiographic scores and other BL variables.

Results: Among the 664 pts included in the analysis, change in employment status was significantly associated with BL radiographic scores (TSS OR=0.980), JSN (OR=0.954), Health Assessment Questionnaire (HAQ; OR=0.482), age (OR=0.932) (all p<0.0001), JE (OR=0.974, p<0.001), female sex (OR=0.617, p<0.01), Short Form 36 [SF-36] Physical Component Score (PCS; OR=1.031, p<0.01) and Mental Component Score (MCS OR=1.016, p<0.05), but not with Disease Activity Score 28 [DAS28] and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Missing work was associated with HAQ (OR=2.083), PCS (OR=0.950), MCS (OR=0.955), FACIT-F (OR=0.953) (all p<0.0001), and DAS28 (OR=1.326, p<0.05). VAS-work was associated with HAQ (r=0.32), PCS (r=-0.21), DAS28 (r=0.22), and FACIT-F (r=-0.20) (all p<0.0001), and MCS (r=-0.19, p<0.001). Missing work and VAS-work were not associated with BL radiographic scores. Multivariate logistic regression indicated that a 1-point change in BL TSS was associated with decreased odds of retaining/gaining employment by 1.1% and a 10-point change decreased odds by 10.4% (p<0.05).

Conclusion: Baseline joint damage in early RA is an independent predictor of a patient's ability to maintain or gain employment. Treatments that are more effective in controlling radiographic damage should be considered when treating pts with early RA.

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The Structure of Certolizumab Pegol, A Novel Design of An Anti-TNF Molecule

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Background: Certolizumab pegol (CZP) is a novel anti-tumour necrosis factor (TNF) biopharmaceutical. In this molecule, 40 kDa of polyethylene glycol (PEG) is conjugated to a specific site at the C-terminus of the heavy chain of an *E coli*-derived recombinant humanised antibody fragment (Fab') directed against TNF. The PEG is designed to increase the serum half-life of the molecule. The objective of our study was to determine the structure of CZP to better assess its pharmacokinetic properties.

Methods: Crystals of certolizumab Fab' were grown and analysed by x-ray crystallography. The structures of certolizumab Fab' and Fab'-PEG conjugates in solution were investigated by a variety of spectroscopic, analytical ultracentrifugation, small angle x-ray scattering (SAXS) and viscometric techniques.

Results: The structure of the Fab' moiety of certolizumab was determined by crystallography at 2.25 Å resolution as confirmed by orthogonal, in-solution spectroscopic techniques (circular dichroism and Fourier transform infrared spectroscopies), for the Fab'. The Fab' was found to have a typical Fab'-like structure. SAXS and analytical ultracentrifugation showed that CZP is a highly flexible, asymmetrical molecule with solution properties dictated by the PEG. The PEG is tethered to the Fab' at a specific point near the Fab' C-terminus, but does not interact directly with the surface of the Fab'. The Fab' was unaffected by any interaction, rearrangement or modification by the PEG. The PEG dictated the solution properties of CZP as reflected in the viscosity, which is significantly greater than that of molar-equivalent solutions of certolizumab Fab' (without PEG). However, even at 150 mg/mL (at 20ºC), the viscosity of certolizumab Fab'-PEG solution was 35 mPa.s, at which manual injection through a narrow-gauge hypodermic needle was feasible. Viscosity was not affected by alteration of pH or ionic strength of the solution. The PEG also acted as a protectant to the Fab' at air-liquid interfaces, inhibiting CZP aggregation there.

Conclusion: The PEG moiety of CZP has been shown to prolong circulating half-life of the certolizumab Fab' in vivo to that of an intact monoclonal antibody, while not affecting the Fab' structure but acting as a protectant under some circumstances.

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The AMBITION Study: Superiority Of Tocilizumab vs Methotrexate Monotherapy in Patients with Rheumatoid Arthritis

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Objective: The AMBITION study (**A**ctemra versus **M**ethotrexate double-**B**lind **I**nvestigative **T**rial **I**n m**ON**otherapy) compared the efficacy and safety of tocilizumab (TCZ) monotherapy, a novel anti-interleukin-6 receptor monoclonal antibody, versus methotrexate (MTX) monotherapy in patients with active rheumatoid arthritis (RA).

Methods: This international multicenter, randomized, double-blind trial included patients (n=572) with moderate to severe active RA who had not failed prior MTX or biologic therapy. Patients received either TCZ 8 mg/kg every 4 weeks, or MTX 7.5 mg/week titrated up to 20 mg/week within 8 weeks, over a 24-week period. Primary efficacy endpoint was non-inferiority of TCZ ACR20 response

at Week 24 vs MTX in the PP population (n=524). Secondary endpoints were the superiority of TCZ over MTX for other efficacy outcomes in the ITT population (n=570), provided non-inferiority was established.

Results: TCZ demonstrated non-inferiority to MTX: 70.6% of TCZ and 52.1% of MTX patients achieved an ACR20 response by Week 24 (PP population; weighted difference 0.21, 95% CI 0.13, 0.29). TCZ was superior to MTX in the ITT population, with a significantly higher proportion of TCZ patients achieving Week 24 ACR20/50/70 responses. Achieving DAS28 remission was >5 times more likely, and good/moderate EULAR response were >4 times more likely, with TCZ vs MTX in this population. Mean change in CRP level from baseline to Week 24 was -2.6 mg/dL for TCZ vs -1.9 mg/dL for MTX; 88.5% of TCZ and 31.0% of MTX patients achieved CRP normalisation (hsCRP <0.3 mg/dL). Hemoglobin levels improved in TCZ patients by Week 24 (adjusted mean change from baseline +1.2 g/dL vs +0.1 g/dL with MTX). Adverse event (AE) rates were comparable: 79.9% with TCZ and 77.5% with MTX. Patients experienced serious AEs at a rate of 3.8% with TCZ vs 2.8% with MTX, with serious infections occurring in 1.4 vs 0.7% of patients, respectively.

Conclusion: After 24 weeks of treatment, monotherapy with TCZ was superior to that of MTX for alleviating RA symptoms in patients who had not failed prior MTX or biologic therapy. TCZ was generally safe and well tolerated in these patients.

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Ocular Toxicity of Chloroquine: A Question of Screening, Progression and Prevalence

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Objective: A series of diagnoses of chloroquine (CQ) induced ocular toxicity at our institution prompted a review of the recent cases of this complication. This review illustrates a number of issues in the ongoing controversy regarding screening modalities for CQ and hydroxychloroquine (HCQ). CQ, and subsequently HCQ have been used in the treatment of inflammatory conditions including RA and SLE for over 50 years. The use of these medications, however, has been tempered by the finding that they can cause ocular toxicity which is often irreversible. A number of different guidelines exist regarding the screening of patients receiving quinolones. In review of recent cases of quinolone induced ocular toxicity at our institution, it was found that all patients had been following recommended screening with annual ophthalmologic exams, monthly Amsler grids and were on 250mg of CQ daily. Three cases will be presented:

Mrs LA, a 48 year old woman with a 26 year history of SLE had been taking CQ intermittently throughout her disease course. 5 months following a normal ophthalmologic screening exam, the patient developed visual symptoms and was found to have bilateral retinopathy. Mrs PP a 66 year old woman with seronegative rheumatoid arthritis had taken CQ for 72 months after having shown intolerance to HCQ. 6 months following a normal ophthalmologic exam, the patient developed "smokey vision" and was found to have CQ induced retinopathy. Mrs AF, a 52 year old woman with a 25 year history of SLE treated with CQ. After 49 months of treatment, the patient developed the insidious onset of visual loss and was found to have bilateral ring scotoma. The patient first developed visual symptoms 12 months after a normal ophthalmologic screening.

Discussion: There has been much controversy regarding screening for patients on quinolones. Currently ACR guidelines recommend annual ophthalmologic examinations (starting at 5 years in low risk patients and yearly in high risk patients). Despite following the recommended screening, the above patients all developed visual symptoms within 5-12 months of normal examinations. Moreover, the modalities used to screen for toxicity including self-testing grids, visual field testing, colour vision and electroretinogram all have limitations in diagnosing ocular toxicity.

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Compliance with Statin Therapy and Predictors of Compliance in Rheumatoid Arthritis (RA)

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Objective: To assess compliance with statin therapy and identify predictors of statin discontinuation in RA.

Methods: We performed a prospective study using administrative data from a previously described pop.- based cohort of RA for British Columbia (N=37,161). Cases with a 1st statin prescription between 05/1996 & 09/2005 were selected & followed until March 2006. Compliance was measured by: 1) Rate of permanent statin discontinuation (d/c) & Kaplan-Meier analysis to describe survival time on statin. 2) Adherence, evaluated with the Proportion of Days Covered (PDC) (total days supplied divided by time drug used). Good adherence was defined as PDC > 80%. Potential predictor variables, measured at the time of starting statin therapy, included: socio-demographic factors, comorbidities, meds & health services used. RA treatments over the entire RA course were also measured as markers of disease severity. Multivariable Cox Regression analysis was used to identify significant predictors of permanent d/c. HR and 95% CI for statin d/c were calculated.

Results: Sample: 5865 incident statin users with RA (61% women, mean (SD) age: 65(11) yrs). 37.5 % discontinued statins at follow-up. At 1 yr 95% remained on statins, at 5 yrs: 64%, at 10 yrs: 45%. Mean(SD) PDC was 0.79%(0.23), 63% had good adherence (PDC >80%). In multivariate Cox regression analysis, risk of statin d/c was less in people with previous MI or CVA [HR,95%CI = 0.82, 0.71-0.95], diabetes [0.86,0.75-0.98], use of ßblockers [0.79,0.71-0.88], ACEinhibitors [0.83,0.75-0.92], annual lipid test [0.62,0.58-0.67], comorbidity [0.82,0.75-0.90], who were older [0.994,.99-.99) per 1 yr inc.], who used DMARDs [0.89,0.24-0.98], or had orthopedic procedures [0.79,0.69-0.90] (markers of RA severity).Risk of d/c was greater in people who co-paid for their statin [1.26,1.03-1.53,] & with more medical visits [1.004,1.001-1.006 per visit/yr].

Conclusion: Compliance with statins in RA cohort was better than reported in the general population, but was still suboptimal. People without traditional risk factors for CVD other than RA, i.e. younger, female & without co-morbidity, and people with co-payment were at greater risk of statin d/c. This has important implications for reducing CVD in RA.

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Early Recognition of Juvenile Systemic Lupus Erythematosus (JSLE) Patients at Risk for Poor Long Term Bone Outcome

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Objective: To prospectively study bone mineral density (BMD) of JSLE patients, correlate BMD with lupus activity, treatment, bone turnover markers and identify JSLE patients at risk of poor long term bone outcome.

Methods: Prospective study of consecutive newly diagnosed JSLE patients followed between 2001 to 2008. Patients underwent Dual Energy X-Ray Absorptiometry (DEXA) within 6 months of diagnosis and serially. Demographic factors (age, gender, body mass index (BMI), ethnicity), clinical and bone turnover markers (25 OHVitamin D, PTH, AP bone isozyme) were determined at each DEXA. Definitions: 1) low BMD: Lumbar Spine (LS) BMD Z <-2.0 or femoral neck (FN) BMD <80%; 2) low/ normal: LS BMD -1< Z ≤-2.0; 3) normal: LS BMD Z ≥-1.0. Poor bone outcome was defined as either low BMD for LS or FN BMD at 3 years. Analysis: t-tests/chi-square for comparison, Pearson's correlation coefficient, logistic regression to model risk factors of poor bone outcome.

Results: A total of 52 patients was included, 7 males: 45 females; median age at diagnosis 12.0 (3.5-16.0) years, mean SLEDAI 13.9 ± 7.6 and 58% had nephritis. At diagnosis, 20% (10/52) of patients had low LS or FN BMD, 80%

(8/10) remained persistently low. Of the 9 with low/normal LS BMD at diagnosis, 44% (4/9) worsened to low BMD at 3 years. Of the 38 with normal LS BMD at diagnosis, 37% (14/38) worsened into the low/normal (13) or low (1) group. At 3 years, 27% (14/52) had low BMD. Correlations: BMD at diagnosis strongly correlated with subsequent BMD results in LS (r=0.8-0.9, p<0.001) and FN (r=0.5-0.6, p<0.001). Higher doses of prednisone associated with worse BMD at LS (r= -0.36, p= 0.0085) and FN (r=-0.31, p=0.016). Higher BMI at diagnosis could be protective against poor bone outcome (OR= 0.8, 95% CI 0.65-1.04). Disease activity and bone markers not associated with bone outcome.

Conclusion: We identified a high risk cohort for poor long term bone outcome in JSLE. Patients with low BMD at diagnosis were at highest risk. Contributory factors included low BMI and high doses of steroids. In contrast, JSLE patients with high BMI and high BMD at diagnosis appeared to be protected. At risk patients could be identified at diagnosis and additional bone protective measures should be considered to prevent poor long term bone outcome in JSLE.

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Achieving Remission in Rheumatoid Arthritis with Biologic Therapies
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Objective: The purpose of this study was to determine how many patients with rheumatoid arthritis achieve remission when treated with a biologic agent.

Methods: RA patients who started treatment with a biologic agent between 1/2007 and 7/2008 were assessed for achievement of remission by EULAR and ACR criteria. Data on these patients are stored on our biologics data base. Patients are assessed at baseline, 3 months, and then every 6 months thereafter provided they remain on the same biologic therapy. If they switch agents they begin the same assessment process for the new agent. Patient assessment included duration of am stiffness, fatigue level, physician and patient global assessment, number of tender and swollen joints, ESR, CRP, cHAQ, ACR20 and DAS28 scores.

Results: One hundred fourteen patients started the biologic of their choice during this period: 72 etanercept, 29 adalimumab and 13 infliximab. The average DAS28 improvement achieved at 3 , 9 and 15 months was 43.6%, 45.9% and 59% respectively. The same timeline improvements for individual agents were as follows: etanercept 42.5%, 47.7% and 55%; adalimumab 48.4%, 48.6% and 63%; infliximab 39.9%, 41.5%, data not available. By EULAR remission criteria 40 patients (35.1%) achieved remission. By ACR criteria however only 4 (3.5%) patients achieved remission.

Conclusion: These data show that RA patients continue to improve in their response to biologic therapies between their 3 and 15 month assessments. Renewal of prescriptions based on a 3 month assessment may deny some patients an opportunity to respond to therapy. Remission of disease is achievable by EULAR criteria but does not appear to be as easily achieved using ACR criteria. Further assessment of criteria for remission is needed.

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Childhood Cutaneous Polyarteritis Nodosa (CPAN): Impact of Streptococcus A Infections
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Objective: The aims of this study were: 1/ to characterize the clinical and laboratory features, treatment and outcome of children with cutaneous polyarteritis nodosa (CPAN); 2/ to determine the impact of concurrent Streptococcus A infection on disease manifestation and outcome.

Methods: A single-center cohort study of consecutive patients diagnosed with CPAN between 1991-2008 was performed. Standardized assessments included clinical and laboratory features, skin biopsies, treatment regimens and outcome. Cohorts of Streptococcus A positive and negative CPAN patients were compared using student's t-test for continuous data and Chi squared analysis or Fisher's exact test for categorical variables.

Results: A total of 22 patients were included in the study (mean age at diagnosis 9.2 years, mean follow-up 3.9 years). Nine children had concurrent group A Streptococcal infections. The majority of CPAN patients presented with painful subcutaneous nodules, fever, fatigue, arthritis, lymphadenopathy, pain and elevated systemic inflammatory markers. Immunosuppressive treatment consisted of NSAIDs, systemic corticosteroids plus IVIG, azathioprine, methotrexate or cyclophophamide. A third of patients were given Penicillin. At last follow-up 96% of patients were in remission, 38% of whom required an immunosuppressive medication. Flares were seen in 55% of patients. Comparison of Streptococcus related and non-Streptococcus related CPAN cohorts revealed no significant differences in clinical manifestations or outcome.

Conclusion: Children with CPAN present with painful skin nodules, constitutional symptoms and elevated inflammatory markers. Disease flares are common. However, disease control can be achieved with immunosuppressive therapy. Group A Streptococcal infections are frequently associated with CPAN but do not impact on disease outcome.

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Longitudinal Numbers-Needed-to-Treat (NNT) Analyses of Analgesic Treatments To Achieve Varying Treatment Response Levels And Stability Over Time: A Pooled Analysis of 7 Randomized Controlled Trials from the Etoricoxib Osteoarthritis Development Program
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Objective: This analysis in osteoarthritis (OA) patients evaluated the stability of NNTs over time and at different levels of response (using 15%, 30%, 50%, and 70% improvements from baseline) for individual patients and were calculated at 2, 4, 8, and 12 weeks.

Methods: This post-hoc pooled analysis included 7 OA (knee or hip) trials of etoricoxib 30 and 60 mg of 12 weeks duration, except 1 trial lasting 6 weeks. Active comparators included celecoxib 200 mg, naproxen 1000 mg, and ibuprofen 2400 mg. The outcome was WOMAC Pain Subscale (WPS, 100-mm VAS). Percent improvement from baseline in WPS at Week 2, 4, 8 and 12 (6-week trial included in Week 8 and12 analysis using its study end data) was computed for each patient. Dropouts, for any cause were assigned 0% improvement at subsequent time points. The proportion of patients achieveing 15%, 30%, 50% and 70% improvement were calculated within each treatment group and at each time point. Resulting NNTs reflect treatment effect thresholds as well as time effects.

Results: Maximal response for all treatments (lowest NNTs) was generally achieved at week 2, while stability of response (change in NNT from week 2 through week 12) varied depending on the treatment. NNTs for 30% improvement were 3.87, 3.09, 4.17, 2.91, and 4.87 (Week 2), and 4.09, 3.81, 5.43, 4.72, and 6.73 (Week 12) for etoricoxib 30 mg, etoricoxib 60 mg, celecoxib, naproxen, and ibuprofen, respectively. There was a consistent ordering of treatment efficacy at all pain relief thresholds over the 2 to 12 weeks. Using NNTs for 30% improvement for illustration, NNTs for etoricoxib 30 and etoricoxib 60 mg were among the lowest (highest efficacy) in the group with little change over time (6% and 23% change between week 2 and week 12, respectively) vs. celecoxib 200mg (30% change), naproxen (62% change), or ibuprofen (38% change). Results for other cut-off levels of improvement at all time points showed similar patterns.

Conclusion: The cut point used for efficacy assessment and its time point of measurement both influence resulting NNT. Here, etoricoxib provided the most robust NNT compared to other treatments, regardless of improvement thresholds and assessment timepoint while Ibuprofen consistently ranked as least effective (highest NNTs). Population mean change analyses blunted these differences, highlighting the complementarity of both of these approaches. Longitudinal responder analyses may be more sensitive in detecting treatment differences and may offer insight into clinical observation of perceived treatment differences.

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IL6 Correlates with Clinical Disease Activity in Patients with Rheumatoid Arthritis

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Objective: Humira, Enbrel, and Remicade are biologic agents that inhibit tumour necrosis factor-α (TNFα) signalling. Up to 60% of patients with rheumatoid arthritis (RA) do not completely respond to these agents. In search of potential biochemical predictors of response to anti-TNFα therapy, this study was an attempt to identify patterns of cytokine profiles in patients with different responses to biologic agents.

Methods: 57 RA patients (44 on anti-TNFα agents and 13 controls on disease modifying anti-rheumatic drugs (DMARDs)) were studied. Demographic and clinical data were collected and patients were assessed using five validated clinical disease activity tools (CDATs): HAQ, DAS28, DAS28-CRP, CDAI, and SDAI. Blood was collected for ESR, CRP, and cytokine analysis on the day of the clinical visit. 12 cytokines (IL2, IL4, IL6, IL8, IL10, VEGF, IFN-γ, TNF-α, IL1α, IL1ß, MCP1, and EGF) were measured by protein microarray technique. Preliminary statistical analysis was performed on 36 patients (28 on biologic agents, 8 on DMARDs) using Microsoft Excel and SAS® statistical kits.

Results: Several cytokines showed correlation with clinical disease; the correlation was strongest for patients on DMARDS. IL6 correlated with DAS-CRP (r=0.491, p=0.003), SDAI (r=0.408, p=0.02), DAS (r=0.354, r=0.03), and HAQ (r=0.352, p=0.04). DAS-CRP also correlated with IL10 (r=0.437, p=0.01) and INFγ (r=0.431, p = 0.01). We did not find significant differences in cytokine profiles between patients on biologic agents and those on DMARDs alone, although a trend was seen towards greater levels of most cytokines in patients on biologics. When patients were grouped according to EULAR classification of disease control, a non-significant trend was observed towards increased levels of IL6, IL8, IL10, TNFα, IL1α, IL1ß, and EGF with worsening disease. We also demonstrated excellent correlation of CDAI and SDAI with other CDATs (CDAI and SDAI versus DAS-CRP: r=0.96; SDAI versus DAS-ESR: r=0.92; CDAI versus DAS-ESR: r=0.91).

Conclusion: A correlation between disease activity and the levels of IL6, IL10, and INFγ points to the central role of these cytokines in rheumatoid arthritis. Anti-TNFα agents appear to weaken such correlation, perhaps by affecting the natural cytokine cascade.

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Serositis in Systemic Lupus Erythematosus: Prevalence and Associated Clinical and Serologic Features

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Objective: An estimated 1/3 of systemic lupus erythematosus (SLE) patients will have serositis during their disease course; little is known about its predictors or associated clinical features. We set out to determine the prevalence of serositis and its associated clinical and serologic variables.

Methods: Consecutive adult SLE patients seen at the University of Manitoba Arthritis Center who satisfied the American College of Rheumatology (ACR) classification criteria for SLE were assessed. Pulmonary symptoms, measures of disease activity (Systemic Lupus Erythematosus Activity Measure (SLAM)) and damage (Systemic Lupus International Collaborating Clinics damage index (SLICC)), and autoantibodies (antinuclear antibody, anti-DS DNA, anti-Sm, anti-RNP, anti-Ro, anti-La, lupus anticoagulant, and antiphospholipid antibodies) were recorded. Serositis was defined as having serositis according to the ACR criteria.

Results: There were 62 patients (59 women, 74% Caucasians) with a mean ± (SD) age of 47.4 (± 12.4) years, disease duration of 13.0 (+ 9.9) years, mean number of fulfilled ACR criteria of 5.8 ± 1.5; the mean + (SD) SLAM score and SLICC scores were 7.4 ± 3.8 and 1.0 ± 1.1 respectively. Twenty two patients out of 62 (36%) had serositis.

Clinical and serologic variables significantly associated with serositis in univariate analyses were: active dyspnea [OR= 7.0, 95% CI of 1.8-27.5, p=0.005], active wheezing [OR= 4.7, 95% CI of 1.5-15.2, p=0.009], an anti-DS DNA antibody [OR= 5.1, 95% CI of 1.6-16.6, p=0.007], an anti-Sm antibody [OR= 8.5, 95% CI of 2.0-36.4, p=0.004], an anti-RNP antibody [OR=6.2, 95% CI of 1.6-23.7, p=0.007]. In multivariate analysis controlling for dyspnea, wheezing, anti-DS DNA, and anti-RNP, SLE serositis was significantly associated with dyspnea (p=0.009), wheezing (p=0.02), anti-DS DNA antibody (p=0.01), and anti-RNP (p=0.03).

Conclusion: Serositis is common and present in > 1/3 of SLE patients in this cohort. Further, serositis is related to pulmonary symptoms and seropositivity for RNP and DS-DNA. These findings suggest that treating physicians consider the relatively common occurrence of lung disease and the association of serositis with the presence of anti-RNP and DS DNA.

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Disease Activity States Following One Year of Etanercept Treatment: Outcomes in Moderate vs Severe Rheumatoid Arthritis

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Objective: To examine clinical and radiographic responses to methotrexate (MTX), etanercept (ETN), and combination ETN and MTX in patients (pts) with moderate vs severe RA.

Methods: Data from the Trial of ETN and MTX With Radiographic Patient Outcomes (TEMPO; 3 arms) and the Early RA trial (ERA; 2 arms) were analyzed. Disease Activity Score including 28-joint count (DAS28) was used to classify patients as moderate (>3.2 and ≤5.1) or severe (>5.1) RA. Outcomes included remission (DAS28 <2.6), low disease activity (DAS28 ≤3.2), Health Assessment Questionnaire (HAQ) score, ACR scores, Total Sharp Score (TSS), absence of radiographic progression (annualized TSS change ≤0), and TSS change from baseline.

Results: Analyses included 41 and 636 pts with moderate and severe RA, respectively, from TEMPO and 65 and 349 pts, respectively, from ERA. In all treatment arms, more pts with moderate RA achieved remission than pts with severe RA. Similar results were seen in all treatment arms for low disease activity: 12 months of treatment resulted in DAS28 low disease activity in 68% and 36% of pts with moderate and severe RA, respectively, in TEMPO and 55% and 27% of pts in ERA (*P*<0.05 for each). Differences in low disease activity were significant in each group at months 6 and 12, with the exception of the ETN group in TEMPO. While ACR 20 and 50 were generally numerically greater in the severe group, ACR 70 responses were significantly greater in the moderate vs severe group in the combination arm only (65% vs 40% at 12 months; *P*<0.05). A greater percentage of pts with moderate than severe disease had HAQ ≤0.5, although not all treatment groups showed statistically significant differences. Pts with severe disease activity, while not achieving better disease states, had greater changes from baseline in DAS28 and HAQ scores. No significant differences were seen between pts with moderate vs severe disease activity in terms of radiographic outcomes, although progression of TSS changes tended to be greater for severe vs moderate pts.

Conclusion: Treatment with high-dose MTX and/or ETN resulted in greater improvements in clinical efficacy measures in pts with severe disease activity; however, pts with moderate disease were more likely to achieve better disease activity states.

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Systemic Lupus Erythematosus (SLE): A Comparative Study of Clinical Manifestations and Damage in Two Chinese Populations.

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Objective: To compare the clinical manifestations and damage accrual in Chinese SLE patients from Hong Kong (HK) and Canada (CAN).

Methods: Consecutive SLE patients (N=154) attending a university clinic in Hong Kong (HK) were enrolled between September and December 2007. These were compared to CAN SLE patients of self-reported Chinese ethnicity who had been enrolled in a multicentre observational study (N=146 of 1458). Baseline visit demographics, serology, clinical features, treatment, disease activity, and damage were compared, using the same protocol in both countries. Serology is reported as 'ever-positive'. Validated measures of disease activity and damage were used (SLAM, SLEDAI, SDI [SLICC/ACR damage index]). Cross-sectional analyses included T tests, one-way ANOVA, chi-square tests and binary logistic regression.

Results: Onset age was younger in the CAN patients (HK 30±10 years, CAN 23±13 years; <0.001), but disease duration was similar (HK12±7 years, CAN 10±8 years). HK patients were older (42±10 years, CAN 32±16 years; p<0.001). SLEDAI, SLAM and SDI scores were not different (mean SDI HK=1, CAN=1.2), with about 50% of each group recording no damage. Number of ACR diagnostic criteria met was not different, but pattern of organ involvement differed. CAN had more frequent malar rash (CAN 71% vs. HK 56%; p=0.008), arthritis (CAN 62% vs. HK 48%; p=0.019), serositis (CAN 25% vs. HK 15%; p=0.040), renal (CAN 62% vs. HK 44%; p=0.005), and neurologic (CAN 11% vs. HK 3%; p=0.011) features. HK had more frequent Raynaud's (HK 36% vs. CAN 15%; p<0.001), fever (HK 49% vs. CAN 18%; p<0.001), cutaneous vasculitis (HK 32% vs. CAN 5%, p<0.001), major vasculitis (HK 5% HK vs. CAN 0%; p=0.015), and alopecia (HK59% vs. CAN 22%). HK were more frequently anti-dsDNA+ (HK 88% vs. CAN 53%; p<0.001) anti-Ro+ (HK 78% vs. CAN 58%; p<0.001) and less frequently anti-Sm+ (HK 13% vs. CAN 35%; p<0.001). In multivariate analysis, autoantibodies did not predict organ involvement.

Conclusion: These two groups had similar disease duration, disease activity, treatment, and damage, but onset age, autoantibody profile and pattern of organ involvement differed. Both differences in genetic make-up and environmental factors may influence the expression of autoantibodies and clinical lupus manifestations in persons of Chinese origin.

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Does Baseline C-reactive Protein Reflect Disease State in Real-world Treatment of Rheumatoid Arthritis in the Optimization Trial of Humira?

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Objective: Rheumatologists do not always follow CRP results when managing patients with active RA. In addition, a non-elevated CRP is a common exclusion criterion for RCTs of new therapies. The purpose of this analysis was to determine if CRP added value above other commonly measured variables in active RA.

Methods: The data for this analysis were obtained from the Optimization of Humira study that compared the effectiveness of intensive management targeting 0 swollen joints or minimal DAS28 score to routine care in RA patients initiated on treatment with adalimumab. Association between CRP and other baseline characteristics, specifically ESR, TJC, SJC, DAS28 and patient global assessment of disease activity (PGA, 100mm VAS, with 0 = no disease activity) were assessed. CRP was classified as low (≤30 mg/L) or high (>30 mg/L) (with normal CRP <10 mg/L).

Results: A total of 300 patients enrolled in the study. Mean (SD) baseline characteristics were: age: 54.8 (13.3); SJC: 10.7 (5.6); TJC: 12.5 (7.3); DAS28: 5.8 (1.1); PGA: 63.4 (26.4); and ESR: 29.6 (20.6). Mean values (SD)

for the following parameters in low-CRP versus high-CRP groups respectively were: ESR: [25.9(16.6) vs. 48.5 (28.3), p<0.001]; SJC: [10.2 (5.7) vs. 12.0 (5.7), p=0.053]; TJC: [12.0 (7.7) vs. 13.6 (6.4), p=0.202]; PGA: [62.6 (26.7) vs. 73.4 (21.5), p=0.004]; and DAS28: [5.7 (1.2) vs. 6.5 (0.8), p<0.001]. Of the 188 patients with DAS28-ESR >5.1, 44 (23.4%) patients were in the high-CRP group, and 66 patients with ESR-DAS28 ≤5.1, 64 (97.0%) were in the low-CRP group. These results indicate poor agreement between CRP and DAS28-ESR (Kappa=0.120). CRP appears to underestimate disease activity as measured by the other parameters included in DAS28-ESR.

Conclusion: Patients in the high-CRP group had greater disease severity compared with patients in the low-CRP group. However, CRP appears to underestimate disease activity vs. DAS28-ESR.

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Regional Differences Between Patients With Rheumatoid Arthritis (RA) in Canada at Initiation of Adalimumab Treatment in Canada: Results of the Optimization of Humira Trial

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Objective: Despite global health care in Canada, access to anti-TNF therapies for RA varies by provincial formularies. We compared profiles of RA patients who received adalimumab in Ontario (ON), Quebec (QC), and other provinces (OTH). Data were obtained from the Optimization of Humira Trial, which evaluated effectiveness of intensive management (targeting SJC=0 or DAS28<2.4) vs. routine care.

Methods: RA patients received adalimumab via routine care (usual means), including private and provincial insurance. Numbers and types of DMARDs and baseline characteristics in ON, QC, and other provinces were compared.

Results: 300 patients enrolled. Mean (SD) age was 54.8 (13.3) years and 81.0% were female. Patients from each region were: ON (n=151, 50.3%), QC (n=57, 19.0%), and OTH (n=92, 30.7%). The following were compared: mean (SD) number of DMARDs [ON: 3.8 (1.4), QC: 3.1 (1.1), OTH: 3.3 (1.4), p<0.001]; SJCs [ON: 10.9 (5.9), QC: 9.0 (4.4), OTH: 11.3 (5.6), p=0.033]; TJCs [ON: 12.2 (7.5), QC: 10.3 (5.7), OTH: 14.4 (7.6), p=0.003]; ESR [ON: 31.0 (20.4), QC: 26.3 (17.1), OTH: 29.2 (23.0), p=0.333]; CRP [ON: 14.7 (17.3), QC: 23.2 (28.6), OTH: 19.8 (26.9), p=0.062]; patient's global assessment [ON: 63.9 (27.0), QC: 64.4 (22.0), OTH: 62.0 (28.1), p=0.820]; DAS28 [ON: 5.8 (1.2), QC: 5.6 (1.0), OTH: 6.0 (1.1), p=0.076]; and HAQ [ON: 1.4 (0.7), QC: 1.7 (0.7), OTH: 1.5 (0.7), p=0.060]. Significant differences between regions were observed for types of DMARDs used: gold (ON: 9.3%, QC: 0.0%, OTH: 15.2%, p=0.008); hydroxychloroquine (ON: 67.5%, QC: 86.0%, OTH: 66.3%, p=0.018); leflunomide (ON: 74.8%, QC: 21.1%, OTH: 51.1%, p<0.001); methotrexate (ON: 94.7%, QC: 93.0%, OTH: 84.8%, p=0.025); and sulfasalazine (ON: 51.0%, QC: 38.6%, OTH: 25.0%, p<0.001).

Conclusion: Regional variation was observed with respect to patient profiles. Ontario used more DMARDs, especially leflunomide, as mandated by the provincial government. Both access to care and prescribing habits of physicians may contribute to these differences. Canadian rheumatologists may vary in specific parameters used to make treatment decisions, but they generally end up with similar DAS28 scores among their patients. Provinces are more similar than dissimilar, reflecting similar thresholds for guiding care decisions.

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Patient Satisfaction with Current Treatments and Work Limitation Prior to Study Initiation: Baseline Characteristics from the Optimization of Treatment with Adalimumab (HUMIRA®) Study

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Objective: The purpose of this study was to assess the effectiveness of man-

agement of RA patients treated with adalimumab. This report presents the baseline patient satisfaction with therapy and work limitations prior to starting adalimumab.

Methods: The Humira Optimization study is an ongoing, multi-center, randomized, controlled, parallel-group, single-blind trial with 32 sites across Canada. Its goal was to enrol 300 RA patients. Participating RA patients were randomized to 1 of 3 treatment goals: 1) achieving a Disease Activity Score (DAS28) <2.4; achieving SJC=0; or usual care. All patients received adalimumab 40 mg every other week. The primary endpoint was differences in changes in DAS28 scores at 12 months for the first two groups (intensive care) vs. the third group (routine care).

Results: A total of 300 patients enrolled. Mean (SD) age was 55 (13) years and 81% were female. The most frequently reported RA medications followed by reason for discontinuing the medication because of an adverse event (AE) and lack of efficacy respectively were: methotrexate (n=274, 91.3%) (n=55, 18.3%) (n=34, 11.3%); hydroxychloroquine sulfate (n=207, 69.0%) (n=27, 9.0%) (n=54, 18.0%); and leflunomide (n=172, 57.3%) (n=66, 22.0%) (n=42, 14.0%). There were 63 (21.0%) patients who used a prior biologic therapy. The most common prior biologic therapies reported were etanercept (n=35, 11.7% of total group) and infliximab (n=22, 7.3%). The following parameters were assessed: mean (SD) number of DMARDs: 3.5 (1.4); SJC: 10.7 (5.6); TJC: 12.5 (7.3); patient's global assessment of disease activity: 63.4 (26.4); DAS28: 5.8 (1.1); erythrocyte sedimentation rate: 29.6 (20.6); C-reactive protein: 18.1 (23.4); HAQ-DI: 1.5 (0.7); WLQ Time Scale: 49.9 (28.8); WLQ Physical Scale: 40.6 (23.8); WLQ Mental Scale: 58.6 (29.1); WLQ Output Scale: 46.8 (30.3); and WLQ Productivity Loss Score: 13.4 (4.1). The majority of patients (72.3%) were dissatisfied with their current RA treatments at baseline.

Conclusion: Many DMARDs had been discontinued by these patients for AEs and lack of efficacy. Work limitations were substantial for RA patients starting anti-TNF treatment in this study. Patients also reported a substantial degree of dissatisfaction with their current RA therapies at baseline.

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The Minimally Important Difference (MID) for Patient Centred Outcomes in Ankylosing Spondylitis (AS) Including Pain, Fatigue, Sleep and Health Assessment Questionnaire (HAQ)

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Objective: Minimal Important Differences (MIDs) are important in determining clinically relevant changes and for interpretation of trials and treating patients. MIDs have been widely studied in RA, but less in Ankylosing Spondylitis (AS). The objective of this study was to determine the MID for the Health Assessment Questionnaire (HAQ) and pain, fatigue and sleep visual analogue scales (VAS) in patients with AS.

Methods: Patients with AS had to be seen for two consecutive visits within a year, and have filled out their HAQ and 100 mm VAS scores on both visits for fatigue, pain and sleep; and at the second visit complete a change in overall health (from last visit) question from much better, better, same, worse and much worse. The MIDs were the mean changes for those who were either better or worse.

Results: There were 140 patients with a spondyloarthropathy studied, 69% male, mean age 45 and disease duration 14.5 years. The MIDs for better and worse for outcomes were: HAQ (-0,136; 0.220), pain (-6.93, 18.97), fatigue (-1.43; 14.42), and sleep (-2.23; 10.76). No gender differences were observed.

Conclusion: This demonstrates that the MIDs vary depending on better vs. worse (bi-directionally different). MIDs may be smaller in clinical practice than what is observed in trials as most patients are not flaring in practice.

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Tocilizumab (TCZ) Rapidly and Significantly Improves Outcomes in Patients with Rheumatoid Arthritis (RA) Who Have Inadequate Response (IR) to TNF Antagonists

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Purpose: The **R**esearch on **A**ctemra **D**etermining eff**I**cacy after **A**nti-**T**NF failur**E**s (RADIATE) study was designed to determine the efficacy and safety of TCZ + methotrexate (MTX) in RA patients with IR to TNF antagonists.

Methods: A multicenter, randomized, double-blind study with 499 patients who had moderate to severe active RA for ≥6 months. All had experienced an IR to at least 1 TNF antagonist and had received stable-dose MTX for 12 weeks prior to baseline. Every 4 weeks, for 24 weeks, patients received MTX 10-25 mg/week plus either IV TCZ 8 mg/kg, IV TCZ 4 mg/kg, or IV placebo.

Results: All outcomes in the TCZ 8 mg/kg group were significantly better than in placebo, as were most in 4 mg/kg group seemingly with a dose response (more improvement at higher dose). Achieving an ACR20 response at Week 24 was 9 times more likely in the TCZ 8 mg/kg group, and 4 times in TCZ 4 mg/kg, than placebo (p<0.0001). A clear separation occurred in ACR20 response rates between TCZ 8 mg/kg and controls by Week 4, and in ACR50/70 responses by Week 8. Patients first achieved DAS28 remission by Week 2 (1.3% of 4 mg/kg and 1.9% of 8 mg/kg group) compared with Week 12 in the control group (0.7%). DAS28 remission rates increased over time with TCZ 8 mg/kg, reaching 30% at Week 24. Adverse events (AEs) occurred in 84.0, 87.1 and 80.6% of TCZ 8 mg/kg, TCZ 4 mg/kg and placebo, respectively. Withdrawal or need for rescue therapy occurred in 25, 34 and 60% of patients, respectively. Common AEs included diarrhea, abdominal pain, rash and dizziness. Serious AEs occurred in 6.3, 7.4 and 11.3% of TCZ 8 mg/kg, TCZ 4 mg/kg and placebo, respectively, with serious infections in 4.6, 1.8 and 3.1%, respectively. TCZ caused occasional increases in lipids requiring treatment, some cytopenias and transaminitis that were usually transient.

Conclusion: TCZ+MTX therapy was associated with rapid and significant clinical improvements, with 30% of the 8 mg/kg group achieving remission. Treatment was generally safe and well tolerated. The proportion in DAS remission (nearly one third in 8 mg/kg) was very high in TCZ compared to placebo in this difficult to treat group of inadequate responders to anti-TNFs.

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Test-Retest Reliability of Patient Global Assessment and Physician Global Assessment in Rheumatoid Arthritis

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Background/Purpose: Rheumatoid arthritis (RA) is followed by patient and physician (MD) assessments. To guide treatment, MDs use measurement tools to quantify RA activity and severity. One such tool is the Patient Global Assessment (PGA), which asks a patient to rate on a scale how they feel overall. Another is the MD Global Assessment (MDGA), which is a similar item completed by the assessing MD. These are frequently incorporated into other indices, such as the ACR Core Data Set or DAS. Other measures including HAQ, MDGA and fatigue visual Analog Scale (VAS) has not yet been thoroughly studied in RA for test-retest reliability.

Methods: This IRB approved study had 122 RA patients (diagnosis confirmed by rheumatologist) who were >17 years old. Patients who received a steroid injection or change in steroid dose at the visit were excluded (except for MDGA). Patients completed a HAQ, PGA, and VAS for pain, fatigue and sleep. After seeing their MD, another questionnaire set in random order, and a return stamped envelope; was given to be completed within 2 days at same time of day as clinic visit. This interval was chosen as it was unlikely that any medical interventions made at the visit would have had an effect. The physician completed a MDGA at the time of the patient's appointment, and again at the end of their clinic day blinded to previous MDGA. Test-retest was assessed using intraclass correlations (ICC) and Spearman's rho. Good reliability is between 0.61-0.80 and excellent >0.80.

Results: 4 rheumatologists and 146 patients; with 122 returned (response rate 83.6%) were included. Test-retest reliability was 0.702 for the PGA, 0.961 for the MDGA, 0.897 for the HAQ, 0.742 for Pain, 0.741 for fatigue, and 0.800 for sleep. The correlation between PGA and MDGA was -0.172.

Conclusion: The PGA, HAQ and pain, fatigue, and sleep VAS and MDGA show good to excellent test-retest reliability in RA. Interestingly, the MDs

were more reliable than patients. The correlation between PGA and MDGA was poor. As these measures are used clinically and in trials, it is important to have confirmed their reliability.

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Certolizumab Pegol with Methotrexate Improves Performance at Work in Patients with Active Rheumatoid Arthritis

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Background: Work disability, described in terms of increased absenteeism (absence from work) and presenteeism (reduced productivity when at work), is a common, serious problem in working-age rheumatoid arthritis (RA) patients. Certolizumab pegol (CZP) is the first PEGylated, Fc-free TNF inhibitor. The objective of this analysis was to evaluate the impact of CZP on work productivity in patients with active RA.

Methods: RAPID 1 and 2 are two double-blind, placebo-controlled clinical trials. The Work Productivity Survey (WPS-RA) is a validated questionnaire that measures RA-related work and household productivity. The WPS-RA was administered every 4 wks starting at Baseline (BL). Mean changes from BL in absenteeism, presenteeism and self-rated impact of RA on work productivity on a 0-10 point scale (0=no interference, 10=complete interference) were compared between treatment arms, using a non-parametric bootstrap-t method.

Results: 982 (RAPID 1) and 619 (RAPID 2) patients were randomized. At BL, 39.58% (RAPID 1) and 34.67% (RAPID 2) of subjects were employed outside the home. Within each trial, treatment groups were comparable at BL in terms of absenteeism, presenteeism and RA impact on work productivity. By Week 52, patients treated with CZP in RAPID 1 missed significantly fewer full days of work per month, with an average of 1.0 or 1.4 days missed by the CZP 200 mg or 400 mg groups, respectively, compared with 4.5 days in the PBO group. This improvement was already apparent by Week 4. In RAPID 1, measured as early as Week 4, patients treated with CZP + MTX reported less limitation at work due to RA, as seen by a decrease in the number of days per month with reduced productivity compared with no improvement in patients treated with PBO. Patients in the CZP group continued to improve over time and reported a decrease in the number of days with reduced productivity to 2.1 on average per month at Week 52 compared with 4.4 days in the PBO group. In RAPID 1, all these improvements were maintained for up to 1 year.

Conclusion: Certolizumab pegol improves the performance at work of subjects with active RA, as shown by the reduction in presenteeism and absenteeism and the decrease in the RA interference on their work productivity.

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The Effect of Hydroxychloroquine on the Risk of Cumulative Damage in Patients with Systemic Lupus Erythematosus

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Objective: To determine whether the use of hydroxychloroquine (HCQ) protects against the development of damage in lupus as measured by the Systemic Lupus International Collaborating Clinic (SLICC) damage index (SDI).

Methods: Data was prospectively collected according to a standard protocol in patients of the Lupus Clinic followed between 1970 and 2007. A nested, matched case-control study was conducted on inception patients (seen within one year of SLE diagnosis). All patients with SDI>0 at Year-3 (3 years after SLE diagnosis) were considered cases. Controls were patients whose SDI at Year-3 was zero matched on calendar year of diagnosis (± 3 years) and disease activity. The highest SLEDAI score was identified over the study period (3 years) for each patient and the control with the smallest difference in the highest SLEDAI score. Variables analyzed were: age, gender, ethnicity, disease activity (average mean SLEDAI or Adjusted Mean SLEDAI (AMS)), HCQ use, cumulative steroid dose and azathioprine (AZA). As AMS and steroids were highly correlated, they were never used in the same models. Statistical analysis was performed using univariate and multivariate conditional logistic regression models and Odds Ratios (OR) (95%CI) were calculated. To control for organ involvement, 103 case-control pairs who had the same organ involvement (skin or renal) were further assessed.

Results: 143 cases (118 women) with mean age of 39.2 ± 14.9 and 143 controls (126 women) with mean age of 33.5 ± 11.9 were included. Most patients were Caucasians (79.7% of cases, 77.6% of controls). In the 143 pairs, age (OR 1.03, 95% CI 1.01-1.05), steroid (1.06, 1.03-1.09) and AZA (2.21, 1.29-3.80) use were significant. HCQ was borderline (0.65, 0.37-1.13). As HCQ use may be affected by an organ involvement-treatment bias, we repeated this analysis in the 103 pairs matched for organ involvement In multivariate analysis adjusted for AMS, baseline age, HCQ and AZA were significant (1.04, 1.02-1.07; 0.21, 0.04-1.03 and 2.54, 1.21-5.35 respectively).

Conclusion: HCQ appears protective against the development of damage within 3 years of onset of SLE when attention is given to adjust for disease duration (inception), calendar year of diagnosis, disease activity, and type of organ involvement. This further supports the protective role of HCQ and has practical implications for the management of SLE.

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Coarctation of the Aorta in an Infant Exposed to Etanercept in Utero

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Objective and Methods: Etanercept is a commonly used anti-TNF inhibitor biologic agent which has proven beneficial in inflammatory rheumatoid diseases such as rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. As these inflammatory disorders commonly have disease-onset in patients in their reproductive years, it is not surprising that there are reports of the use of etanercept during pregnancy. The safety of etanercept in pregnancy is unknown as adequate literature with controlled studies are lacking. There are many reports of etanercept being used safely and effectively in pregnant women and the FDA rates etanercept as "category B" in pregnancy. However, there have been some reports of congenital defects in fetuses that have been exposed to etanercept during pregnancy. There appear to be a higher than expected number of reported VATER/VACTERL (vertebrae and anal anomalies, tracheal and esophageal problems, radius or renal defects and sometimes cardiac abnormalities and hypospadias) in fetuses exposed to etanercept during pregnancy. Congenital heart defects (CHD) occur in 1% of live born infants, and of infants born with CHD, 7% will have coarctation of the aorta (0.0007% of live born infants). We report the first case of coarctation of the aorta in an infant exposed to etanercept in utero.

Conclusion: The safety of etanercept in pregnancy is unknown. We propose that the TNF antagonists, specifically etanercept, be used with caution during pregnancy and that adverse outcomes should be reported.

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Leading Change in the Transformation of Arthritis Care through Development of an Inter-professional Academic-Clinical Education Training Model in and Academic Healthcare Facility.

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Background: The ACPAC program is a novel, competency-based, rigorously evaluated advanced clinical and academic, post-graduate, interprofessional educational program in arthritis care created in 2005 and hosted by St. Michael's Hospital and The Hospital for Sick Children, Toronto, Ontario.

Objective: The processes driving change and the risks assumed thereof, as well as a description of the successes, challenges and shortcomings of the ACPAC program as it has evolved over a three year period, are intended to be instructive to other healthcare facilities considering similar initiatives. This description is intended equally for programs considering new models of arthritis care or other fields of chronic disease management requiring competency-based training initiatives.

Methods: The inception, development, implementation and operational processes associated with the launching of this novel program are revealed in relation to the series of eight distinct stages considered essential to successful change process in a traditional business model. These transformational processes involved establishing a sense of urgency, creating a powerful guiding coalition, creating and communicating a vision, removing obstacles to the new vision and empowering others to act on the vision, systematically planning for and creating short-term wins, consolidating improvements and producing still more change, and institutionalizing new approaches to arthritis care across diverse clinical settings.

Results: The notion of developing an advanced practice practitioner (APP) program within an academic teaching facility faced implicit obstacles including a paradigm shift at the individual and group level, as well as systemic obstacles, namely physical and economic. There was an extreme sense of urgency to identify appropriate health professionals who could 1. most effectively develop new models of arthritis care in Ontario (Physical and Occupational Therapists) and 2. create a competency-based, rigorous, interprofessional and highly evaluated program that would effectively train the APPs in arthritis care. Key features of the core planning team included being connected, highly motivated, action-oriented problem solvers with a willingness to take a risk and to be leading change agents.

Conclusion: The ACPAC program is offered at a critical time in the context of rapidly changing healthcare delivery, producing highly skilled advanced practitioners across Ontario central to the development of innovative models of chronic disease management in arthritis care and optimizing human health resources. Sustainability of the ACPAC program initiative and the important template it provides for interprofessional care in chronic disease management depends on genuine collaborative go-forward efforts of effective leaders within the community, hospitals, universities and ministries of health.

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Case Report: 24-Year-Old Male With Gout Secondary to Testicular Cancer

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Objective: We report an unusual presentation of gout due to metastatic germ cell tumor of the testis.

Case: 24-year-old Caucasian male previously healthy presents with left shoulder, right hip and pain knee pain. The pain started in the right hip seven weeks prior with difficulty weight bearing and ambulating. No history of specific trauma, preceding flu-like symptoms, history of sexually transmitted diseases or recreational drug use. Returned from a 40 day trip to Thailand 12 weeks ago with s day history of non-bloody diarrhea which has resolved. Subsequently, left shoulder pain started 1-week prior and right knee pain for 24 hours. The pain has been progressively worsening, finds no relief with anti-inflammatory medications but required narcotics for pain relief with frequent visits to the Emergency Department. He also reports of decrease appetite, fatigue, and non-productive cough. Patient reported self testicular exam on monthly basis. Denied constitutional symptoms. On examination, patient was in moderate distress secondary to pain. General examination was unremarkable. Examination of the musculoskeletal system, mild effusion on the right knee with normal ROM. The right hip with decreased rotation and

left shoulder noted to have crepitus without any effusion. Radiographs of the hip and knees were unremarkable except for the effusion in the right knee and demineralization of the right hip. Aspiration of the right knee revealed lack of fluid but needle-shaped crystals were identified extra-cellularly. Patient given prednisone 40mg daily and to taper over three weeks. The symptoms improved the symptoms initially, then worsened requiring re-initiation of the prednisone. Despite this, continued to experience severe pain and was started on colchicines and narcotics.

Disease course: Eleven days later, returned to the ER as he felt like "right hip had popped" and unable to weight bear. Chest radiograph revealed a mediastinal mass and MRI of the hip enhancing lesion with avulsion fracture of the lesser trochanter. Further investigations revealed extremely elevated alpha-fetoprotein close to 50,000.Scrotal ultrasound revealed bilateral abnormal appearing testes that were heterogeneity with right larger than left. CT guided biopsy revealed a non-germ cell with surgical resection of the tumor and metastatic lesions. He received chemotherapy with bleomycin, cisplatin, and, etoposider.

Conclusion: Testicular cancer accounts for only 1% of all male malignancies. Germ cell tumors (GCTs) are a morphologically distinct group of neoplasms with varied clinical presentation and encompass 95% of tumors originating from the testes. Early detection of the tumor offers complete resolution and good survival rates of the tumor(85%).The risk factors for the development of this disease are largely unknown but a history of cryptorchidism seems to be related to the development of GCT with an associated risk of 10-40-fold. GCT is spread by the lymphatic route to the retroperitoneal lymph nodes early in the disease, with hematogenous dissemination developing later. Most common presentation is painless testicular swelling. When young patient presents with bone pain or painless swelling, even if it is an unusual site and isolated, testicular GCT should be considered as a differential diagnosis, as these lesion could be the first evidence of metastatic GCT.

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Comparison of Vertebral Radiographs, Vertebral Fracture Assessment and Lumbar Spine by Bone Densitometry of Patients for Evaluation of Osteoarthritis and Osteoporosis

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Introduction: Assessment of degenerative changes and vertebral fractures can be conducted by a variety of techniques. Currently, radiographs are the mainstay of evaluation of fractures and degenerative changes of the spine. The purpose of this study was to evaluate vertebral fractures and degenerative joint disease by vertebral fracture assessment (VFA) in comparison to radiographs.

Methods: Ninety-seven patients were evaluated by radiographs and VFA between August of 2005 and November of 2007. Majority of the subjects were female (n=88), with an average age of 60 years. Subjects were being evaluated for osteoporosis and the mean T-Score was -1.4. The radiographs of the lumbar and thoracic spine were initially evaluated by radiologists and subsequently reviewed. VFA with lumbar spinal densitometry was analyzed using the Genant quantitative method.

Results: Fractures were identified in 7 subjects by radiographs and 6 by VFA. There were a total of 15 fractures: all identified by radiographs and 10 (66%) by VFA. Vertebral fractures were detected from T8-L4 by both modalities. Detection of fractures in T5-8 was missed using the VFA method due to imaging difficulties. Total of 1232 vertebrae were assessed. Osteophytes were present in 357 vertebrae by radiographs and 288 by VFA (0.81%). Disc height narrowing was identified in 123 by radiographs and 68 by VFA (55%). VFA was comparable to radiographs for kyphosis and scoliosis.

Conclusion: VFA may play a role as a screening modality prior to that of plain radiograph in identification of vertebral fractures and degenerative joint disease of the spine. Radiographs are the gold standard in identifying spinal fractures and are an efficient modality for detection of degenerative changes. In summary, VFA is a quick, safe, and, cost-efficient study that may be used as an initial screening tool for Osteoarthritis and Osteoporosis.

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Treatment Approaches to Juvenile Dermatomyositis Across North America: The Childhood Arthritis and Rheumatology Research Alliance (CARRA): JDM Treatment Survey

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Objective: There are a number of different approaches to the initial treatment of juvenile dermatomyositis (JDM). The primary aim of this study was to assess the therapeutic approaches taken by North American pediatric rheumatologists to inform future studies of therapy in JDM.

Methods: A survey describing clinical cases of JDM was sent to pediatric rheumatologists. The cases described children with varying severities of typical disease, disease with atypical features or refractory disease. Three open-ended questions were asked following each case: (1) What additional investigations would you order? (2) What medicine(s) would you start (dose, route, frequency, adjustment over time) and (3) What non-medication treatment(s) would you start?

Results: The response rate was 84% (141/167). For typical cases of JDM, regardless of severity, almost all respondents used corticosteroids and another medication, with methotrexate (MTX) being the most commonly used. The route and pattern of corticosteroid administration was variable. Intravenous immunoglobulin (IVIG) was used more frequently for more severe disease, for refractory disease, and prominent cutaneous disease. Hydroxychloroquine was often used in milder cases and cases principally characterized by rash. Cyclophosphamide was reserved for ulcerative disease and JDM complicated by lung disease.

Conclusion: For the majority of North American pediatric rheumatologists, corticosteroids and MTX appear to be standard of care for typical cases of JDM. There is variability, however, in the route of administration of corticosteroids and use of IVIG and hydroxychloroquine.

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An Evaluation of Sleep Quality in Rheumatology Clinic Patients

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Objective: To evaluate sleep quality by utilizing the Pittsburgh global sleep quality index (PSQI) in a rheumatology clinic patient population. Secondly to compare pain, fatigue, global functioning, and modified Health Assessment Questionnaire scores in patients with and without abnormal sleep quality scores.

Methods: Consecutive Rheumatology Clinic patients were invited to participate in a self-administered questionnaire study. The questionnaire included: visual analogue scale (VAS) measures for patient perceived pain, fatigue, and global functioning, the modified Health Assessment Questionnaire (mHAQ), the SF-36 quality of life measures as well as the Berlin sleep questionnaire, the Epworth Sleepiness Score (ESS) and the PSQI. A PSQI of > 5 is considered abnormal and consistent with poor sleep quality.

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. The diagnostic categories included: RA (n = 98) 35 %, seronegative arthritis (n =79) 28.2%, osteoarthritis and crystalline arthropathies (n = 47) 16.8 %, connective tissue diseases (n = 33) 11.8 % and soft tissue musculoskeletal disorders (n = 23) 8.2%. The mean age was 52.6 years (range 18-87). 25.9% were male. A previous medical evaluation for a sleep disorder was reported by 10% of patients. Pre-existing diagnoses of sleep disorders were reported by 13 % of patients (6% with OSA, 4 % with insomnia, 2 % with RLS, and 1 % with 'other' sleep disorders). Of the 280 study participants, 262 correctly completed the PSQI. The proportion of patients in which the PSQI was abnormal (> 5) was .664 (95% CI: ± .0563). The mean PSQI was 7.98 (SD 4.12). Statistically significant

relationships were observed between the PSQI and other measurements of abnormal sleep (ESS and Berlin scores). Additionally significant associations are observed between the PSQI scores and patient reported pain, fatigue, global function, mHAQ scores, and quality of life summary measures, but not with age, marital status, gender or BMI.

Conclusion: Two thirds of all participating rheumatology clinic patients had abnormal PSQI scores, consistent with poor sleep quality. PSQI scores were significantly associated with a number of other measured variables, including worse pain, fatigue, mHAQ scores and global function.

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Does Depression Play a Role? A Comparison of Depression Scores to Sleep Quality and Other Measures in Rheumatology Clinic Patients

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Objective: To evaluate the prevalence of depressive mood symptoms utilizing the Centre for Epidemiologic Studies-Depression (CES-D) score. Secondly, to compare the depression scores in these rheumatology clinic patients with pain, fatigue, global functioning, modified Health Assessment Questionnaire (mHAQ), and sleep assessment instrument scores.

Methods: Consecutive Rheumatology Clinic patients were invited to participate in a self-administered questionnaire study. The questionnaire included visual analogue scale (VAS) measures for patient perceived pain, fatigue and global functioning, the mHAQ, Stress scores as well as the Epworth Sleepiness Score (ESS), the Pittsburgh global sleep quality index (PSQI), and the CES-D. A CES-D > 15 is considered abnormal and consistent with depression.

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. The diagnostic categories included: RA (n = 98) 35 %, seronegative arthritis (n =79) 28.2%, osteoarthritis and crystalline arthropathies (n = 47) 16.8 %, connective tissue diseases (n = 33) 11.8 % and soft tissue musculoskeletal disorders (n = 23) 8.2%. The mean age was 52.6 years (range 18-87). 25.9% were male. A previous medical evaluation for a sleep disorder was reported by 10% of patients. Pre-existing diagnoses of sleep disorders were reported by 13 % of patients (6% with OSA, 4 % with insomnia, 2 % with RLS, and 1 % with 'other' sleep disorders). The mean CES-D was 14.58 (9.99) with a median of 14.0. The mean psychosocial stress score was 6.4 (SD 2.5). The CES-D was abnormal (>15) in 41.7% of all patients. Comparison between those with and without abnormal CES-D revealed higher pain, fatigue, mHAQ, ESS, PSQI, and stress scores in those with abnormal CES-D scores. No significant differences in age or BMI were observed between groups.

Conclusion: Over 40% of all general rheumatology clinic patients had abnormal CES-D scores in this study population. Higher scores were associated with poorer global function, worse sleep quality and increased pain and fatigue.

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Does Disease Activity Influence Sleep Quality? A Comparison of RADAI and Sleep Instrument Scores in a Rheumatoid Arthritis Patient Population

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Objective: To evaluate the influence of disease activity on sleep instrument scores by comparison of RADAI scores in a Rheumatoid Arthritis (RA) patient population.

Methods: Consecutive Rheumatology Clinic patients were invited to participate in a self-administered questionnaire study. The questionnaire included visual analogue scale (VAS) measures for patient perceived pain, fatigue and global functioning, the modified Health Assessment Questionnaire (mHAQ), the Epworth Sleepiness Score (ESS), the Berlin sleep score, the Pittsburgh global sleep quality index (PSQI), diagnostic criteria for restless legs syndrome (RLS) and the Rheumatoid Arthritis Disease Activity Index (RADAI) for patients with RA.

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. Of these 84 completed the RADAI and were identified by their attending rheumatologist as having RA. The mean age was 56 years, 26% of patients were male, 74% of patients were married or cohabitating. The mean RADAI score from patients with abnormal ESS (28% of population) was 4.5 compared to 3.3 in those with ESS < 11 (p = .004). The mean RADAI score from patients with abnormal PSQI scores (66% of population) was 4.3 compared to 2.6 in those with normal PSQI scores (p < .001). In those patients identified by the Berlin score as at high risk for obstructive sleep apnea (OSA) (40% of population), the RADAI was 4.4, compared to 3.1 in the low risk group (p = .001). The RADAI was 4.3 in those meeting RLS criteria, compared to 3.5 in those who did not (p = .06). The RADAI score was significantly associated with the VAS pain, fatigue, global functioning, mHAQ, and SF-36 physical component summary scores.
Conclusion: Rheumatoid arthritis disease activity as reflected by the RADAI score was significantly higher in RA patients with abnormal ESS, abnormal PSQI scores, or high risk Berlin scores for OSA than in RA patients with normal values on these assessment measures.

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Correlates of Pain in an Inception Cohort of Children with Juvenile Idiopathic Arthritis (JIA): Research in Arthritis in Canadian Children
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Objective: Pain is a common complaint of children with JIA, but few studies have examined the correlates of pain in the early stages of disease. In this study, we examine correlations of pain with QoL and potential determinants of pain in an inception cohort of Canadian children with JIA, ReACCh.
Methods: Children with newly diagnosed JIA (≤6 mo since diagnosis) from 16 pediatric rheumatology centres in Canada were enrolled into a longitudinal outcome study, with routine data collection at 6 month intervals. Parents completed a set of quality of life (QoL) questionnaires at study entry (baseline) and 6 months. Correlations of pain (measured by a 0-10 cm visual analogue scale) with QOL scales were assessed. Variables examined as possible *determinants* of pain include: age, sex, ethnicity, socioeconomic measures, JIA subtype, and disease activity measures. Relationships between these variables and the pain score were examined, and regression analysis performed using variables showing associations at a significance of p<0.10.
Results: 321 patients (65%F) are included in this study. Median pain score at baseline was 2.4 (range 0-9.8), and at 6 months was 0.6 (range 0-10). The highest median pain at baseline was reported by patients with polyarticular rheumatoid factor + JIA (5.4), followed by enthesitis related JIA (4.2), compared with the lowest pain in systemic onset JIA (1.15). There were strong correlations between all scales of the QoL questionnaires and the pain score (Spearman correlations coefficients 0.096 to 0.63), with strongest correlations between physical functioning scales and lowest correlations with psychosocial and behavior scales.
Patient age, gender and ethnicity were not correlates of pain. There were weak correlations with parental employment or educational level. There were strong correlates between pain and disease activity measures: active joint count, number of limited joints, and parent/patient and MD global assessments Active joint count was an independent predictor of pain at baseline (p<0.0001) and 6 months (p<0.0001). Decrease in active joints and ESR at 6 months predicted decrease in pain (p=0.027 and <0.0001).
Conclusion: Pain, QoL, and parent/patient global assessment are closely related in children with early JIA. Objective measures of disease activity were the strongest predictors of pain while demographic and socioeconomic variables did not influence pain in this cohort. We postulate that pain is an important determinant of quality of life, particularly early in disease course.

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Cytokine Profiles at Diagnosis of Juvenile Idiopathic Arthritis (JIA)
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Objective: The aims of this study were to identify cytokine signatures within the JIA cohort and to test the association of cytokine signature with JIA diagnostic categories, extent of joint disease and inflammatory markers.
Methods: A prospective national multi-center cohort study of newly diagnosed JIA patients seen between January 2005 and June 2007 was performed. Patients were included if they met ILAR JIA criteria, were DMARD-, steroid-, and biologic agents-naïve and had pre-treatment blood work. Patients were allowed to receive NSAIDs and topical eye drops. Baseline characteristic including clinical, serological and cytokine data. A specific panel of 18 cytokines and chemokines were determined by multiplex assay (Luminex) and tested by K-means cluster analysis. Frequencies of clinical and laboratory variables were examined within each cluster. Associations of defined clusters with standard inflammatory markers and JIA subclasses were explored.
Results: During the study period, 192 children with new onset JIA from 5 different centers fulfilled inclusion criteria. Cluster analysis revealed 4 distinct cytokine profiles in the peripheral blood of children at diagnosis of JIA. All 4 clusters demonstrated similar concentrations of leukocyte recruitment molecules including MCP-1, MIP-1a, MIP-1b, RANTES and Fractokine. Similarly, Th2 associated cytokines such as IL-4 and IL-10 did not have any demonstrable differences between the clusters, nor did the pro-inflammatory cytokines IL-6 and IL-1a, and the osteoclastogenesis associated cytokine RANK-L. Interestingly, specific cytokines related to the Th1 (IFNg, IL-12, IL-2) and Th17 (IL-17) subset of T-lymphocytes; those involved with the final common pathway of a pro-inflammatory response (TNFa, IL-1b) and OPG — an antagonist to osteoclastogenesis and apoptosis, were clearly grouped and able to distinguish between clusters. Specifically, OPG, IL-1b, IL-2 and IL-12 (IL-12p70 and IL-12p40) was statistically significant different between clusters. Clusters did not have association with standard markers of inflammation, extent of joint disease or JIA classifications.
Conclusion: Distinct biologic fingerprints of treatment naïve JIA patients were identified. Cytokines clustered in functional classes, suggesting a corresponding biological homogeneity of these JIA patients. Standard inflammatory markers and JIA classifications did not mirror the biologic signature suggesting the need to further define the underlying pathogenic processes.

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The Use of Micronutrient Supplements among Patients with Systemic Lupus Erythematosus
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Objective: To assess the prevalence of micronutrient supplement use among patients with Systemic Lupus Erythematosus (SLE); and its potential associations with disease activity, perceived health status and health care resource utilization.
Methods: 202 patients with SLE from 4 institutions across Canada were enrolled. Disease activity was determined according to the Systemic Lupus Activity Measure (range 0-86), with scores >8 considered clinically active. Subjects were classified as micronutrient supplement users (MSU) if they took multivitamin/mineral or any single vitamin/mineral supplement at the time of enrolment. The Medical Outcomes Study 36-item Short Form (SF-36) was used to assess general, physical and mental health. Un-paired student t-test or Chi square test was used to compare MSU and non-MSU.
Results: Subject's age ranged from 9 to 68 and disease duration from 3.1-58.9 years. 54.2% of the sample was employed, 88.5% were in clinical remission and 11.5% had an active disease. Vitamin/mineral supplements were used by 56.4% of participants. Among MSU, 82.6% had post-secondary education and 37.7% were smokers. These values were 78% and 42.7% in

non-MSU respectively with no statistical significance between the two groups. Disease activity scores were similar between MSU (4.76±0.35) and non-MSU (4.95±0.367). Perceived self-rated health status was considered fair/poor in 33.6% of MSU and 25% of non-MSU (p=0.058). The general health score (scale of 1-5; 1=excellent and 5=poor) was significantly worse in MSU (3.21±0.08) than non-MSU (2.94±0.11; p =0.04). The physical (MSU: 38.5±1.12; non-MSU: 40.5±1.31) and mental (MSU: 46.0±1.07; 47.5±1.24) component score of SF-36 were similar between the two groups. MSU were more likely to visit health care professionals (85.2% of participants) than non-MSU (74.2%, p=0.048) and the use of diagnostic tests was more prevalent among MSU (80.5%) than non-MSU (59.1%; p=0.001).

Conclusion: Micronutrient supplements are frequently used by SLE patients with no clear benefit on disease activity or self-reported health status. Considering that many options are available, but with limited research demonstrating benefits in SLE, patients need to be more educated about the use/choice of nutritional supplements.

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Outcomes At 30 Months In Patients With Recent-Onset Polyarthritis (EPA): Does Stability Of Rheumatoid Arthritis (RA)-Associated Antibodies Have An Impact?

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Objective: To evaluate the outcomes at 30 months into disease associated with stability or fluctuation of RA-associated antibodies in patients with recent-onset polyarthritis (EPA).

Methods: We measured IgM-RF, anti-Cyclic Citrullinated Peptide (CCP) and anti-Sa in a cohort of 208 consecutive EPA patients at baseline and at 18 and 30 months after disease onset DAS-28, M-HAQ, and Sharp (SHS) scores were obtained at each assessment. Severity was defined as an M-HAQ score of at least 1.0 and/or belonging to the upper third of the Erosion component of the SHS.

Results: Between baseline and 30 months, RF, anti-CCP and anti-Sa remained positive in 68 (33 %) vs 70 (34%) vs 20 (10%); remained negative in 116 (56%) vs 122 (59%) vs 155 (75%); became positive (seroconversion) in 3 (1%) vs 11 (5%) vs 5 (2%); and became negative (seroreversion) in 21 (10%) vs 5 (2%) vs 28 (13%).

The initial value of DAS-28 and its variation over 30 months were not associated with stability of any antibody. Remaining positive for any antibody was associated with the worst outcomes.

Relative to Remaining RF+, seroreversion of RF was associated with a smaller Erosion score at 30 months (median 5 vs 9; p=0.008), a slower progression (median increase in Erosion 4 versus 6; p=0.041), and a lesser risk of severity (OR= 0.3; p=0.035). Seroconverting anti-CCP, relative to remaining anti-CCP negative, was associated with a higher erosion score (median 12 versus 4, p=0.012) and a higher increase in the erosion score (median 9 vs 2; p=0,002). Remaining anti-Sa negative, compared with remaining positive, was associated with better outcomes (OR for severity = 0.25; p=0.0019) and lower Erosion score (4 vs 11). Disappearance of anti-Sa was also associated with worse outcomes than remaining anti-Sa negative (OR for severity = 2.5; p=0.027 and Erosion score 8.5 vs 4).

Conclusion: Persistence of RA antibodies over 30 months is strongly associated with poorer outcomes. Anti-CCP seroconversion is associated with poor radiological outcomes. Seroreversion of anti-Sa is associated with intermediate outcomes between remaining positive and remaining negative. As disease activity was not linked with conversion and reversion of RA antibodies, additional predictors need to be defined.

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Methotrexate Drug Interactions: a Systematic Review of the Literature

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Objective: The purpose of this investigation was to determine what drugs used in combination with MTX, excluding DMARDs, folic and folinic acid, corticosteroids and biologic agents, do enhance side-effects or toxicity of MTX or lower its efficacy.

Methods: A systematic literature research with Medline, Embase, Cochrane central register of controlled trials, Cochrane database of systematic reviews and abstracts from annual congresses of American College of Rheumatology 2006-2007 and European League Against Rheumatism 2006-2007 was performed. References from retrieved papers were reviewed. Articles in English or French were selected.

Results: A total of 1172 articles were found. 1024 articles were excluded on the basis of titles and abstracts and 81 were excluded after detailed review. 21 pharmacokinetics studies, 5 observational studies and 78 case reports, representing a total of 67 papers, were included. Studies were heterogeneous. 19/21 pharmacokinetics studies evaluated non-steroidal anti-inflammatory drugs (NSAIDs). Most did not significantly affect the pharmacokinetics profile of MTX, but 4/5 (80%) studies evaluating high-dose acetylsalicylic acid (ASA) (1,3-4,5g/d) reported an increase of serum concentration of MTX. One observational study found no difference in toxicity between NSAIDs and high-dose ASA. Among the clinical studies, cytopenia and elevation of liver enzymes were the main reported toxicities. The use of trimethoprim-sulfamethoxazole (TMP-SMX) was mentioned as a risk factor for developing cytopenia in one observational study and 17 case reports. Thirty case reports of cytopenia were attributed to the use of concomitant NSAIDs, including ASA. Two studies described mild abnormalities of liver enzymes with the use of isoniazid and one study with the use of high-dose ASA.

Conclusion: Based on the published literature, MTX has limited drug interactions with the exception of TMP-SMX and NSAIDs more specifically high-dose ASA, which can exacerbate toxicity of MTX. However, the clinical significance of many of these drug interactions is not known or has not been substantiated by extensive clinical observations.

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Clinical Correlates of Health Related Quality of Life in Early Inflammatory Arthritis

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Objective: In Early Inflammatory Arthritis (EIA), there are few studies regarding Health Related Quality of Life (HRQoL). This study aimed to identify predictors of the Medical Trust Short Form 36 (SF-36) Physical Component Summary (PCS) score.

Methods: We studied patients enrolled in the McGill University Early Arthritis Registry. Patients referred to the registry are over 16 years of age, have had inflammation in at least one joint for > 6 weeks and < 1 year, and do not have any specific diagnosis other than RA or undifferentiated inflammatory arthritis. Factors influencing HRQoL, such as age, sex, race, income level, McGill Range of Motion Index score (McROMI), HAQ, DAS-28 CRP, were identified using multivariate linear regression with forced entry.

Results: There were 394 patients with EIA studied (70.6% female, 83% Caucasian, mean age 56 ± 15 years, 20% smokers, 17.8% met ACR criteria, mean tender joint count 11.70 ± 10.71, mean swollen joint count 6.43 ± 7.09, mean CRP 24.58 mmol/L ± 40.93, mean HAQ 0.84 ±0.75, mean McROMI 5.84 ±8.2, DAS-28 CRP 4.7 ±1.6, mean SF-36 PCS score 38.1 ± 9.6). Significant Predictors of HRQoL inlcuded the HAQ (p < .001), DAS 28 CRP(p<0.001), and sex (p=0.009). Oher factors, including age, race, education, smoking status, alcohol use, and corticosteroid use were not found to be significant predictors of impaired physical HRQoL. The final model explained 58.7% of the variance in the SF-36 PCS.

Conclusion: The physical component of the SF36, a measure of HRQoL, is significantly reduced in EIA. Physical function and degree of disease activity are important clinical correlates of HRQoL in EIA. Demographic features and RF positivity are not independent predictors of HRQoL. Longitudinal studies will be needed to determine how HRQoL in EIA evolves as these disease related clinical parameters change over time.

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Soluble LIGHT: a Novel Cytokine in Spondyloarthropathies

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Introduction: LIGHT (TNFSF14) is a newly identified member of the TNF superfamily. LIGHT is expressed by a number of activated immune cells and immature DCs. LIGHT has been shown to recruit TRAF2 and TRAF5 leading to release of NFκB and AP-1. We have shown previously that infliximab results in significant reduction in the gene expression of LIGHT by microarray analysis. We estimated the serum level of soluble LIGHT (sLIGHT) in patients with spondylarthritides and the effect on the same following infliximab infusion in patients with AS.

Patients and methods: Thirty-six patients and 5 normal controls were enrolled in the study. The patients had AS (N=15), IBD associated AS (16) or psoriatic arthritis (PsA; N=5). The 15 patients with AS were given infliximab and were followed up regularly with clinical parameters like BASDAI and laboratory parameters like CRP and ESR. Seven of these patients were randomly selected to be given placebo initially and observed for 14 weeks before starting infliximab. Serial samples obtained after 2 weeks were used for estimating change in sLIGHT following infliximab or placebo. Soluble LIGHT was assayed by commercial ELISA. Statistical tests used include Spearman's Rank correlation and Mann-Whitney test where applicable.

Results

• The mean (± SD) sLIGHT value for patients and normal controls were as follows; AS 243.95 (± 144.5), IBDAAS 332.47 (±155.7), PsA 430.2 (±252.4) and controls 91.62 (± 31.2). The sLIGHT level in all forms of spondylarthritides was significantly higher than normal controls. The sLIGHT level was highest in patients with PsA (not statistically different from other spondylarthritides.

• Change in clinical parameters 2 weeks after infliximab: There was significant (p=0.001) decrease in BASDAI, CRP and ESR

• sLIGHT decreased following infliximab (p=ns). There was strong correlation between the fold-change in sLIGHT and fold-change in CRP (R=0.664; p=0.007) and ESR (R=0.722; p=0.002. There was no correlation with fold-change in BASDAI.

Conclusion: sLIGHT is significantly elevated in patients with spondylarthritides compared to normal population. There is a strong correlation between changes in sLIGHT and inflammatory laboratory markers after infliximab in patients with AS.

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Long-Term Neurological Outcome of Children with Biopsy-Confirmed Small Vessel Primary CNS Vasculitis

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Objective: To report the neurological outcome of children with angiography-negative, brain biopsy-positive primary small vessel CNS vasculitis (SVcPACNS).

Methods: A prospective cohort study of children <18 years of age diagnosed with SVcPACNS between October 1998 and February of 2008 was performed. Inclusion criteria: a) diagnosis of primary CNS vasculitis according to Calabrese criteria with normal CNS angiography and positive brain biopsy, and b) treatment with standardized immunosuppressive protocol. All patients were treated with a 24-month standardized cPACNS treatment protocol of 6 months induction therapy with 7 pulses of cyclophosphamide IV and high dose corticosteroid, followed by 18 months of maintenance therapy with azathioprine or mycophenolate mofetil. Standardized outcome assessments were completed at 0, 3, 6, 9, 12, 18 and 24 months. Clinical neurological outcome was measured using the Pediatric Stroke Outcome Measure (PSOM). An overall PSOM score of normal, mild, moderate or severe deficit was calculated. Inflammatory markers, MRI imaging of the brain and neuropsychological testing were performed at regular intervals.

Results: A total of 13 SVcPACNS patients (9 F: 4 M) were included and treated with the cPACNS protocol. Median age at diagnosis was 7.1 years (5.2 - 17.1 years); mean duration of follow up was 22 months (7 - 124 months). At diagnosis: 69% (9) of patients had a severe neurological deficit as measured by PSOM, 23% (3) of patients had a moderate deficit, and 8% (1) of patients had a mild deficit. At 12 months: 42% (5) of patients had attained a normal PSOM neurological assessment, 25% (3) of patients had a mild deficit and 25% (3) had a moderate deficit, with 8% (1) of patients still having a severe deficit. At 24 months: 50% (3) of patients had a normal PSOM neurological assessment, and 50% (3) had a residual mild deficit. Residual deficits included mild sensorimotor abnormalities and difficulties with memory and concentration.

Conclusion: The neurological manifestations of SVcPACNS are devastating, with significant neurological deficits present at diagnosis. The reversibility of this inflammatory brain disease with aggressive and effective immunosuppression is evidenced by the remarkable neurological recovery the patients in this series achieved.

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Attracting Internal Medicine Trainees to Rheumatology — A Review of Canadian Data

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Objective: To determine when & on whom rheumatology program directors (PD) should focus their efforts in order to increase recruitment of rheumatology trainees (RT) from General Internal Medicine (GIM) programs in Canada.

Methods: 1) Using data from CAPER (Canadian Post-MD Education Registry), we calculated the percentage of trainees at each of the 13 English speaking Canadian GIM programs who entered a Canadian rheumatology training program from 2005 to 2007. We correlated this with the opportunity they had to do a rheumatology rotation in each of their 3 post graduate years (PGY) of GIM training. Elective opportunity information was collected from the Canadian Residency Matching Service (CaRMS) website, & weighted based on the number of elective choices available, with an assumed maximum of 10 choices. 2) Using CAPER data, we calculated the overall

percentage of residents who remained at the same training institution as their GIM program from 2005-2007. We then compared this rate to 4 similar sized subspecialty training programs.

Results: From 2005-2007, 3.5% (23/651) of GIM trainees began rheumatology training. A positive relationship existed in PGY1 between more elective opportunities & chance of entering rheumatology (p<0.05); there was no significant relationship in PGY2 or 3. 78% of RTs remained at the same GIM training institution, greater than the trainees from gastroenterology (70%-73/105), nephrology (68%-41/60), endocrinology (67%-33/49), & infectious diseases (76%-25/33).

Conclusion: The opportunity for a rheumatology rotation in the first year of GIM training increases the likelihood the trainee may choose rheumatology as a career. Further, most RTs continue at the same institution as their GIM training, which is proportionally more than other subspecialties. This information may assist rheumatology PDs in their recruitment efforts to increase RTs & the overall rheumatology workforce. Further, this data should influence GIM program directors & curriculum developers in re-evaluating their program of study in order to influence trainee career choices & plan better for future workforce requirements in all internal medicine specialties.

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Osteopenia and Osteoporosis Already Present in Newly Diagnosed Juvenile Systemic Lupus Erythematosus Patients

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Objective: To assess the effects of SLE and therapy on bone mineral density in new JSLE patients.

Methods: Prospective single center study of consecutive newly diagnosed JSLE patients, who underwent Dual Energy XRay Absorptiometry (DEXA) for study of bone mineral density (BMD) within 3 months of diagnosis. Z score for lumbar spine and mean femoral neck bone density were computed. Z score <-1 and >-2.5 indicated osteopenia and ≥ -2.5 osteoporosis. Mean femoral neck bone density <80% was considered abnormal. BMD measurements were correlated with: 1) demographics (age, body mass index (BMI), ethnicity); 2) markers of disease activity (SLEDAI, major organ system involvements, ESR, C3 and C4). Markers of bone turnover including ionized calcium (iCa), phosphate, alkaline phosphatase (ALP), bone specific ALP, Parathyroid hormone (PTH), 25 hydroxyvitamin D (25OHD) and urine N-telopeptide were also studied. Associations were assessed using t-tests, chi-square (Fisher's exact) or Pearson correlations as appropriate.

Results: 69 consecutive patients had a DEXA performed within 3 months of diagnosis (mean 44.2±34.0 days). The female to male ratio was 4:1. Median BMI was 20.5 (range 13.8-27.8). Median SLEDAI was 11.0 (0.0-32.0). Median cumulative prednisone dose to BMD was 22mg/kg; 12/69 were not on any steroids. Mean lumbar spine BMD was different from age matched norms (p=0.02) with osteopenia present in 23%, osteoporosis in 4%. 9% had low mean hip density. Lumbar spine and femoral neck bone densities were moderately correlated (r=0.57, p<0.001). Both lumbar spine BMD and femoral neck correlated with PTH: r= -0.44 and -0.51 respectively, p<0.01. There was a trend towards an association with BMI (r=0.24, p= 0.051) and iCa (r=0.35, p=0.052) in the spine. The femoral neck BMD correlated with the BMI (r=0.31, p< 0.01). There was no correlation of either site with ethnicity, cumulative dose prednisone, major organ involvement, disease activity or markers of bone turnover.

Conclusion: More than 25% of newly diagnosed JSLE patients had osteopenia and/or osteoporosis. We found an association of BMD with PTH but not vitamin D. There was a trend for associations with BMI and iCa. Disease activity, major organ manifestations or prednisone dose were not associated with osteopenia/osteoporosis.

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Pulmonary Dysfunction in Systemic Lupus Erythematosus (SLE)

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Objective: Pulmonary function test (PFT) abnormalities are common in SLE. We set out to determine the relationship of PFT abnormalities with clinical features and exercise capacity in SLE.

Methods: Consecutive SLE patients, seen at a university center, who met the ACR criteria for SLE, enrolled into the Lupus Lung Study. Clinical and serologic variables were recorded, including: self-assessed pulmonary symptoms, a Systemic Lupus Erythematosus Activity Measure (SLAM), SLICCACR damage index (SDI), and autoantibodies. Patients had PFTs and 6-minute walk tests (6-MW). Restrictive lung disease (RLD) was defined as having a forced vital capacity or total lung capacity of ≤80% predicted; an abnormal DLCO was ≤80% predicted on PFT. An abnormal 6-MW was ≤80% predicted meters walked. Patients with no physician recorded respiratory symptoms on SLAM were analyzed.

Results: Of 62 patients enrolled, 38 had no SLAM lung symptoms (35 women, 74% Caucasians) with a mean ± SD age of 48.7 ± 12.5 years, disease duration of 13.3 ± 9.6 years, number of fulfilled ACR criteria of 5.4 ± 1.3, and SLAM score of 6 ± 2.8. By self-assessment, 22 (58%) reported dyspnea, 16 (42%) had a cough, 12 (32%) had pleuritic chest pain, and 10 (26%) had wheezing. Abnormal PFT results were seen in 21 (55%) patients; 11 (29%) had RLD and 18 (47%) had an abnormal DLCO; 8 patients (24%) an abnormal 6-MW.

RLD was significantly associated with a cough (p=0.02) and serositis by ACR criteria (p=0.02) using simple logistic regression (SLR). Controlling for age, cough, serositis, disease duration, serositis [OR=12.4, 95% CI of 1.6-96.9, p=0.02] and cough [OR=10.1, 95% CI of 1.4-72.5, p=0.02] remained significantly associated with RLD. In SLR, dyspnea (p=0.005) was significantly associated with an abnormal DLCO. Controlling for dyspnea, age, and disease duration, dyspnea remained significantly associated with an abnormal DLCO [OR= 13.8, 95% CI of 2.4-78.7, p=0.003). An abnormal 6-MW was not associated with either RLD or an abnormal DLCO.

Conclusion: Abnormal PFTs and exercise capacity are common and occur in 55% and 24% of SLE patients despite no SLAM respiratory symptoms. RLD was associated with serositis and cough and an abnormal DLCO with dyspnea. PFTs should be considered in the evaluation of SLE patients, particularly in those reporting dyspnea or who have had a history of serositis.

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The Efficacy of Treatment for Systemic Sclerosis Interstitial Lung Disease: Results from a Meta-Analysis

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Objective: Scleroderma interstitial lung disease (SSc-ILD) is a significant cause of death and trials have demonstrated modest or borderline effects comparing treatment to placebo. This meta-analysis examined all randomized controlled trials (RCTs) comparing pharmacotherapy for SSc-ILD with placebo or alternative drugs on pulmonary function tests (PFTs), quality of life, dyspnea, skin thickness and adverse events.

Methods: Pubmed and Embase were searched for RCTs of SSc and lung as a primary outcome, where lung function was provided using a Cochrane search strategy.

Results: Two RCTs examining cyclophosphamide and one examining bosentan met inclusion criteria out of 40 identified studies, where trials had to be randomized, study at least 20 subjects and have PFTs as primary outcomes. Differences between groups on PFT change scores between baseline and 12 months were non-significant when the three trials were combined. The treatment effect of cyclophosphamide versus placebo on forced vital capacity (FVC) revealed a mean difference of 3.30% (95% CI 0.06, 6.54). Diffusing capacity (DLCO) and total lung capacity (TLC) did not change. This conservative yet significant effect demonstrates the need for further investigation of its effectiveness on patient-important outcomes such as dyspnea and quality of life, which could not be meta-analyzed.

Conclusion: It may be that studies in SSc-ILD need outcomes that are more

sensitive to change, the treatment effect of cyclophosphamide is weak, or the patient selection should be enriched for those who will not be stable over the treatment period.

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The Minimally Important Difference (MID) for Patient-reported Outcomes in Psoriatic Arthritis (Psa) Including Health Assessment Questionnaire (HAQ), Pain, Fatigue, Sleep, and Global VAS

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Objective: Patient-reported outcomes are often used to gauge the impact of psoriatic arthritis (PsA) in clinical trials. However, there is currently no knowledge about the minimally important difference (MID) for patient-reported outcomes in PsA. The objectives were to determine the MID for the Health Assessment Questionnaire (HAQ) and pain, fatigue, sleep and global visual analogue scales (VAS, 0-100mm) in patients with PsA using a patient-reported overall health status anchor.

Methods: Patients with a diagnosis of PsA who had answered outcomes at two consecutive visits and an overall health status question: "How would you describe your overall status since your last visit: *much better*, *better*, *the same*, *worse*, *much worse*" were included in the study. MID was calculated as the mean change between visits for those who rated their disease as 'better' or 'worse'. Scales on VAS were from 0 (best) to 100 (worst).

Results: 200 patients met inclusion criteria; 58.5% female, with a mean age of 51 and mean disease duration of 11 years. The mean baseline HAQ score was 0.732 (0.677) and follow-up HAQ was 0.711 (0.707) with a mean change of -0.0211 (0.369). Eighteen percent of patients rated their status as 'better' and 25.0% of patients rated their status as 'worse' than the previous visit. MID estimates for improvement / worsening (SD) respectively were: -0.131 (0.411)/ 0.131 (0.309) for HAQ, -9.37 (24.37)/13.96 (22.05) for pain VAS, -8.15 (23.52)/ 3.63 (27.62) for fatigue VAS, -10.97 (29.74)/ 13.81 (27.32) for sleep VAS, and -8.41 (21.17)/ 11.53 (21.03) for global VAS. Spearman's rho correlation coefficients for the patient-reported outcomes were 0.374 (HAQ), 0.448 (pain VAS), 0.239 (fatigue VAS), 0.326 (sleep VAS), 0.490 (global VAS), $p < 0.01$.

Conclusion: This is the first study investigating MID of patient-reported outcomes in PsA. The MID for the HAQ is smaller than what has been suggested in RA RCTs (0.2 to 0.22). It is likely that patients can detect even a single change on the HAQ scale (ie change on HAQ of 0.15).

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SLEDAI-2K Describing Features Over the Past 10 Days and 30 Days

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Objective: The SLEDAI (Systemic Lupus Erythematosus Activity Index) was developed in 1985 through a nominal group process and is based on the presence of 24 features in 9 organ systems over the patient's past 10 days. An updated version SLEDAI-2000 (SLEDAI-2K) was introduced and validated in 2002 again documenting findings in the past 10 days. However, both SLEDAI and SLEDAI-2K have been used in clinical studies and clinical trials documenting features over the past 30 days to make them comparable with other disease activity indices.

The objective of this study was to compare SLEDAI-2K values when features were scored first if the variables occurred within the last 10 days and then if they occurred within the last 30 days.

Methods: 131 consecutive lupus patients seen at a single centre Lupus Clinic, over 6 weeks were enrolled. A complete history, physical exam and laboratory tests were performed to allow the determination of SLEDAI-2K. The SLEDAI-2K score was completed twice, once for a 10 day window and the second for a 30-day window. Since the same values would be counted in both forms, we excluded from the analysis the SLEDAI-2K items related to laboratory investigations, including serology, urine and blood tests.

Results: Among the 131 patients, 97 had a SLEDAI-2K of 0 and 34 patients had varying levels of disease activity (12 had SLEDAI-2K of 2; 11 had 4; 2 had 6; 3 had 8; 1 had 10; 2 had 12; 1 had 14 and 2 had 16). In all but 1 patient-

there was agreement between the SLEDAI-2K 10 and 30 days. This patient experienced inflammatory skin rash at -30-21 days prior to his visit and the use of local steroid resulted in a total resolution of the findings.

Conclusion: SLEDAI-2K 30 days was validated against SLEDAI-2K 10 days, both in patients in remission and in patients with a spectrum of disease activity levels. It is extremely unusual for patients to display features of disease at -11-30 days prior to a visit and have those features totally resolved in the 10 days prior to a visit. SLEDAI-2K may now be used in clinical studies and clinical trials to describe disease activity over the previous 30 days.

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Longitudinal Study of Vascular Markers of Premature Atherosclerosis in Pediatric Systemic Lupus Erythematosus

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Objective: Patients with pediatric Systemic Lupus Erythematosus (pSLE) are at increased risk of premature atherosclerosis. The goals of this study were to determine the progression of vascular markers of premature atherosclerosis in a prospectively followed pSLE cohort and the role of treatment and disease activity related factors.

Methods: Forty-three pSLE patients (mean age: 14.0 years SD=2.8, 81% female) who were enrolled into a longitudinal study were assessed following the first follow-up visit. Drug therapy and disease activity were recorded. Fasting lipid and glycemic profiles, carotid intima-media thickness (CIMT), flow-mediated dilatation (FMD) and pulse wave velocity (PWV) were performed. Patients were then classified as improved, worsened, or no change, according to a change of ± 0.5 SD in these vascular markers.

Results: Patients at the start of the study had a mean disease duration of 2.3 yrs (SD=2.4), a mean BMI of 22.7 (SD=4.6), a median SLEDAI score of 2 (0-15) with a mean follow-up time of 1.6 years (SD=0.5). Although there was no overall significant difference in CIMT (mean change 0.01 mm SD=0.05 p=0.15), 17% of patients improved, 29% worsened, and 54% did not change. Similarly there was no overall significant difference in FMD (mean change 0.19% SD=5.0 p=0.81), 26% of patients were found to have improved, 26% worsened, and 48% did not change. Again there was no overall significant difference in PWV (mean change 0.15 m/s SD=1.0 p=0.31), 29% of patients were found to have improved, 53% worsened, and 18% did not change. When considering the time-dependent effects of disease activity and immunosuppressive drug use on vascular indices, only corticosteroid use was found to be negatively associated with CIMT at follow-up (r= -0.44 p=0.004). This association remained significant in a multiple variable model that included the baseline CIMT measure and log time (R^2=0.63, p<0.001).

Conclusion: In pSLE of relatively short duration, progression of vascular markers of premature atherosclerosis was not observed over short-term follow-up, but an increase in CIMT was found to be negatively associated with the amount of corticosteroid use. This suggests aggressive immunotherapy may reduce the atherogenic burden of chronic inflammation in pSLE and warrants further investigation.

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Severe Thrombocytopenia on Initial Presentation of Systemic Lupus Erythematosus (SLE): A Case Report

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Objective: SLE is an uncommon disease in males. Mild thrombocytopenia (TP) is a relatively common manifestation of SLE but severe TP (< 50x 10 (9)/L) is uncommon and is associated with increased disease activity and

higher mortality. We present a case of acute onset severe TP in a male patient.
Case: A 59 y.o. previously healthy male, presented with a 10 day history of flu-like symptoms including fever, chills, myalgia, arthralgia, a pruritic excoriating rash (chest) and 20 pound weight loss over 3 months. Initial blood work showed marked TP of 7x10(9)/L & normal hemoglobin (Hgb) and WBC. Renal function was normal. Peripheral blood smear showed minimal schistocytes, liver transaminases were slightly elevated and urine showed 2+ protein, 4+ Hgb & no casts. A diagnosis of post viral (mononucleosis) TP vs Thrombotic thrombocytopenic purpura was made. He was treated with intravenous methyprednisone 1 gm/day for 3 days and IVIG 1gm/kg/day for 2 days. Platelets continued to drop with a mild drop in Hgb. Rheumatology was consulted for severe TP. ANA was positive (+ve) homogenous pattern, anti ds-DNA +ve, low complements, lupus anticoagulant mildly elevated. On hemolytic work up, haptoglobin was elevated, DAT was +ve, IgG +ve, cold agglutinins and C3 were negative. Skin biopsy was consistent with SLE with lichenoid dermatitis with mucin. Immunoflourecence was negative. A diagnosis of SLE was made and he was started on Hydroxychloroquine (HCQ) and prednisone was tapered. He was discharged home; unfortunately readmitted with pericarditis and asymptomatic severe TP of 8x10(9)/L and was treated with high dose prednisone for few days and followed by a slower steroid taper and continued on HCQ.

Results: There is data to suggest severe TP is associated with more aggressive disease with multisystem involvement and higher mortality, although initial presentation with severe TP is rare.

Conclusion: This is a unique case of Lupus induced severe TP in a male, which was initially misdiagnosed as post infective. Lupus though uncommon, should be included in the differential of acute onset severe TP as it is an independent predictor of more severe disease and higher mortality.

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The Excess of Endothelial Dysfunction in SLE Is Not Explained By Framingham Cardiac Risk Factors

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Objective: 1)to test if there is an excess of endothelial dysfunction in women with systemic lupus erythematosus (SLE); and 2) to test if Framingham cardiac risk factors are associated with endothelial dysfunction in SLE.

Methods: We studied 136 women with lupus at two centers of the Health Improvement and Prevention Program (HIPP) study. Patients with prior cardiovascular disease were excluded. All patients underwent FMD (flow mediated dilatation) study using high resolution ultrasound of brachial artery, performed by a single scanner in each centre. The use of vasodilator, alcohol, and smoking was not allowed on the day of the study. The proportional change in pre/post-brachial artery obstruction by cuff pressure is a valid measure of endothelial-dependent dilatation. We defined low FMD as a percentage change of < 6%. Demographic, cardiovascular risk factors, SLE manifestations and organ involvements, and Framingham cardiac risk factors variables were collected. Student's t test and Wilcoxon test are used to compare continuous variables, Chi-square test is used to test binary variables, general and logistic regression were used to test the association between risk factors and outcomes.

Results: The average age of the 136 female patients is 44, 66% were Caucasian and 38% were postmenopausal at baseline. Average SLE duration is 14 years. Median SLEDAI total score is 4 and median SLICC total score is 1. Steroids were used by 43% and immunosuppressive drugs by 41% of patients. There were 2 % diabetic, 27% hypertensives, 78 % with family history of heart disease, 17 % with BMI above 30, and 45 % smoker. Mean total cholesterol was 4.58 (±1.35). Average (median) FMD of the patients was 9.4 (4.9, 15.6) and there were 46 patients (34%) who had low FMD. Using dichotomous FMD (low versus normal), we did not find any association with Framingham cardiac risk factors or lupus variables in univariate analyses.

Similarly, using FMD cuff change as a continuous variable, only use of anti-hypertensive medication was significant (p=0.02).

Conclusion: We observed a high prevalence of endothelial dysfunction measured by FMD in this cohort and could not explain this excess despite a high prevalence of Framingham cardiac risk factors. This suggests that SLE it self plays an important independent role in endothelial dysfunction.

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Pediatric Takayasu Arteritis: Significance of Central Nervous System Manifestations

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Objective: To determine characteristics of childhood TA at diagnosis, disease course, treatment regimens and risk factors for adverse long-term outcome.

Methods: Single-center cohort study of consecutive children diagnosed with TA from 1986 to 2008

Data: demographics, presenting clinical, laboratory, magnetic resonance (MRA)/ conventional angiography (CA) characteristics and treatment regimens. Outcome: death or persistently active TA at last follow-up.

Results: Total of 19 children with TA; 6 boys, 13 girls (ratio 1: 2.2). *Ethnicity:* 10 Caucasians (53%), 5 Blacks (26%), 2 Asians (10%), 2 Arabs (10%); median age at diagnosis 10.0 years (range 0.6-18); median follow-up 36 months (range 12-156).

Presenting features: hypertension in 11 (58%). CNS manifestations in 10 (53%), all had ≥ 2 CNS features: severe headache in 7 (37%), hypertensive seizures in 4 (21%), arterial ischemic stroke in 5 (26%). Claudication seen in 6 (32%). 8 had murmur (42%), 1 unstable angina. Constitutional features in 3 (16%); 2 (10%) had uveitis. History of TB in 3 /8 tested (37.5%).

Laboratory: ↑ESR in 10/ 15 tested (67%), anemia in 7/19 (37%), ↑IgG in 3/10 tested (30%), ↑CRP in 2/9 (22%); thrombocytosis in 4/19 (21%)

MRA/CA: *At diagnosis:* stenoses in 100% patients, additional dilations in 4(21%); vessel wall enhancement in 4 (21%). *Follow-up:* Stenoses in 100%, additional dilatations in 6 (31%), aneurysms in two (10%).

Vessels by MRA and angiography: 12 (63%) had supra and infra-diaphragmatic vasculitis; 6 (32%) had infra-diaphragmatic aortitis and 1 patient had supra-diaphragmatic vascular involvement .

Treatment: 14 children (74%) treated with corticosteroids; 13 (68%) received additional agent: MTX in 6 (31%), Cyclophosphamide in 6 (31%), Azathioprine in 5 (26%), MMF in 1; 2 patients with refractory disease received Infliximab; 8 (42%) required surgical interventions.

Remission at last follow-up in 7/19 (37%). Flares noted in 5/19 (26%), all on immunosuppression.

Outcome: 5 adverse TA outcome (26%): 2 deaths, persistent active disease in 3.

Risk factors: Non-Caucasian ethnicity, younger age at diagnosis, hypertension, extensive disease and high inflammatory markers were associated with adverse TA outcome.

Conclusion: CNS manifestations and hypertension are the leading diagnostic features of pediatric TA. Severe headache, hypertensive seizure, and/or stroke in a child should raise the suspicion for TA. Young non-Caucasian children presenting with extensive vasculitis, high inflammatory markers and hypertension had the highest risk for adverse outcome.

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Peer to Peer Mentoring: Facilitating Individuals with Early Inflammatory Arthritis to Manage their Arthritis

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Objective:
1. To review qualitative literature of the impact of peer support on improving the health and well-being of individuals with rheumatic disease
2. To conduct a needs assessment
3. To develop an intervention for feasibility testing

Methods: This study is in early stages and consists of the following three phases: 1. Qualitative Research Synthesis: Using a meta-ethnography technique, qualitative data on the processes, circumstances and contexts under which peer support interventions are effective for individuals with rheumatic disease will be synthesized. 2. Needs Assessment: Interviews and focus groups will be conducted to explore the learning needs (informational needs, educational preferences) of individuals with early and established inflammatory arthritis (IA) from the perspectives of patients, family and friends, and health care providers. Data will be analyzed using a constant comparative approach. 3. Peer Support Intervention: The literature synthesis and primary qualitative research will inform the development and evaluation of a peer support intervention for decision-making by individuals newly diagnosed with IA. A feasibility study will test the intervention using mixed (qualitative and quantitative) methods.

Results: We anticipate that by February 2009 the meta-ethnography and primary qualitative data collection will be underway. The process of how the meta-ethnography is being undertaken will be outlined and an update on the primary qualitative data collection of phase 2 will be available. We are hypothesizing that well-supported patients (informational, emotional and appraisal support) will be better able to make informed decisions and manage their disease. It is expected that early peer support will result in improved concordance with therapy, higher self efficacy, improved coping, and reduced healthcare utilization in the first two years post-diagnosis of IA.

Conclusion: Peers may be considered an instrumental part of decision support and stress management and adjunct to clinical care for arthritis.

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Study Design For The Validation Of An Early Inflammatory Arthritis Detection Tool Within Primary Care Practices In Canada

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Objective: To determine the sensitivity, specificity, positive and negative predictive value of the Early Inflammatory [EIA] Detection Tool, within primary care practices.

Methods: A prospective cohort of adult patients presenting to primary care with MSK complaints will be recruited. Inclusion criteria: At least 18 years of age, read English, self-reported MSK symptoms of 6-52 weeks duration and availability to attend a Rheumatology clinic for assessment. Exclusion criteria include: diminished capacity to provide informed consent, a medical history of an inflammatory arthritis. Patients who meet criteria and provide consent will be assigned an anonymous study number and will complete the 11 question EIA detection tool. Their primary care practitioner (PCP) will record their diagnosis on the tool and fax it to the study centre for data entry, and will refer the patient to rheumatology for assessment and confirmation of diagnosis. The rheumatologist, blinded to results of the EIA detection tool, will report the patient diagnosis to the study team via a fax-back form. Complete data on 1152 subjects will be recruited to capture 288 EIA participants, while the recruitment of 864 non-EIA study participants will result in a precise estimate of the specificity of the tool.

Results: To evaluate the optimal EIA Detection Tool score for EIA, the Se, Sp, PPV and NPV will be calculated using sequential unweighted cutoff scores. To determine the optimal cutoff point on the Detection Tool, a Receiver Operating Characteristic (ROC) curve will be plotted and used to show the relationship of probability of false positive (x-axis) to the probability of true positive (y-axis) for the Detection Tool scores of 0-11 in this study

population. The optimal EIA Detection Tool score will also be evaluated using the weights determined from the Guttman analysis.

Conclusion: Early IA classification by rheumatologists will be determined by reported diagnoses of Ankylosing Spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), rheumatoid arthritis (RA), or undifferentiated Spondyloarthropathy (SpA) or other inflammatory arthritis, including polyarthritis, seronegative arthritis, or undifferentiated inflammatory arthritis.

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Efficacy and Safety of Repeat Treatment Courses of Rituximab in RA Patients with Inadequate Response to Tumor Necrosis Factor (TNF) Inhibitors: Long-term Experience from the REFLEX Study

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Objective: To update the long-term efficacy and safety of repeated courses (C) of rituximab (RTX) therapy in patients with active RA and a previous inadequate response (IR) to TNF inhibitors.

Methods: Eligible patients were those from the original REFLEX study who had responded to an initial course of RTX and had received repeated open-label treatment courses of the same RTX regimen. Placebo patients in the original study were also eligible, and received their first course of RTX within the extension study. Efficacy was measured against the original baseline.

Results: In the REFLEX study population to date, 235 patients have received at least a third course (C3) of RTX. Efficacy data were available for 179 patients, each of whom had completed at least 24 weeks of follow-up in each treatment course. A comparison of efficacy within these patients at 24 weeks following C1, C2 and C3 showed that, by all measures, repeated treatment with RTX was effective (Table). Response rates were generally higher for the C2 and C3 compared to C1, with DAS remission rates increasing from 8.8% to 17.6% from C1 to C3. Repeated courses of RTX were generally well tolerated, with the main safety findings being infusion-related reactions, which were generally mild and required no treatment, and infections. The overall rate of serious infection was consistent with previous data (6.75 events per 100 patient-yrs; 95% CI 5.47-8.33). There were no reports of opportunistic infections or tuberculosis cases.

Conclusion: These results demonstrate that repeated courses of RTX produced sustained efficacy relative to original baseline and were generally well tolerated.

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An Evaluation of the Potential Effects of a National Consensus Statement on Optimal Treatment of Early Rheumatoid Arthritis in Ontario

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Earlier population-based assessments demonstrated that many Canadians are not provided optimal rheumatoid arthritis (RA) therapy, especially older persons with RA. In 2004, CRA convened an expert panel regarding optimal therapy in early RA (ERA).This led to a consensus statement, reinforcing the importance of early treatment, with methotrexate (MTX) as the cornerstone. The Ontario Biologics Research Initiative(OBRI)represents a collaboration of stakeholders aiming to improve RA management. One goal is to provide real-world surveillance through administrative database linkages.

Objective: We used Ontario's provincial administrative data to determine whether drug therapy for older individuals with RA has improved since the CRA consensus statement was established.

Methods: We assembled an incident RA cohort using physician billing data, limiting analyses to persons aged>65.An incident RA diagnosis was based on a standardized billing code algorithm. Cohort was stratified into 3 sub-cohorts, according to calendar year of RA diagnosis:1997-2000,2001-

2003;and 2004-2006.We followed subjects for 1 year and assessed whether a subject had been exposed to MTX(defined as U≥U2 prescriptions).We then compared the percent of ERA patients exposed to MTX over 2001-2003vs.2004-2006,calculating the difference, with 95%confidence intervals(CIs). To assess prescription trends that may have been unrelated to consensus statement, we looked for changes between 1997-2000vs.2001-2003.

Results: A significant increase in MTX use occurred over 2004-2006vs.2001-2003.Percent of ERA patients exposed to MTX in 2001-2003 was 16.8%(95%CI15.4,18.3) compared to 28.4%(26.5,30.3)in 2004-2006.This substantial increase was statistically significant(11.5%, 95%CI 9.2%,13.9%). Percent of ERA patients exposed to MTX in 1997-2000 was 9.9% (95%CI9.1,10.9), indicating a very slight increase between 1997-2000 vs. 2001-2003(6.8%,95%CI 5.2%,8.5%), even before implementation of the consensus statement.

Conclusion: Though not conclusive, our results suggest that a national consensus statement may have led to some improvements in RA care. Given slight increase in MTX use evident even prior, other factors might explain some of results. Most persons with ERA still do not receive optimal care, suggesting need for further efforts.

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Medication Exposures and Serious Infections in a Population-based Cohort of Older Individuals with Rheumatoid Arthritis (RA)

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The OBRI has commenced real world surveillance of RA therapy through administrative database linkages along with physician and patient reported data.

Objective: To assess drug exposures and risk of hospitalization for infections, using a case-control sample nested within an RA cohort.

Methods: Our RA cohort was assembled using Ontario billing and hospitalization data (1992-2007) for persons aged>65.Cohort entry criteria were an RA diagnosis based on ≥2 billing diagnoses, ≥60 days apart but within 5 years. Cohort members were further required to have ≥1 prescription for a glucocorticoid, DMARD, or biologic. Our primary outcome, assessed over 1998-2007, was a 1st-time infection, based on 'most responsible' hospital discharge diagnoses. Cases were matched (on age, sex, year of cohort entry) to RA controls using risk-set sampling. Based on the index date (date of infection for each case-control set), current drug exposures were defined using estimated duration of each prescription, plus a 50% grace period. Past exposures (in the 365 days prior to the index date), were similarly defined. Multivariate logistic regression assessed the independent effects of exposures, adjusting for demographics (age, sex, income, rurality index), co-morbidity, and markers of RA severity/activity (rheumatology visits, history of joint replacement, extra-articular features, and NSAIDs).

Results: Cohort members experienced 4,376 first-time infections requiring hospitalization. Comparing drug exposures of the cases to controls (N=9,783), the crude odds ratio, OR (for all infections requiring hospitalizations) with current anti-TNF exposure was 3.4 (95% confidence interval 1.7. 6.8) and for past exposure, 6.0 (2.5, 14.8). The respective adjusted ORs were 3.2 (0.4, 26.8) and 2.8 (0.2, 43.8). For methotrexate, the crude OR for current exposure was 1.3(1.2, 1.5) and for past exposure 1.5 (1.3, 1.8). The respective adjusted ORs were 1.0(0.8, 1.3) and 1.0 (0.7, 1.4). For cyclophosphamide, the crude OR for current exposure was 3.2 (1.1, 9.5) and for past exposure, 7.8 (2.1, 28.6). The respective adjusted ORs were 1.2 (0.1, 10.4) and1.7 (0.2, 13.3). The most precise estimate of an independent effect was for current systemic corticosteroid exposure (adjusted OR 1.5, 1.2, 1.8).

Conclusion: Our results emphasize corticosteroids as an important independent risk factor for serious infection in RA. Crude ORs suggested increased risk of infection with several other agents; however our adjusted estimates were imprecise, likely related to relatively infrequent exposure to specific agents. Ongoing prospective data collection in the context of the OBRI will provide additional insights.

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Use of Biologic Response Modifying Drugs by Ontario Rheumatology Specialists: 2008 Update

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Objective: To assess use of biologic response modifiers (BRMs) by Ontario rheumatology specialists since the introduction of these agents.

Methods: We studied prescribing patterns of the 154 rheumatology specialists in Ontario between 2001- 2007. Anonymized patient and provider data from the Ontario Health Insurance Plan Database and the Registered Persons Database were used. Data on BRM (infliximab, etanercept, anakinra, adalimumab) use and costs were obtained from the Ontario Drug Benefit Plan Database, which captures information on publicly reimbursed drugs for Ontario residents aged U ≥U65 years and social assistance recipients, and the PharmaStat Database (Brogan Inc.), which provided aggregate data on public- and privately-insured BRM expenditures. The latter database contains drug claim data for Ontario beneficiaries of 12 private drug plans, representing approximately 85% of Ontario's private drug insurance business. Quarterly PharmaStat data were used to estimate the proportions of BRM expenditures paid for by public vs. private drug insurance. We also estimated the number of Ontario rheumatology patients receiving BRMs. Analyses were conducted at the Institute for Clinical Evaluative Sciences.

Results: As expected, the number of rheumatology patients receiving publicly-funded BRMs for any arthritis indication has risen significantly over time (165 in 2001; 1793 in 2004; and 3879 in 2007). In 2007, under 40% of BRM costs were covered by the public drug plan.. We estimate that just under 10,000 Ontarians received a BRM for a rheumatic indication. This represents < 10% of the estimated number of Ontarians living with inflammatory arthritis. In 2007, approximately 2 in 3 publicly-funded BRM users were aged < 65 years. Etanercept was the most frequently prescribed BRM in this group. Information regarding the number of rheumatology patients new to BRMs was available for patients aged U≥ U65 years. Although the annual number of new (incident) users of BRMs continues to rise, the proportion new users comprise of all publicly-funded use appears to have stabilized. In 2006 and 2007, new users represented approximately one-quarter of rheumatology patients treated with BRMs.

Conclusion: There has been substantial growth in BRM use in usual rheumatology care in Ontario. This emphasizes the urgent need for systematic post-marketing surveillance of these agents. The Ontario Biologic Research Initiative represents a novel collaboration of stakeholder groups representing patients, providers, researchers, and government. Current research will further delineate BRM practice patterns, funding patterns, and the real-world effectiveness and safety of these agents.

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Effect of Denosumab vs Alendronate on Bone Turnover Markers and Bone Mineral Density Changes at 12 Months Based on Baseline Bone Turnover Level

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Objective: Denosumab, an investigational RANKL inhibitor, suppresses osteoclast-mediated bone resorption by a different mechanism than bisphosphonates. We report the effect of denosumab vs. brand alendronate (ALN) on bone turnover marker (BTM) changes over time, and BMD changes based on the baseline levels of serum C-telopeptide (sCTx) and procollagen type 1 N-propeptide (P1NP) in postmenopausal women with low BMD.

Methods: Postmenopausal women (lumbar spine or total hip T-score ≤ -2.0) were randomized 1:1 to receive subcutaneous (SC) denosumab injection (60 mg, every 6 months [Q6M]) + oral placebo weekly or oral ALN (70 mg) weekly + SC placebo injection Q6M. All received calcium and vitamin D. BTM changes from baseline were assessed over 12 months. BMD gains at the total hip, lumbar spine, femoral neck, and radius at month 12 were compared across quartiles of baseline sCTX.

Results: Subjects (N = 1189; 594 denosumab; 595 ALN; mean age 64 yrs) had a mean lumbar spine T-score of -2.6. With denosumab sCTx decreased by a median of 89%, 77%, and 74% vs. 61%, 73%, and 76% with ALN at month 1, 6, and 12, respectively ($P ≤ 0.0001$ month 1 and 6; $P = 0.5$ month 12). Median P1NP decreases at these times were: 26%, 72%, and 72% for denosumab vs. 11%, 62%, and 65% for ALN ($P < 0.0001$ all times). As reported earlier, denosumab resulted in significantly greater gains in BMD vs. ALN ($P ≤ 0.0003$ all sites). BMD increases at the total hip were greater for subjects in both groups with higher baseline bone turnover (i.e. sCTx ≥0.836 ng/mL); BMD gains were significantly greater for denosumab vs. ALN regardless of baseline bone turnover. Results were similar for BMD gains at the lumbar spine, femoral neck, and radius. Adverse events were similar for each group.

Conclusion: Denosumab suppressed bone remodeling and increased BMD at all measured sites more than ALN. BMD gains were consistent across different levels of baseline bone turnover. The differences in results between these drugs may be due to their different mechanism of inhibiting bone turnover.

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Successful Clinical Outcomes in Canadian Early Inflammatory Arthritis Patients: Data from the CATCH Study

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Objective: To provide a preliminary analysis of clinical outcomes in Canadian patients with early inflammatory arthritis (EIA) who have been recruited to the Canadian Early Arthritis Cohort (CATCH) study.

Methods: Data were collected from CATCH, a multi-centre observational prospective "real world" cohort of patients with early inflammatory arthritis (EIA). Patients included are >16 years old with a symptom duration of 6 to 52 weeks of persistent synovitis, have ≥2 effused joints or 1 swollen MCP or PIP + >1 of: positive RF, positive anti-CCP, morning stiffness >45 minutes, response to NSAIDs, or a painful MTP squeeze test. Patients were treated with initial DMARD therapy, usually consisting of medications approved by provincial formularies, including methotrexate ± hydroxychloroquine ± sulfasalazine. Patients were evaluated according to a standardized protocol at baseline and every 3 months. Therapy was adjusted targeting for remission. Patient reported outcomes, tender and swollen joint counts, and routine laboratory measures were collected at each routine visit.

Results: Baseline characteristics were: mean age (years) ± SD 51.6±16, 75% female, 83% Caucasian, 26% college educated, 53% employed, 57% smoking/ex-smoker, 46% RF positive, 68% RA (ACR criteria), mean symptom duration (days) 189 ±170. Baseline parameters of disease activity (means ± SD) were: TJC(28) 10±7, SJC(28) 8±6, ESR 27±20, CRP 18±29, DAS28 ESR 4.0±1.82, HAQ-DI 1.0±0.5. In patients with ≥ 6 months follow up joint counts and DAS28 scores (as means ± SDs) were: baseline (n=344) TJC(28) 9.8±7.2, SJC(28) 8.1±6.4, DAS28 4.0±1.8, and DAS28 CRP 4.9±1.5; 6 months (n=197) TJC(28) 4.8±5.8, SJC(28) 3.7±4.5, DAS28 2.9±1.7, and DAS28 CRP 3.5±1.7; 12 months (n=113) TJC(28) 3.3±4.4, SJC(28) 2.5±3.8, DAS28 2.8±1.8, and DAS28 CRP 2.8±1.4. The proportion (%) of patients in high, moderate, low and remission DAS28 states at baseline (n=344) were: 29.0, 34.0, 12.2, 24.7; at 6 months (n=197) were: 12.7, 25.9, 15.2, 46.2; at 12 months (n=113) were: 9.7, 26.6, 8.8, 54.0.

Conclusion: With early implementation of DMARDs ± oral or parenteral glucocorticoids, high levels of remission were rapidly achieved in CATCH patients with EIA. Further studies will attempt to identify early predictors of good and poor patient outcomes.

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Hepatic Aminotransferases and Bilirubin Levels During Tocilizumab Treatment of Patients with Rheumatoid Arthritis: Pooled Analysis of Five Phase 3 Clinical Trials

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Objective: In five phase 3 clinical trials, the IL-6 receptor inhibitor tocilizumab (TCZ) significantly improved signs and symptoms of moderate-to-severe RA, and was well tolerated. This pooled analysis evaluated trial levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin.

Methods: Five randomized, double-blind, placebo-controlled, international, 24-week trials included patients with RA who received IV infusions of TCZ 4 mg/kg, TCZ 8 mg/kg, or placebo (control) every 4 weeks, in combination with DMARDs (OPTION, TOWARD, RADIATE, and LITHE), or who received TCZ 8 mg/kg or methotrexate (MTX; control) monotherapy (AMBITION). An exploratory post-hoc analysis of liver enzyme levels was performed at Week 2, and then every 4 weeks for 24 weeks.

Results: Shifts in ALT and AST from normal at baseline to >upper limit of normal (ULN) during treatment occurred more frequently with TCZ+DMARD vs control, and at similar rates with TCZ monotherapy vs MTX (table). Amongst patients with elevations 1-3xULN in ALT and AST, this was a single occurrence in 33.3% and 45.6% of TCZ-treated patients, respectively, compared with 40.7% and 56.7% of MTX-only patients. Dose modification was not required to achieve ≤ULN in the majority of these patients. Few TCZ+DMARD and TCZ patients had more than one elevation >3xULN in ALT (2.1% and 0.4%) or AST (0.4% and 0%), and none were sustained. Hepatic transferase elevations were not associated with clinically relevant increases in total bilirubin, as changes in total bilirubin were driven by indirect bilirubin.

Conclusion: In RA patients with varying disease duration and DMARD use, the incidence of elevations of hepatic transferases (>3xULN) was <5% with TCZ+DMARD, <2% with TCZ monotherapy, and <3% with MTX monotherapy. These elevations were not associated with clinical signs or symptoms of liver disease, and the majority of elevations 1-3xULN returned to normal limits without any adjustment in TCZ therapy.

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Abatacept Use in Daily Practice : Report on Early Improvement after 3 Months of Utilisation in 50 Patients from the Rhumadata Database.

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Background : Phase III trial have shown efficacy of abatacept in controlled set-up. Patients from clinical practice are oftenly very different from those of

clinical trial. Efficacy data can thus be somewhat different from those trial. Observational prospective cohorts such as the one from the Institute of Rhumatology of Montreal, Rhumadataâ, provides us with the possibility to extend this knowledge to standard clinical practice.

Methods: Data from the Rhumadataâ electronic database was used. Data collected from the first 51 rheumatoid arthritis(RA) patients exposed to abatacept is shown. All patients underwent clinical evaluation at baseline, 3 and 6 month by one of the investigators. Data collected include demographics, disease duration, rheumatoid factor assessment, erosive status, prior medication use, 28 joint count, ESR and CRP, HAQ, patient and physician global evaluation (VAS10cm), morning stiffness (Minutes) , fatigue scale (VAS), pain global scale (VAS). Abatacept was dosed according to patient as per the product monograph in Canada.

Results: Mean age is 53 years . 82% of the group is of female gender. Average duration of disease is 14 years. 54% are RF + and 75% anti-CCP +. 61% have erosions. Mean previous DMARDS failure is 3.1. Average dose of methotrexate for those who are taking it at initiation of abatacept is 18.8 mgs. 50% have used more than one biologic agent. 12% were biologic naïve. Mean baseline tender joint count is 11.3 and swollen joint count 9.75. Mean baseline DAS 28esr is 5.46 , DAS 28crp 4.93, CDAI 33.7 and SDAI 27.29. Mean improvement in TJC at 3 month is 6,52 (p=0.0005), SJC 4,00 (p=0.001). Mean DAS 28esr improvement was 1,57 (p=0.006). Mean improvement in TJC at 6 month is 8,09 (p=0.001), SJC 6.18 (p=0.01). Mean DAS 28esr improvement was 2.72 (p=0.006).

Conclusion: In a population of RA patients with several markers of severity and resistance to treatment, abatacept was able to induce a clinically and statistically significant improvement in several measures parametersas early as 3 months post-initiation.

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Injection Site Pain, Burning, and Stinging Are Important, Under-reported Side Effects of Subcutaneous Anti-TNF Therapies for Patients with Rheumatoid Arthritis

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Background: Subcutaneous (sc) anti-TNF therapies provide convenient administration options for patients with rheumatoid arthritis (RA). Clinical trials have documented injection-related side effects from sc administration; however, these effects may be under-reported compared with real-world experience. The objective of this analysis was to determine the rates of injection-related side effects in real-world use of sc anti-TNF therapies for the treatment of RA.

Methods: RA patients in the US were asked to complete an Internet survey regarding their disease, current therapies and treatment experience. Patients were >18 years of age, formally diagnosed with RA and currently receiving care from a rheumatologist. Patients currently receiving sc anti-TNF therapies were asked questions regarding injection site side effects related to administration. Rheumatologists and RA nurses were recruited to complete a corresponding Internet questionnaire and were asked questions regarding their perceptions of patient's injection site side effects.

Results: 2039 RA patients, 500 rheumatologists, and 101 RA nurses completed the surveys. Among RA patients, mean age was 54 years, 79% were female, mean disease duration was 8 years, and 83% reported moderate to severe RA. A total of 92% of patients were taking prescription RA medication, and 23% were currently receiving a sc anti-TNF therapy. Similar proportions of patients (38%) and nurses (42%) reported that patients' experience a moderate to high level of injection site pain (ISP; ≥5 on a 1-10 scale, where 10=extremely painful), compared with only 20% of physicians. Similarly, 5% and 8% of patients and nurses, respectively, reported extremely painful ISP (≥8) compared with only 1% of physicians. Stinging/burning was reported in 66% of patients, and bruising in 44% of patients.

Conclusion: These results indicate that pain on administration among patients receiving sc anti-TNF therapy is higher than physicians perceive. Nurses' perceptions are in alignment with patients' reported levels of ISP. Stinging/burning and bruising are also common among patients receiving sc anti-TNF therapy. Further analyses are needed to determine the reasons for these differences in perception and the impact of these side effects on patient care.

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Computerizing Common Tools in the Rheumatology Practice

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Objective: Computer technology can increase the efficiency of visits to the rheumatology clinic. To demonstrate this, we have implemented three commonly used tools in assessing and recording patients' clinical course: 1) the Stanford Health Assessment Questionnaire Disability Index (HAQ), 2) the Pain Scale (PS), and 3) the Joint Man (JM).

Methods: Used: HTML and JavaScript were the chosen programming languages. Programs generated using these languages are readily accessible everywhere there is an internet browser, without requiring installation of any additional software. As web pages, they are also easily distributed via a URL. As verification, rheumatologists were consulted for assessment of the programs' accuracy, usability, and utility.

Results: The HAQ was translated into an interactive web form that calculates the disability score automatically and displays a summary for the rheumatologist to review. The computerized PS allows patients to drag a slider along a 15 cm horizontal line, and it remains very similar to the standardized paper version of the visual analog scale. The score is then automatically computed. The computerized JM has selectable joints and displays a summary of the affected joints as well as categorizes the joints based on size and left versus right.

Conclusion: The application of computer technology to the setting of the rheumatology practice has the potential to save time, improve record-keeping, and even improve care. Our programs would allow patients to document their condition at home in between visits, and in the waiting room before meeting with the physician. Future versions of these programs can incorporate trending functions to improve usefulness in the clinical and research setting. The next step is to distribute the programs to rheumatology offices, and quantitatively evaluate any improvements in office efficiency.

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Continued Inhibition of Structural Damage in Rheumatoid Arthritis Patients Treated with Rituximab at 2 Years: REFLEX Study

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Objective: This report describes the sustained inhibition of structural damage progression by RTX in rheumatoid arthritis (RA) patients at 2 years (Week 104) given rituximab (RTX) plus methotrexate (MTX), which was shown to inhibit the progression of structural joint damage in these patients having an inadequate response (IR) to TNF inhibition at Week 56 of the REFLEX study (ACR 2006; A1307).

Methods: The REFLEX study design was previously described by Cohen (Figure 1). Analysis was based on the intent-to-treat (ITT) principle, including patients who were randomized at baseline (BL) to placebo (PLA) (BL-PLA) and subsequently received RTX, as well as patients randomized to RTX who subsequently received standard of care. Radiographs of the hands and feet were performed at BL, Week 24, Week 56, and Week 104. Trained radiologists rescored X-rays for the 2-year analysis, and were blinded to treatment group assignment and order of the radiographs using the Sharp-Genant method.

Results: The ITT population included 187 BL-PLA and 281 RTX-treated patients who had a BL and post-BL film. RTX demonstrated significant structural damage progression inhibition over 2 years (Total Sharp Score [TSS]: RTX 1.14 vs. BL-PLA 2.81; p<0.0001). This effect was seen between BL and 1 year (TSS: RTX 0.66 vs. BL-PLA 1.78; p=0.0003) and from 1 year to 2 years (TSS: RTX 0.48 vs. BL-PLA 1.04; p=0.0019). Erosion scores and joint space narrowing were similarly affected. 60% of RTX patients had no pro-

gression in TSS over the first year vs. 46% of BL-PLA patients, with 68% of RTX and 54% of BL-PLA patients not progressing in the second year. RTX demonstrated consistent progression inhibition, with 87% of RTX-treated patients exhibiting no progression the first remaining progression-free through the second year. All patients missing Week 104 X-rays (RTX 30% vs BL-PLA 28%) had either a Week 24 or Week 56 X-ray available for linear extrapolation.

Conclusion: Earlier treatment with RTX was previously shown to inhibit structural damage progression at Week 56 in RTX-treated patients when compared to BL-PLA. The results of this study demonstrate that RTX treatment continued to inhibit joint damage with longer treatment in patients with an IR to TNF inhibitors.

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The Efficacy and Safety of Abatacept in Methotrexate-naïve Patients with Early Erosive Rheumatoid Arthritis and Poor Prognostic Factors

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Objective: To present 1-yr efficacy and safety results from a 2-yr study of abatacept in seropositive methotrexate (MTX)-naïve patients with early erosive rheumatoid arthritis (RA) and poor prognostic factors.

Methods: In this Phase IIIb, double-blind study, patients with RA for ≤2 yrs were randomized (1:1) to receive abatacept + MTX or placebo + MTX. Patients were MTX naïve, seropositive (RF/anti-CCP) and had evidence of erosions (hands, wrists or feet). Abatacept was administered at ~10 mg/kg according to weight range; MTX was initiated at 7.5 mg/wk and titrated to 20 mg/wk by Wk 8. Primary endpoints were: DAS28 (CRP)-defined remission (<2.6) and joint damage progression (Genant-modified Sharp total score [TS]) at Yr 1. Other efficacy measures included ACR responses. Safety was monitored throughout.

Results: Patients had high baseline disease activity (mean number of tender joints was 31; mean number of swollen joints was 22.4) with a mean disease duration of 6.5 months.

Patients were positive for RF (96.5%), anti-CCP (89.0%) or both (89.0%). Of the 256 and 253 patients treated with abatacept + MTX or MTX alone, 90.6 and 89.7% completed Yr 1, respectively. Fewer patients in the abatacept + MTX vs MTX group discontinued due to lack of efficacy (0 vs 3.2%) or AEs (3.5 vs 4.3%). At Yr 1 significantly more patients treated with abatacept + MTX achieved DAS28 (CRP)-defined remission, ACR 50 and ACR 70 responses, and Major Clinical Response [(MCR) (ACR 70 for 6 consecutive months)]. Mean change from baseline in TS was 0.63 for patients treated with abatacept + MTX vs 1.06 for patients treated with MTX alone (p=0.04). AEs and SAEs occurred in 84.8 vs 83.4% and 7.8 vs 7.9% of patients in the abatacept + MTX vs MTX groups, respectively. Serious infections occurred in 2 (0.8%) vs 4 (1.6%) and autoimmune disorders occurred in 6 (2.3%) vs 5 (2.0%) abatacept + MTX- vs MTX-treated patients, respectively; no malignancies were reported. Acute infusion reactions (mostly mild/moderate), occurred in 16 (6.3%) vs 5 (2.0%) of abatacept + MTX- vs MTX-treated patients.

Conclusion: Abatacept + MTX provided significantly better efficacy and favourable safety compared with MTX alone in an MTX-naïve population with early erosive RA and poor prognostic factors.

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Durable Impact on Diseases Activity and Consistent Safety Through 5 Years in Abatacept-Treated Rheumatoid Arthritis Patients Receiving Background Methotrexate

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Objective: To evaluate the efficacy and safety of abatacept through 5 years in patients with rheumatoid arthritis (RA) and an inadequate response to methotrexate (MTX).

Methods: This was a long-term extension (LTE) of a Phase II 1-yr, randomized, double-blind (DB), placebo-controlled trial. During the DB period, patients received abatacept 10 or 2 mg/kg or placebo + MTX. Patients completing the DB period could enter the LTE (all received ~10 mg/kg abatacept + MTX). Low disease activity score (LDAS: DAS28 [CRP] ≤ 3.2) and remission (DAS28 [CRP] < 2.6) were assessed for patients originally randomized to abatacept 10 mg/kg who entered the LTE, with available data at the visit of interest (as-observed). Safety was assessed at each visit for all randomized patients who received ≥ 1 dose of abatacept.

Results: Of 235 patients completing the DB period, 219 patients entered the LTE (abatacept 10 mg/kg=84; abatacept 2 mg/kg=68; placebo=67). Of these 219, 130 (59.4%) were ongoing at Yr 5 (91 and 39 pts randomized to abatacept (2 or 10 mg/kg) or placebo, respectively). For patients originally randomized to 10mg/kg abatacept, DAS28 responses were sustained through 5 years (LDAS: 48.2 and 58.5%; and Remission: 25.3 and 45.3%, at Yrs 1 and 5, respectively). The types and incidence of adverse events (AEs) and serious AEs were similar between the DB versus cumulative (DB + LTE) periods (489.7 vs 374.9/100 pt-yrs and 20.0 vs 18.9/100 pt-yrs, respectively). Forty-nine (17.1%) patients discontinued therapy in the cumulative period due to AEs.

Conclusion: Through 5 yrs, abatacept 10 mg/kg was well tolerated and provided durable improvements in disease activity. No unusual safety events were reported during the LTE. These data, together with the relatively high retention rates, confirm that abatacept provides sustained clinical benefits in RA.

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Achievement of Sustained Low Disease Activity State Predicts the Absence of Structural Damage Progression in Patients with Rheumatoid Arthritis: Insights from the Abatacept Database

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Objective: To analyze the relevance of assessing disease activity using sustained Low Disease Activity State [(LDAS) defined as DAS28 (CRP) ≤ 3.2] in predicting the lack of structural damage progression (an important parameter from a physician's perspective).

Methods: This was a post-hoc analysis of a 1-year, Phase III, randomized, double-blind (DB), placebo-controlled trial. Abatacept (~10 mg/kg) was given on Days 1, 15 and 29 and every 4 wks thereafter, plus background MTX. Data were pooled for the abatacept and placebo groups over the first 6 months. Status of disease was assessed using the DAS28 (CRP)-derived criteria. To determine the clinical relevance of evaluating the sustainability of a successful response to treatment, the percentage of patients with LDAS (DAS28 [CRP] ≤ 3.2) for ≥1, ≥2, ≥3, ≥4, ≥5 and 6 consecutive visits over 6 months was assessed. Structural damage progression was determined using the radiographic changes from baseline to 1 yr, assessed by the Genant-modified Sharp scoring system. Data were dichotomized as the % of progressors

(total score [TS] >0) versus non-progressors (TS ≤0). The relevance of sustained LDAS in predicting the lack of structural damage progression was scored as a positive likelihood ratio (LR+). Higher values of LR+ are indicative of better techniques; LR+ values >2 may be considered to have relevant prognostic value.

Results: After 1 year, 15% (97/638) of patients in the pooled abatacept and placebo population demonstrated no radiographic damage progression from baseline (change in TS < 0). In total, 79% and 34% of patients achieved an ACR20 or LDAS, respectively, within the 6-month period. LDAS were achieved by 12% of patients at three or more visits during the 6-month period. Sustainability of LDAS for three or more visits over 6 months was shown to be a predictor of inhibition of structural damage progression. Positive LRs were ≥ 2 when LDAS was sustained for three or more visits.

Conclusion: This post-hoc analysis of the abatacept database reveals that sustainability of good disease status, as measured by LDAS in the first 6 months was predictive of no radiographic progression at Yr 1.

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Sleep Disturbance in Patients with Rheumatoid Arthritis: An Analysis of Abatacept Clinical Trial Data

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Objective: Determine the sensitivity to change of sleep disturbance and investigate the relationship of sleep disturbance with other patient reported outcomes (PROs).

Methods: 2 randomized, double-blind, placebo controlled trials in patients with active RA were considered in this assessment: ATTAIN 6-month trial comparing treatment with abatacept (n=258) to placebo (n=133) on a background of DMARD therapy in patients who were anti-TNF therapy failures; and AIM 12-month trial comparing treatment with abatacept (n=433) to placebo (n=219) on a background of methotrexate therapy. Sleep disturbance was measured as an independent domain in the MOS-sleep module. In addition, outcomes assessed included the ACR core set measures, activity limitation, fatigue and the 8 domains and 2 component scores of the SF-36. Sensitivity to change was assessed by comparing treatment and placebo groups on sleep disturbance for treatment difference, relative percent improvement, standardized response mean (SRM) and relative efficiency (RE) for detecting a treatment effect relative to tender joint count. Correlation and regression analyses were conducted to evaluate the relationship between sleep disturbance and other PROs.

Results: Comparing treatment to placebo in the ATTAIN trial, the treatment difference of -8.6 (95%CI -13.4, -3.9), relative percent improvement of 18%, SRM of 0.38 (95%CI 0.17, 0.60) and RE of 0.39 for sleep disturbance were found. Similarly for the AIM trial, the corresponding results found were: -4.6 (95%CI -6.9, -2.4); 10%; SRM 0.19 (95%CI 0.03, 0.35); and RE 0.20. Moderate correlations were found between sleep disturbance and other PROs; for example, in the ATTAIN trial, correlations of 0.37, 0.35, 0.34, 0.36, 0.31, -0.23, -0.43 with fatigue, activity limitation, patient global assessment, pain assessment, HAQ, physical and mental component scores of the SF-36 and in the AIM trial, very similar correlations of 0.31, 0.27, 0.30, 0.31, 0.32, -0.29, -0.38 respectively were found.

Conclusion: Treatment with abatacept improves sleep disturbance and the psychometric property of sensitivity to change of this sleep dimension is confirmed. Sleep disturbance is consistent with other PROs and provides a unique contribution, and so would be a candidate for inclusion in a core set of measures of PROs.

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Technology Failure —How "Simple" Electronic Processes Can Fail

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Introduction: Rheumatologists found personal digital assistants slow and costly to use in a previous project involving practice audit. A new technical

process using fax technology was introduced to overcome these objections.

Objective: The use of technology for automatic data capture from paper to digital is assessed as a tool to facilitate the data entry process.

Material and Methods: Two questionnaires were developed to investigate the characteristics of the rheumatologist's practice and their choice of treatment for RA. The format used for the questionnaires was compatible with Remark ® software for processing and automatic data capture, through the use of bar codes to identify practice, and "bubbles" to be filled with the applicable information. The questionnaires were received by fax, named, saved, and then read by the Remark ® software through specially developed templates.

Results and Discussion: We received 457 faxes from 27 rheumatologists and encountered the following series of problems. On manual scrutiny, seventy-six questionnaires had missing, angled, upside down pages, or other significant defects (e.g., blurred text, small font, multiple pages on a single page). Processing of "good" files was followed by quality control that discovered an unacceptably large number of miss-read fields; many of these related to questionnaires from individual practices. There were also technical problems associated with the construction and layout of the questionnaire, such as some "bubbles" had the letters "Y" or "N" inside which caused reading problems by the Remark ® software. Fax errors may be due to old fax machines, or poorly maintained ones, while other errors may be related to send/receive and transmission problems.

Conclusion: Problems in the process lead to a failure of this technology as a tool compared to the conservative manual data entry process. Although this technology is potentially a valuable tool in practice audit, revisions in the steps of the process are required.

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Inadequately Managed Depression in Fibromyalgia Drives Referral to Specialists

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Objective: although the cornerstone for diagnosis of fm is pain, mood disorders are reported to occur frequently in these patients. Recognition and appropriate management of mood may impact on suffering and quality of life in fm patients, and may be a factor contributing to poor response to standard treatments. We have evaluated the frequency of depression and treatments thereof, in fm patients newly referred to a tertiary care centre.

Methods: demographic, disease related variables and measurements for functional status (fibromyalgia impact questionnaire, fiq), mood (arthritis impact measurement scale, aims), and pain catastrophizing (pain catastrophizing scale, pcs) were recorded for fm patients newly referred. Depression was defined on the aims depression scale as 4 or greater. Using this cut-off, comparisons were made between depressed (d) and non-depressed (nd) subjects with respect to selected variables. Univariate comparisons of continuous variables were made using student's t-tests, and for categorical variables using chi-squared tests. Logistic regression was used to model the association between age, gender, pain duration, catastrophizing, disability and pain intensity.results: 137 consecutively attending fm patients referred to a multidisciplinary clinic were evaluated. Depression (d) vs. No depression (nd) was present in 110 (80%) vs 27 (20%). No differences between groups (d vs nd) were noted for age (48 vs. 46 yrs), employment status (32 vs.42%), disability status (35 vs 37%) or pain intensity vas (6.6 vs 6.0). D vs nd had longer disease duration, 12.2 vs 7.3 years (p=0.03), scored higher for pain catastrophizing, 30 vs. 21.5% (p=0.002), anxiety 6.6. Vs 5.5% (p=0.05), and total fiq 65 vs. 57% (p=0.048). After adjusting for other covariates, duration of pain was the only factor associated with depression in multivariate analysis, adjusted or 1.11, 95% ci 1.03, 1.19). Use of any antidepressant for d vs nd was 48% vs. 63% (p=0.2), with tricyclic antidepressant (tca) use in 19 vs 44% (p=0.006) and non-tca use in 39% vs. 22% (p=0.024).

Conclusion: important depression was identified in 80% of fm patients. Of greater concern was the lack of any treatment to address depression in more than 50% of depressed patients, with the remainder treated for depression but

mostly with inadequate effect. Tca use in the nd reflects treatment patterns for fm pain and sleep, rather than use for mood effect. Prolonged pain duration was independently associated with depression. Poorly controlled depression may be an important factor driving referral of fm patients for specialist consultation.

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What Pain Related Behaviour Tells the MD about a Patient with Fibromyalgia?

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Objective: the entire clinical assessment of patients with fibromyalgia (fm) is subjective and depends upon patient report and interpretation of this report by the physician. There has been debate regarding the validity and reliability of the complaint of symptoms by patients with fm, who frequently report important functional impairment. Pain related behaviour (prb) may be defined as overt demonstrations by an individual indicating the presence of important pain. These behaviours may be perceived by the health care professional as compatible with, or as an exaggerated response to the underlying condition. Some have even suggested that the presence of these behaviours may reflect a conscious effort by the patient to emphasise the severity of symptoms.

Methods: We examined the frequency and associations of prb in fm patients attending a specialized multidisciplinary fm clinic in a tertiary care centre.methods: we evaluated 136 consecutively attending fm patients for the presence of prb. These was defined as behaviours that occurred during the physician interview and examination, appeared out of proportion to that expected for the symptom complaint, and which conveyed the subjective impression of exaggeration of pain and discomfort. Associations with demographic variables, pain and mood measurements and functional status were explored using the following: mcgill pain questionnaire (mpq), pain catastrophizing scale (pcs), pain disability index (pdi), the arthritis impact measurement scale (aims) and the fibromyalgia impact questionnaire (fiq).

Results: prb was present in 28 (21%) vs. No prb in 108 (79%). There were no differences between groups for age, gender, duration of symptoms or current employment status. Patients with prb vs. No prb scored higher on all pain assessments including mpq vs. 39, (p=0.03), affective component of mpq 7.2 vs. 5.5 (p=0.04), pain vas 7.2 vs. 6.2 (p=0.04), pdi 42 vs. 35 (p=0.03) and tended to be receiving disability compensation, 50% vs. 31% (p=0.06). There were no differences for pain catastrophizing (pcs), severity of depression and anxiety, presence of allodynia or fiq.

Conclusion: prb were observed in one in five of fm patients. All measurement of pain associated with the presence of these behaviours, but there was no association with mood disorders or functional impairment. Contrary to expectations, pain catastrophizing was not more prevalent in those with these overt behaviours. Prb may reflect a truly severe pain experience in fm, rather than a manifestation of attention seeking and histrionic behaviour.

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A Comparison Between Old and Newer Methods for the Detection of Anti-ribosomal P Autoantibodies

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Objective: Anti-ribosomal P (Rib-P) autoantibodies represent a highly specific serological maker for the diagnosis of systemic lupus erythematosus (SLE). A variety of methods are currently available for the detection of anti-Rib-P antibodies. The objective of this study was to compare the well established methods with newer technologies for the detection of anti-Rib-P autoantibodies.

Methods: Sera (n=51) with putative anti-Rib-P reactivity were identified by an addressable laser bead assay (INOVA) and tested for anti-Rib-P antibodies by ELiA® Rib-P (Phadia), Ribosomal P ELISA (Dr. Fooke), line immunoassay (LIA: Mikrogen), immunoblot (IB: in house assay Phadia) and indirect immunofluorescence (IIF: ImmunoConcepts) and the results were compared. Chi-square test was used to analyse association between anti-Rib-P reactivity and other autoantibodies.

Results: Of the 51 sera that tested positive by ALBIA, 43% and 37% were positive by ELISA and LIA, respectively. By IB, 35% reacted with P0, 29% with P1 and 16% with P2. When the results of the IB were used as reference excellent to moderate discrimination between anti-Rib-P aab was observed. Area under the curve (AUC) values determined by receiver operating characteristic analysis were: 0.90 (ELISA), 0.87 (LIA), 0.62 (IIF as CSP) and 1.0 (EliA®). For IIF as reference the AUC were: 0.72 (ELISA), 0.62 (LIA), 0.69 (IB), 0.78 (EliA®). Good quantitative agreement was observed between EliA® Rib-P and ELISA (r = 0.71, 95% CI 0.54 to 0.83; p < 0.0001) according to Spearman. Anti-Rib-P reactivity was strongly associated with other autoantibodies, most notably with anti-Ro60 (p < 0.0005).

Conclusion: Based on our findings we conclude that the agreement between various methods for the detection of anti-Rib-P autoantibodies varies significantly from assay to assay and this supports a call for wider and more rigorous standardization of Rib P testing kits.

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Impact of Adalimumab on Presenteeism for Patients with Psoriatic Arthritis and Reliability and Validity of the Work Limitations Questionnaire: Results of ACCLAIM

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Objective: The Work Limitations Questionnaire (WLQ) is a 25-item, self-administered instrument measuring the impact of disease on productivity of currently employed patients (pts). We assessed the reliability and validity of the WLQ in pts with psoriatic arthritis (PsA) and described the impact of adalimumab (ADA) on presenteeism (ie, lost productivity at work because of illness).

Methods: Data were obtained from ACCLAIM, a Canadian, prospective, open-label cohort study of 127 pts with PsA treated for 12 weeks (wks) with ADA. Internal consistency of the 4 WLQ scales, measured by Cronbach's alpha, was used to assess reliability. Overall construct validity was assessed by a correlation matrix of change in WLQ scales over the 12-wk treatment period with changes in clinical measures of the disease, as well as pt and physician measures of disease activity and pain. We hypothesized that the WLQ measures have constructs different from but related to those of physical and clinical assessments; therefore, statistically significant correlation coefficients of 0.2 to 0.7 demonstrated construct validity. Sensitivity to change was assessed by response to ADA therapy.

Results: In ACCLAIM, 99 of 127 pts (78%) were employed and are included in the analysis. Mean (SD) age was 47 (10) years, 42% were female, mean (SD) psoriasis duration was 20.4 (11.0) years, and mean (SD) PsA duration was 10.8 (8.8) years. Cronbach's alpha estimates of the 4 WLQ scales were 0.851 at baseline, 0.847 at 12 wks, and 0.614 for change from baseline to 12 wks (all p<0.001). ADA therapy for 12 wks produced significant mean (SD) reductions in the Physical (-14.5 [31.5]), Time (-12.58 [27.31]), Output (-8.1 [25.4]), and WLQ-Index (-2.4 [5.7]) scales (p<0.001), demonstrating sensitivity to change. Linear regression analyses demonstrated significant linear relationships between change in Pt's Global Assessment of disease activity (PGA) and WLQ-Index, indicating that for every 6.5% improvement in PGA, WLQ-Index improved by 10% (p<0.001).

Conclusion: The WLQ is reliable and valid as an outcome assessment tool in pts with PsA and provides valuable information beyond clinical and physical assessments. As early as 12 wks, adalimumab was associated with significant improvements in presenteeism.

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Impact of Adalimumab (HUMIRA®) on Work Productivity in Patients With Psoriatic Arthritis: Results From ACCLAIM

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Objective: We assessed the impact of 12 weeks (wks) of treatment with adalimumab (ADA) on work limitations and productivity measured by the Work Limitations Questionnaire (WLQ) in patients (pts) with active psoriatic arthritis (PsA) who did not respond to prior PsA treatment.

Methods: Data were obtained from ACCLAIM, an open-label, Phase IIIb study of Canadian pts with PsA who had not responded to DMARD therapy and were treated with ADA 40 mg by subcutaneous injection every other week for 12 wks. The WLQ is a 25-item, self-administered questionnaire measuring the impact of disease on the productivity of employed pts, specifically: difficulty in time-related demands (Time), physical impairment (Physical), cognitive function and interpersonal interactions (Mental), and ability to successfully meet task demands (Output). The WLQ Index is a weighted sum of the 4 WLQ scales, and the WLQ Productivity Loss Score represents the percentage of time in the prior 2 wks that respondents were limited in performing job tasks. Student t-tests were used to assess the mean change in WLQ from baseline to 12 weeks in the entire group and in relevant subgroups defined by baseline characteristics.

Results: A total of 127 pts enrolled and completed 12 wks of treatment. Mean (SD) age was 49 (11) and 54.3% were male. All 99 employed pts (78%) completed the WLQ. Mean (SD) significant changes in all WLQ scales were observed between baseline and Wk12: Physical, -14.5 (31.5); Time, -12.6 (27.3); Work Productivity, -2.3 (5.1), (all p<0.001); Mental, -4.4 (22.1; p=0.060); and Output, -8.1 (25.4; p=0.003). Significant changes between baseline and Week 12 were observed for the majority of subgroups analyzed, including age (<50 years and ≥50 years); sex (male and female); DMARDs users and non-users; and disease duration (≤3 years and >3 years).

Conclusion: As all patients in this study received adalimumab (no comparator arm), this stratified analysis further describes the impact of adalimumab on work productivity, especially in consideration of potential of confounding variables. Adalimumab was associated with significant improvements in work productivity, as measured by the WLQ in employed pts with PsA. Treatment benefits were observed across relevant pt subgroups in the ACCLAIM study.

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ACR and DAS 28 Response Over 24 Weeks in RA Patients Treated with Rituximab after an Inadequate Response to One TNF Inhibitor

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Purpose: To determine the safety and efficacy of rituximab (RTX) plus methotrexate (MTX) in patients with active rheumatoid arthritis (RA) who had an inadequate response (IR) or were intolerant to treatment with one prior TNF inhibitor.

Methods: This open-label, multi-centre study was conducted in Canada and Sweden; results are from an interim analysis of 50 patients who had 24 weeks of follow-up after 2 infusions of RTX. RA patients receiving background MTX (10-25 mg/week) received 1000 mg of RTX on Days 1 and 15, as per approved labeling. Key inclusion criteria included moderate/severe RA with SJC ≥6 and TJC ≥6 (28 joint count) at baseline (BL) and treatment history of one prior anti-TNF therapy. Efficacy assessments were conducted at Weeks 4, 12 and 24, including ESR, CRP, patient and physician global assessments of disease activity, HAQ-DI, TJC, SJC and FACIT questionnaire.

Results: Patients (34 females and 16 males) had a mean age of 55.6 years, mean disease duration of 13.6 years, and mean DAS of 6.4. ACR 20, 50 and 70 improvements were achieved in 60%, 28% and 8% of patients, respectively, at Week 24. Major improvements (>50%) were observed in all ACR core components with the exception of HAQ (31%) and ESR (48%). The mean BL values vs. Week 24 were as follows: SJC: 13.7 to 6.8; TJC: 15.5 to 6.2; patient global: 67.3 to 36.4; physician global: 65.5 to 28.9; HAQ: 1.8 to 1.3; CRP (mg/dL): 3.0 to 1.2; ESR (mm/hr): 39.0 to 20.4. Fatigue levels decreased by 34% (FACIT-F score) by Week 24 (BL: 28.3; Week 24: 18.6). DAS changed as early as Week 4 (-1.1 vs. BL) and decreased by -2.2 by Week 24. EULAR good/moderate response at 4, 12 and 24 weeks was 54%, 74% and 78%, respectively. DAS remission was observed in 8% of patients by Week 24, with low disease activity obtained in 20% of patients.

Conclusion: At 24 weeks, a single course of RTX (2 x 1000mg) with MTX provided clinically significant improvements in disease activity in this cohort of patients with active, long-standing RA. Smaller improvements in the HAQ are likely due to the irreversible damage seen in these patients. These data confirm earlier findings that RTX is an effective treatment option in RA.

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Safety of Tocilizumab in Patients with Rheumatoid Arthritis: An Interim Analysis of Long-Term Extension Trials with a Mean Treatment Duration of 1.5 Years

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Objective: To further assess the safety and tolerability of tocilizumab (TCZ) as demonstrated in patients with rheumatoid arthritis (RA) in phase 3 clinical trials, an interim analysis of long-term extension studies was performed.

Methods: Patients with RA who had already completed one of four international, randomized, double-blind, placebo-controlled, 24-week, phase 3 trials (OPTION, TOWARD, AMBITION, and RADIATE) could transition into two ongoing, open-label, extension studies assessing the long-term safety of TCZ (8 mg/kg; every 4 weeks). Safety outcomes were evaluated up to October 1, 2007 (the cut-off date).

Results: A total of 2562 patients (94.3%) entered the extension studies, with a median TCZ exposure of 1.5 years, and a total cumulative duration of observation of 3693.0 patient years. The rate of withdrawals due to adverse events (AEs) remained low (6.2%) by the cut-off date. The most common of these AEs were neoplasms (1.1%), elevations of liver enzymes (1.0%), and infections (0.9%). The rate per 100 patient years of serious AEs was 13.5 (95% CI: 12.4-14.8), and 3.9 for serious infections (95% CI: 3.3-4.6), with no evidence of increased risk with continued TCZ exposure. Alanine and aspartate aminotransferases (AST and ALT) were elevated >3x the upper limit of normal in 7.6% and 2.4% of patients, respectively. Elevations were single occurrences in most cases and there was no association with clinically relevant changes in direct bilirubin. The mean total cholesterol, high density lipoprotein, low density lipoprotein, and triglyceride values were elevated from the first measurement at Week 6, and remained elevated without further increases with continued TCZ treatment. The overall rate per 100 patient years of myocardial infarction was low at 0.27 (95% CI: 0.1-0.5), and the rate was stable over 6-month intervals.

Conclusion: TCZ showed a favourable safety profile over the treatment extension period, with a low discontinuation rate. Insight into TCZ as a long-term treatment option will be provided by the results of these continuing extension studies.

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Differences in Inflammatory Arthritis Disease Severity Among Mexican Mestizos and Native American Indians Compared to Caucasians

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Objective: Ethnic differences are reported in inflammatory arthritis (IA). We compared the presenting features and clinical outcomes of IA in three ethnic groups: Mexican Mestizos (MM), Canadian First Nations (FN) and Canadian Caucasians (CC) in early and established disease.

Methods: Patients with early IA (EIA) of less than 12 months (Rheumatoid arthritis (RA) =126; undifferentiated arthritis (UA) n=63; MM n=52, FN n=23, CC n=114) were followed in outpatient clinics in Canada and Mexico and compared to patients with late RA (LRA) with first clinic visit after Jan 2000 (MM=121, FN=120, CC=295). Clinical features, treatment, and patient global assessments (VAS) were assessed at the initial visit and at one year. Disease remission was defined as DAS3ESR < 2.6. Associations were tested using non-parametric tests and binary logistic regression (BNR).

Results: MM and FN with EIA were younger than CC at their initial clinic visit (39 and 36 vs 51 years p<0.0001) and had higher baseline VAS (EIA 58 vs 36 and 39 p<0.0001). MM were more likely to have received corticosteroids prior to first rheumatology visit and had greater use of combination DMARDS. DMARD use over the first year (none vs anti-malarials (AM) vs methotrexate (MTX) or sulfasalazine (SSZ)) was similar across groups. At one year, MM and FN were less likely to achieve remission than CC (MM 1/19(5%); FN 3/15(20%); CC 54/93 (58%) p<0.001). Comparing LRA patients, MM and FN were also younger at initial visit (46 and 46 vs 55 years p<0.0001) with higher VAS (50 vs 43 vs 40 p=0.03). The groups were equally likely to receive MTX or SSZ and combination therapy although CC tended to use fewer total numbers of DMARDs than MM or FN ((1.9 vs 2.7 and 2.6 p=0.05). At one year, LRA MM and FN were also less likely to achieve remission than CC (p<0.001). BNR models to predict remission at one year in EIA included ethnicity, baseline DAS3ESR, and DMARD treatment (MTX or SSZ vs AM vs none over the first year). Ethnicity and baseline DAS predicted remission at one year in EIA (p<0.0001).

Conclusion: MM and FN have an early age of onset of IA and are less likely to achieve remission at one year. These two ethnic groups tend to be more socially disadvantaged. Factors leading to poor outcomes, genetic or environmental need to be explored.

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Class V Nephritis in Pediatric SLE: Treatment and Long-term Outcome
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Objective: To evaluate presenting features, treatment regimens and long-term outcome of membranous lupus nephritis in pediatric systemic lupus erythematosus (pSLE).

Methods: A single-center cohort study of consecutive patients diagnosed with pSLE at age < 18 years between January 1990 and July 2008 was performed. Data collection: demographics including ethnicity, clinical features, laboratory test results, medications and SLE disease activity (SLEDAI). Outcome: 1) survival, 2) renal survival, 3) renal flares and time to flare, and 4) proteinuria as measured by total urine protein/24 hours and urine protein:creatinine ratio (UP:CR) at last follow up.

Results: A total of 150 of 453 consecutive pSLE patients (33.1%) had lupus nephritis. Of these, 25 patients (16.7%) had biopsy-confirmed class V nephritis, alone or in combination with Class II (WHO class Va/Vb). These were 4 boys and 21 girls with a mean age at first renal biopsy of 13.4 years (5.6-18.4), mean nephritis follow-up 3.6 years (0.23-13.4). 23 patients (92%) were followed ≥9 months. Ethnicity: Asian (48%), Black and Caucasian (16% respectively); mean SLEDAI at presentation 9.35 (0-27); proteinuria: mean urine protein at diagnosis 2.73 g/24h (0.1-21.0g/24h, 21/25); mean UP:CR 316.8 g/mol (21.0-2020.8 g/mol, 18/25), Treatment: prednisone in 24 (96%), mean initial dose 51.3 mg/day, azathioprine in 9 (36%), cyclosporine in 7 (28%). Cyclophosphamide was given to 2/3 patients for nephritis recurrence (class IV). Outcome: 1) overall survival: 100%, 2) renal survival: 96%; end-stage renal failure and transplant in 1 patient at age 14.5 years (5.5 years post diagnosis) for nephritis recurrence (class IV), 3) flares: 13 renal flares in 8/25 patients (32%) (mean time to 1st flare: 10.8 months), 3 developed class IV nephritis on subsequent biopsy (at 0.57, 3.0 and 7.4 years), and 4) proteinuria: mean urine protein excretion 0.33 g/l (0.01-2.3 g/l, 22/24) and mean UP:CR 30.91 (7.7-155.6 g/mol, 22/24) at last follow up.

Conclusion: Pediatric patients with membranous lupus nephritis have an excellent renal outcome. Only patients who transformed on subsequent biopsies to proliferative lupus nephritis were at risk for adverse renal outcome. These data question the need for aggressive immunosuppressive therapy in pediatric patients with pure Class V nephritis.

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Knee Osteoarthritis and Overpronation of the Foot among Different Patient Populations
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Objective: The purpose of this study was to prospectively evaluate consecutive patients with knee osteoarthritis who presented to a community Rheumatology clinic in Brampton to determine the prevalence of varus deformities of the knees and the incidence of forefoot overpronation in three different populations — a Canadian-born population, Indian (Punjabi)-born population and Portuguese-born population. Correlations were also evaluated between forefoot overpronation and hypertension, hypercholesterolemia, diabetes mellitus, Angina/Myocardial infarction, and cardiac revascularization.

Methods: Data were collected on patient age, sex, Body-Mass Index (BMI), Visual Analog Scale (VAS) pain, ethnic background, Valgus/varus deformity at the knee and overpronation of the forefoot. Two radiologists who were blinded to patient demographics reviewed plain radiographs of the knees and Kellgren-Lawrence scores were assigned.

Results: There was no significant difference between the groups in terms of age. There was a trend to lower BMI in the Punjabi-born group, and lower VAS pain in the Canadian-born group. The VAS pain was not significantly different between men and women. Significantly more forefoot overpronation was noted in the Portugese-born group (chi-square=6.327, P=0.04) vs. the Canadian-born group; and patients who had overpronation of the forefoot had a trend to greater VAS pain compared with those who did not (VAS=63.1 vs. 50.1 N.S.). There was no significant correlation between BMI and VAS pain, nor age and VAS pain (r=0.01 and 0.003 respectively). There was no significant association with either BMI or age and forefoot overpronation. 16/31 patients with forefoot overpronation also had hypertension, while 10/36 patients without forefoot overpronation had hypertension.

Conclusion: Patient populations differed significantly in terms of prevalence of overpronation of the foot and a trend to differences in VAS pain was noted in patients with overpronation of the foot.

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Canadian Internal Medicine Musculoskeletal Education Survey (CaIMES): Preliminary Review of Program Directors' Reponses
Steven J. Katz (University of Alberta); Anna E. Oswald (University of Alberta)

Objective: CaIMES is envisioned as a multi-centre national survey examining how musculoskeletal (MSK) education is provided to internal medicine (GIM) residents. Resident confidence in their MSK clinical skills & factors that may influence it are being studied. We present preliminary results from the program director's (PD) portion of this project.

Methods: A 5 minute opinion based survey was designed & posted online at Surveymonkey.com. An email invitation was sent to rheumatology & GIM PDs across Canada. The survey differed between the two groups with a broader scope of questions to the GIM PDs, although for the purposes of this review, the majority of questions examined were posed to both groups unless indicated. Ethics approval was obtained. Raw results are reported, with rheumatology & GIM PDs results combined.

Results: 7 GIM & 10 Rheumatology PDs completed the survey representing 14/16 Canadian sites. 16/17 PGs felt GIM residents had the most MSK exposure during a rheumatology rotation. Degenerative joint disease was the most commonly seen MSK abnormality, with a need for more experience with inflammatory arthropathy. A variety of formal & informal teaching methods are used at most sites, with rheumatology staff physicians & fellows nearly

unanimously felt to be the most frequent & best teachers. GIM PDs ranked resident MSK clinical skills at 6/10, lower than 7.7, 7.7, & 6.9 scored for cardiology, respirology & gastroenterology respectively. When asked to rank how confident they are in their residents' abilities to diagnose common MSK problems & perceived resident confidence, PD's average score was 5 & 4.5/10 respectively.

Conclusion: Program Director's confidence in their residents' MSK abilities appears cautious at best. The perception of MSK confidence in residents is low, & worse than other clinical skills. This may be related to a lack of experience, since it appears most MSK exposure occurs during a small portion of GIM training, the rheumatology rotation. Further study, including a survey of internal medicine residents, is required & ongoing.

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The Association of Anti-CCP Antibodies with Primary Sjögren's Syndrome

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Objective: To determine the prevalence of anti-cyclic citrullinated peptide antibody (anti-CCP Ab) in patients diagnosed with primary Sjögren's syndrome in a University based rheumatology cohort.

Methods: The University of Alberta Rheumatic Disease Unit Autoimmune Testing Laboratory stores serum on all samples, and when possible links them with an associated clinical rheumatologic diagnosis. We identified and confirmed by chart review, patients at the University of Alberta Rheumatic Disease Unit who have been diagnosed with Primary Sjogren's Syndrome, as defined by the 1993 European classification criteria. Patients with a secondary rheumatic disease were excluded. Anti-CCP Ab status was determined on those patients with previously submitted serum. Anti-CCP Ab was measured by a semi-quantitative ELISA kit. Results were reviewed and tabulated.

Reults: 31 patients were identified with primary Sjogren's syndrome who also had serum previously submitted to the rheumatology lab. Of these, 3 patients were positive for anti-CCP antibody, conferring a rate of 9.7% anti-CCP antibody positivity.

Conclusion: Anti-CCP antibodies are present in nearly 1 in 10 patients diagnosed with primary Sjogren's syndrome in this cohort. While small, this is significantly more than previous studies have identified. A positive anti CCP antibody does not appear to rule out a diagnosis of Sjogren's syndrome; its utility in this disease remains uncertain. It is important to consider Sjögren's syndrome in the differential diagnosis with a positive anti-CCP Ab test, if features of Rheumatoid Arthritis are not present.

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Sustained Clinical Remission and Response for Early RA Patients with Adalimumab and Methotrexate Initial Combination Therapy: 5-Year Results of the PREMIER Trial

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Objective: In a long-term, open-label extension (OLE) of the 2-year (yr) PREMIER study,[1] we evaluated efficacy and safety of open-label adalimumab (ADA), with and without methotrexate (MTX), for an additional 3 years.

Methods: 799 patients (pts) with active, early rheumatoid arthritis (RA) (<3 yrs) received ADA (40 mg every other week [eow]) and MTX (7.5 mg/week rapidly increased, as needed and tolerated to a maximum of 20 mg/week), ADA alone, or MTX alone for 2 yrs.[1] All pts still on blinded therapy at Yr 2 could enroll in an OLE and receive monotherapy ADA 40 mg eow. Blinded MTX/placebo were discontinued. MTX could be restarted at any time during the OLE at investigator's discretion. Efficacy was evaluated for pts with available American College of Rheumatology (ACR) responses and radiographic data at Yr 5. We evaluated ACR response rates, major clinical response, remission (28-joint Disease Activity Score [DAS28] <2.6), and safety.

Results: 354 pts had available ACR responses and radiographic scores at Yr 5 (124 originally randomized to ADA+MTX; 115, to ADA monotherapy; 115, to MTX monotherapy). Clinical responses were greatest for pts initially treated for 2 yrs with ADA+MTX followed by 3 yrs of OL ADA (34% achieved ACR90 and 60% in clinical remission by DAS28 at Yr 5). Responses for pts originally randomized to either ADA or MTX monotherapy were similar following 3 yrs of OL ADA therapy (24% and 31%, respectively, achieved ACR90; 52% and 57%, respectively, were in clinical remission). For the 497 pts who received ≥1 dose of study drug during the OLE, rates per 100-pt-yrs (100-PYs) for serious adverse events and serious infections (SIs) were 21.9 and 3.3. The SI rate for pts with long-standing RA treated with adalimumab was 5.1/100-PYs.[2]

Conclusion: Initial combination therapy with ADA+MTX resulted in greater percentages of pts with early RA achieving sustained clinical response and DAS28 remission at 5 yrs compared with pts randomized to ADA or MTX monotherapy followed by OL ADA. Long-term efficacy and safety of adalimumab in the PREMIER trial suggest a favorable benefit-risk profile in the early RA population.

1. Breedveld FC, et al. *Arthritis Rheum*. 2006;54:26-37.
2. Schiff MH, et al. *Ann Rheum Dis*. 2006;65:889-94.

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Characteristics of a Psoriatic Arthritis Cohort in Newfoundland and Labrador

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Background: Psoriatic arthritis (PsA) is a serious chronic condition that affects 10-35% of patients with skin psoriasis and is associated with increased patient morbidity and mortality.

Objective: Examine the clinical characteristics and associated co-morbidities of a cohort of patients with psoriatic arthritis.

Methods/Materials: An ongoing retrospective chart review of patients diagnosed with psoriatic arthritis in a rheumatology practice with special interest in psoriatic arthritis was performed. Patient demographics, disease characteristics, treatment received and co-morbidities were extracted. Descriptive statistics were performed. Patients who received or currently receiving biologic therapy were analyzed as a subgroup and compared to a larger cohort. Additionally, results were compared to a small cohort of PSO patients seen in the same period in the same centre with no arthritis symptoms or signs.

Results: At the time of the report preparation nearly 200 patients with PsA were identified. Data collection was completed on 59 patients (53% male) with a definite diagnosis of psoriatic arthritis and who met the CASPAR criteria. Their mean age was 51.8 ± 11.3 years. All patients have or had a definite history of skin psoriasis (duration of skin disease: 20.4 years ± 14.2). Of those surveyed: 69% had a family history of psoriasis; 82% had a family history of arthritis; 28 patients (47%) had nail involvement; 26% of patients tried a biological agent (most TNF antagonists); 40% tried or were taking Methotrexate; 14 patients (23%) had hypertension; 2 (3%) had IHD and 11(18%) had diabetes. These percentages were overall higher than those obtained from the patients with psoriasis only.

Conclusion: Preliminary data suggests patients with psoriatic arthritis have a high prevalence of cardiovascular co-morbidities, body mass and prevalence of diabetes and hyperlipedimia.

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Safety of Other Biologic Therapies Following Rituximab Treatment in RA Patients

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Purpose: To assess the rate of serious infection events (SIEs) in rheumatoid arthritis (RA) patients previously treated with rituximab (RTX) who received a subsequent biologic RA therapy.

Methods: Patients with moderately-to-severely active RA who received RTX + methotrexate in an international study were included. Following withdrawal from their respective studies, patients entered a safety follow-up (SFU) during which patients were permitted to receive additional biologic therapies. All SIEs were collected throughout the SFU period, and peripheral B-cell counts were monitored at regular intervals for ≥ 48 weeks. SIEs were defined as infections that required intravenous antibiotics, or to which at least one of the following applied: in-patient hospitalization or prolongation of an existing hospitalization was required, considered immediately life-threatening, resulted in persistent or significant disability or incapacity, judged medically significant, an intervention was required to prevent one of the previously mentioned outcomes, or the infection was fatal.

Results: 2578 RA patients had received at least 1 course of RTX at the time of data cut-off (November 2007), providing 5013 patient-years of follow-up. The overall rate per 100 patient-years of SIE was 4.31 (95% CI: 3.77, 4.92). Of patients who withdrew from SFU, 185 were treated with another biologic (150 received TNF inhibitors, 25 abatacept, and 10 anakinra or experimental biologics), with a median SFU of 11 months (range: 0-45 months). Peripheral B-cell depletion with CD19 levels below the lower limit of normal was seen in the majority of patients when receiving further treatment. During RTX treatment, this subgroup reported a total of 13 SIEs in 186.05 patient-years follow-up (6.99 events/100 patient-years; 95% CI 4.06, 12.03) (Table). Following biologic initiation, 10 SIEs in 182.31 patient-years were reported (5.49 events/100 patient-years; 95% CI 2.95, 10.19]. Overall, infections were variable and typical for RA patients, with no opportunistic or fatal infections.

Conclusion: The use of other biologic therapies in RA patients previously treated with RTX was not associated with an increase in the rate of SIEs in this SFU.

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Diagnosis Of Scleroderma With "Normal" Skin And Abnormal Skin Biopsy

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Objective: We describe the diagnosis of a patient with systemic sclerosis (SSc) with initial normal skin examination, and biopsy of visibly normal skin which was diagnostic for SSc.

Case: A 51 year old woman with idiopathic pulmonary fibrosis (IPF), presented with a 1 week history of fatigue, nausea, dyspnea, recent Raynaud's and acute renal failure. The patient's symptoms started 9 months previously with progressive dyspnea, fatigue, myalgias and arthralgias. A CT chest had shown interstitial markings with diffuse ground glass appearance and she was started on prednisone and azathioprine for treatment of IPF. On examination, the patient was hypertensive and had a III/VI systolic murmur at the left sternal border. Peripheral exam revealed periungal ulceration on the right second digit but no skin thickening or other abnormalities. Laboratory investigations showed elevated WBC count 22.8 x 10^9/L, creatinine of 492 mmol/L and peripheral blood smear revealed red cell fragmentation with schistocytes. Preliminary renal biopsy results demonstrated thrombotic microangiopathy. The patient's clinical status deteriorated and she was found to have *S. aureus* endocarditis. Dermatology was consulted to perform a skin biopsy of the patient's upper arm which showed sclerosis of the mid-reticular dermis and the patient was diagnosed with SSc. Immunological tests showed a positive ANA with a nucleolar pattern and renal biopsy results found histology consistent with scleroderma renal disease.

Discussion: The patient's presentation included pulmonary fibrosis, renal microangiopathy, hemolysis, Raynaud's and the lack of physical findings of SSc, all of which were complicated by her endocarditis. The skin biopsy provided a definitive diagnosis of SSc despite being taken from a clinically uninvolved area.

Conclusion: Pathologic changes in SSc can be more widespread than what is clinically appreciated and skin thickness is significantly greater in SSc patients (either clinically involved or uninvolved skin) than in controls. One should consider skin biopsy in patients being investigated for possible SSc whether or not cutaneous changes are found on examination.

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Determinants of DMARD Use and of Rheumatologist Referral in RA

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Objective: In previous research we found that despite current RA treatment guidelines, many people with RA are not treated with DMARDs and rheumatologist referral greatly influenced DMARD use but was not frequent. To understand the underlying reasons for the gaps in care identified, we evaluated determinants of DMARD use and rheumatologist care.

Methods: A survey was sent to a random sample of 6500 RA cases identified from administrative data, including measures of disease activity (RADAI), pain and fatigue (VAS), physical function (mHAQ), self-efficacy and questions about information sources and use of services for RA, health benefit plan, visits to allied health professionals (AHP) and complementary and alternative medicines (CAM). Data was linked with MoH administrative data on DMARD use, rheumato referral, local health area (LHA) and Charlson co-morbidity score. Stepwise multivariate logistic regression analysis was used to identify determinants of DMARD use and rheumato referral.

Results: 2007 were ineligible (deceased, incorrect address, age <18, did not report MD diagnosis of RA), 1822 participated in survey, of which 885 could be linked with admin data. Over 1 yr, 32% had used a DMARD and 34% had seen a rheumatologist. After controlling for LHA, people who had seen a rheumato [OR(95%CI): 9.0(5.6-11.5)], had received helpful info about RA from an AHP [1.8(1.3-2.7)], and non-Caucasians [1.7(1.1-2.7)] were more likely, and those who attended a support group were less likely [0.48 (0.2-0.97)] to receive DMARDs. Having attended education sessions on RA was not significant (p=0.06). Removing "seen a rheumato" from the model allowed the selection of other variables, incl. disease variables. For rheumato referral, after controlling for LHA, women [2.2(1.4-3.3)], people with greater co-morbidity, and who attended education sessions were more likely; whereas those with lower education and who received helpful information from GPs or from CAM practitioners were less likely to see a rheumato.

Conclusion: This study provides useful information for targeting interventions aimed at improving quality of care in RA. The lack of association with disease variables is likely related to the cross-sectional nature of the study. Also rheumatologist referral may serve as marker for characteristics associated with DMARD use.

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Factors Affecting Referral and Treatment with Disease Modifying Anti-Rheumatic Drugs (DMARDs) for Patients with Rheumatoid Arthritis: Qualitative Interviews with Primary Care Physicians.

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Objective: ACR guidelines for the treatment of RA recommend that DMARD therapy be initiated within 3 months of symptom onset. Previous research has shown that in British Columbia, many patients are not treated with DMARDs at any time, and that patients managed solely by their primary care physician (PCP) are less likely to be prescribed DMARDs than those referred to a rheumatologist. Our objective was to identify factors influencing PCP's decisions regarding referral to a rheumatologist and initiation of DMARDs.

Methods: PCPs were recruited from a randomly selected sample representative of the PCP population in terms of geographic location and time since graduation. Using an open-ended interview guide developed in collaboration

with PCP academic leaders, we asked PCPs to discuss facilitators and barriers to prescribing DMARDs and referring patients with possible RA to a rheumatologist. Individual interviews lasting 20-30 minutes were conducted over the phone. Interviews were taped, transcribed, coded and analyzed independently by 2 researchers, using a grounded theory compare and contrast approach.

Results: Our sample includes 29 PCPs (11 female), in full-time family practice. Physicians from urban areas and older age were somewhat under-represented. Most PCPs preferred to refer all patients with suspected RA to a rheumatologist for confirmation of diagnosis and initiation of treatment, with only 6/29 prescribing DMARDs prior to a rheumatologic consult. Though the majority of PCPs were aware of the paradigm shift towards earlier and more aggressive treatment for RA, many PCPs expressed their lack of confidence in recognizing 'early' RA. Some PCPs still felt that if symptoms were mild, they would try NSAIDs first. A near universal concern was delays in accessing rheumatologists, though the actual time to be seen varied widely. Another important factor was the influence of local practice patterns. Several PCPs who had been prescribing DMARDs in their previous practice locations were now referring all RA patients since relocating to BC. Patient factors were also identified as important barriers to DMARD treatment, such as PCPs describing some patient's reluctance to take DMARDs, preference for natural treatments, and difficulties in travelling to appointments, particularly for patients in rural areas. System-based factors included underutilization of available resources such as clinical guidelines and drug information sheets, due to lack of awareness.

Conclusion: Delays in referral and treatment initiation appear to be multifactorial, including patient, PCP, and system based barriers. Most PCP interviewed were aware of the need for earlier and more aggressive treatment, but many did not feel confident in making the diagnosis and starting DMARDs.

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Content Validity of Work Productivity Measures in Ankylosing Spondylitis

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Objective: To assess the content validity of the Workplace Productivity and Activity Impairment (WPAI) survey and supplemental work-specific items for measuring workplace productivity in patients with AS.

Methods: This was a cross-sectional, qualitative study of patients with AS recruited from the Arthritis Center of Canada in Vancouver during September 2008. Patients completed a questionnaire on demographics and clinical characteristics, followed by the WPAI, with supplemental items characterizing their workplaces, employment demands, and job satisfaction. Trained interviewers, following an interview guide, conducted one-on-one cognitive debriefing interviews with each patient to assess the interpretation and comprehensiveness of the questions and response items. Responses were grouped by item and summarized, and the data were reviewed to identify whether modifications to the questionnaire were required for its use in an AS population.

Results: The study sample consisted of 13 patients. Mean age was 51 years, and 8 (62%) were female. Eight patients (62%) worked full-time at a variety of occupations. All patients had AS symptoms: 2 (15.4%) reported "very mild" AS, 5 (38.5%) had "mild" AS, 5 (38.5%) had "moderate" disease, and 1 (7%) had "severe" disease. Feedback indicated good content validity for the WPAI in measuring workforce participation and productivity. While AS patients understood the majority of the supplemental work-specific questions posed, they were frequently confused by how questions were structured for employment type (ie, previous work history; reasons for work discontinuation; coverage for disability; classification of profession; and defining place of work). Patients also reported difficulty in recalling events from ≥1 month

ago, as well as difficulty in reporting percentages of time vs. absolute hours or minutes.

Conclusion: These findings suggest that the WPAI and supplemental items are appropriate for assessing workplace-related burden of AS. A cognitive debriefing exercise is beneficial before the application of new questions that have not been validated in a clinical study setting. We anticipate these results will enhance the data relevance and quality of future studies evaluating work burden in AS populations.

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Ultrasound of the Hands and Feet: Effect on Rheumatologists' Diagnostic Confidence and Patient Management

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Objective: The purpose of our study was to quantify the impact that ultrasound (US) of the hands and feet have on rheumatologists' diagnosis and diagnostic confidence and on patient management.

Methods: A prospective controlled observational study was performed with 62 consecutive referrals from 2 rheumatologists to a teaching hospital for sonography of the hands and/or feet. Measurements of diagnostic confidence for both specific clinical findings (synovitis, erosion, enthesitis, tenosynovitis, other/osteophytosis) as well as overall diagnosis (rheumatoid arthritis, seronegative arthropathy, inflammatory OA, OA, gout, septic arthritis, normality, other diagnoses) using a Likert scale were made both before and after the US examination in each case. Certainty was defined as 'very unlikely' or 'definite' on the Likert scale. Proposed management (intra-articular steroids, parenteral steroids, oral steroids, DMARD, surgical referral, NSAID/ review at outpatients, physiotherapy, and discharge) was also recorded before imaging and then with benefit of the US result. The McNemar test was performed to test for differences in diagnostic certainty and proposed management before and after US.

Results: The proportion of physician certainty for specific clinical findings increased for synovitis (9.7 versus 38.7%; p-value <0.001), tenosynovitis (9.7 versus 46.8%; p-value <0.001), erosions (1.6 versus 58.1%; p-value <0.001), enthesitis (50.0 versus 83.9%; p-value <0.001), and other/osteophytosis (53.2 versus 77.4%; p-value 0.003). The physician certainty for overall diagnosis increased for seronegative arthropathy (46.8 versus 61.3%; p-value 0.049), inflammatory OA (46.8 versus 87.1%; p-value <0.001), OA (46.0 versus 73.0%; p-value 0.002). A total of 88.7% of patients had DMARD as a proposed management option before US versus 48.4% after US (p-value <0.001). In addition, 4.84% of patients had NSAID/review at outpatients as a proposed management option before US versus 45.26% after US (p-value <0.001).

Conclusion: Sonography of the hands and/or feet significantly influences the rheumatologists' diagnostic confidence in specific clinical findings and management plans

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Tocilizumab Treatment Results in Rapid Improvements in the Signs and Symptoms of Moderate-to-Severe Rheumatoid Arthritis in Four Patient Populations with Different Prior Therapy Exposure

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Objective: To determine the time to onset and duration of response of tocilizumab (TCZ) 8 mg/kg in the four different patient populations with active rheumatoid arthritis (RA) evaluated in phase 3 trials.

Methods: Safety and efficacy data from four randomized, double-blind, 24-week, international, phase 3 clinical trials investigating TCZ therapy in patients with moderate-to-severe, active RA were evaluated. In TOWARD, patients with inadequate response (IR) to prior DMARDs (DMARD-IR)

received TCZ 8 mg/kg intravenously (IV) or placebo IV (control) every 4 weeks plus DMARDs. In OPTION, methotrexate (MTX)-IR patients received TCZ 8 mg/kg IV or placebo IV plus MTX 10-25 mg/week. The RADIATE study had anti-TNF-IR patients receiving TCZ 8 mg/kg IV or placebo IV (control) plus MTX 10-25 mg/week. AMBITION assessed patients who had not failed previous MTX or biologic treatment (43% DMARD-naïve) and were given TCZ monotherapy (8 mg/kg IV every 4 weeks) or MTX monotherapy (escalating dose 7.5-20 mg/week). Outcome measures included ACR20/50/70 responses, remission rates (DAS28 < 2.6), EULAR response criteria (good or moderate), and change from baseline C-reactive protein (CRP) levels.

Results: The TCZ and control groups separated at the first time point measured (Week 2), regardless of prior RA therapy, with 56%-65% of TCZ-treated patients achieving a good or moderate EULAR response (Table). CRP levels had also normalized by Week 2 in these patients, and 17%-25% had achieved ACR20 responses. The improvements observed with TCZ were sustained in all populations throughout the 6-month study period.

Conclusion: As monotherapy or in combination with DMARDs/MTX, TCZ produced rapid (within 2 weeks) and sustained (over 6 months) improvements in the signs and symptoms of RA as measured by ACR, EULAR and DAS28 criteria, and normalization of CRP levels. Response was consistent regardless of prior therapy.

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A Scientific Basis for Our Empiricism in Treating RA: DMARDs Downregulate Citrullinated Proteins/antigens in Vitro Using Different Mechanisms

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Objective: Citrullinated (cit) proteins are by-products of inflammation but become cit-antigens (e.g. cit-vimentin or the Sa antigen) only in rheumatoid arthritis (RA). DMARDs used in combination or added to biologics are more efficient then any drug given alone and whether there is a common anti-inflammatory/anti-arthritic mechanisms of action of DMARDs is still unclear. Our work explores the in vitro effect of DMARDs on cit-protein and cit-antigen (Sa) production, a central uniquely specific feature of RA.

Methods: Two cell lines, ECV304 and UMR106 were treated with increasing doses of Methotrexate (MTX), Sulfasalazine (SSZ), Azathioprine (AZA), Hydroxychloroquine (HCQ) and Prednisone (Pred) in dose ranges corresponding to those obtained in vivo during treatment of RA patients. The semi-quantitative effect on cit-proteins and cit-antigens production was estimated. ECV304 cells have peptidylarginine deiminase (PAD) activity at all times provided by the PAD2 and 3 isoenzymes. UMR106 only has PAD activity at confluence provided by PAD2. Both lines are capable of producing cit-proteins and cit-antigens detectable by western blot (WB) using a rabbit anti-chemically modified citrulline antiserum and polyvalent RA sera (anti-Sa), respectively.

Results: UMR106 cells are osteoblast-like cells with PAD activity increasing with confluence and ECV304 are endothelial/epithelial-like cells with high amounts at all times. MTX treatment of UMR106 showed a dose dependent decrease in PAD activity with significantly less production of both cit-proteins and cit-antigens. That MTX effect could be prevented by folinic acid and was not mediated via adrenergic receptors. At the same low dosage, MTX had no effect on ECV304. SSZ and AZA decreased the amount of PAD activity under all conditions except in confluent ECV304 assays while Pred had no effect under any conditions. In contrast, HCQ decreased PAD activity under all conditions tested. The amount of PAD2 protein, one of the isoenzymes present in articular tissues (synovium, muscle, cartilage, bone) was influenced quantitatively by SSZ, AZA and HCQ treatments but not by MTX or Pred treatments.

Conclusion: Our observations support the hypothesis that DMARDs are DMARDs because they downregulate the production of cit-proteins/antigens. Some do this by decreasing the quantity of enzyme, others by blocking its activity. In RA patients with antibodies to cit-antigens like anti-Sa, DMARDs

should significantly decrease the antigenic load and eventually the specific immune response by removing one of the elements responsible for chronicity. Those data explain the good results obtained by rheumatologists using empirical selection and combination of DMARD(s).

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Paraneoplastic Raynaud's Phenomenon in A Breast Cancer Survivor

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Objective: Paraneoplastic Raynaud's phenomenon (RP) has been described in association with solid or hematologic malignancies including lymphoma, multiple myleoma, liver, melanoma, and genitourinary tumours. The only reported association of breast cancer and RP, however, has been in the context of systemic sclerosis or chemotherapy treatment. We describe the first case of paraneoplastic RP associated with recurrent breast cancer in the absence of an underlying rheumatic condition.

Methods: A 35-year-old woman with a history of breast cancer, treated three years earlier with surgery, radiation, and chemotherapy presented with a rapid onset of asymmetric, severe RP. On physical examination, she had asymmetric digital ulcers and splinter hemorrhages. There were no signs of an underlying rheumatic condition; specifically, there were no scleroderma skin changes, telangectasias, calcinosis, or abnormal nail-fold capillaries.

Results: Laboratory evaluation revealed anemia and slight depression in her serum complement C3 level. She had an antinuclear antibody at low titre (1:40); the remainder of her serologic evaluation, including extractable nuclear antigens, anti-double-stranded DNA antibody, antiphospholipid antibodies, rheumatoid factor, anti-neutrophil cytoplasmic antibodies, cryoglobulins, and cold agglutins, were negative.

Within weeks of her presentation, she developed acute renal failure and bilateral lower extremity edema. A computed tomography scan of her abdomen and pelvis showed bulky lymphadenopathy and hydronephrosis; a pelvic lymph node biopsy revealed metastatic breast cancer.

Conclusion: She was initially managed with passive rewarming strategies, topical antibiotics, vasodilator and anti-platelet therapy, but had a neglible response. However, once she was started on chemotherapy for her recurrent malignancy, there was a significant improvement in her Raynaud's symptoms, resolution of her digital ulcers, and normalization of her complement levels. She was given the diagnosis of paraneoplastic RP; the presumed mechanism of action being a small vessel vasculitis.

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Serum Dickkopf-1 (DKK-1) Is Unrelated to Radiographic Severity in Ankylosing Spondylitis

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Objective: It has been reported that serum DKK-1 is elevated in rheumatoid arthritis compared to healthy controls. In contrast, DKK-1 in ankylosing spondylitis (AS) is decreased in comparison to healthy controls, and a role for DKK-1 in differential remodeling of joint architecture in AS has been proposed. If such a role for DKK-1 is operational in AS, the level of DKK-1 may correlate with radiographic damage in AS but this question has not previously been addressed.

Methods: AS Patients are evaluated according to a standard protocol in which demographic, clinical, radiographic and laboratory variables are recorded at regular intervals. Radiographic severity was determined by calculation of the mSASSS score. Serum DKK-1 was assessed by ELISA. Serum from normal healthy controls was included. DKK-1 levels were compared using the student t-test. DKK-1 levels were correlated to various clinical variables using Pearson correlation coefficients.

Results: 47 AS patients (43 Male, 4 Female), all fulfilling modified New York criteria, were included. 85% were HLA-B27 positive. The mean age (±SD) was 41.7 (±12.4) years and the mean disease duration was 16.9 (±12.1) years. Mean mSASSS score was 29.8 (±28.7) units. The mean DKK-1 level for the AS group, 83.97 (±55.5) pg/mL, was lower than in the control group,

108.84 (±58.7) pg/mL, but the difference was not statistically significant (p=0.12). AS patients were classified into groups according to the severity of the mSASSS score. The *Lowest group* (N=18) had scores ranging from 0 to 4 (median = 0), the *Middle group* (N=13) scores ranged from 20 to 33 (median = 24) and the *Highest group* (N=16) scores ranged from 48 to 72 (median = 68.2). There was no significant difference in mean serum DKK-1 levels between the *Low* (89.92 pg/ml), *Middle* (72.87 pg/ml) and *High* (90.74 pg/ml) mSASSS groups of AS patients. Overall, there was no correlation between serum DKK-1 levels and mSASSS scores (r=0.042, p=0.78). There was also no correlation between serum DKK-1 levels and ESR, CRP, BASDAI, BASMI, disease duration, swollen or tender joint count, or serum alkaline phosphatase.

Conclusion: There is no difference in DKK-1 values between AS patients and healthy controls. Although DKK-1 may play an important role in bone growth and homeostasis, there was no relationship between serum DKK-1 values and radiographic severity in AS.

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REPArE (Rating Evaluations in Psoriatic Arthritis with Enbrel): Interim Analysis of a Canadian Phase 4 Post-Marketing Study of Etanercept in Psoriatic Arthritis

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Objective: To describe, in a Canadian clinical practice setting, the long-term efficacy of etanercept in improving functionality and quality of life in patients with psoriatic arthritis (PsA).

Methods: In this 24-month, open-label, observational trial conducted at 22 Canadian sites, adults with PsA received etanercept 50 mg/week. Exclusion criteria included active infection, recent malignancy (past 5 years), and previous treatment with biologics. The primary endpoint was a ≥0.50 unit improvement from baseline on the Health Assessment Questionnaire Disability Index (HAQ-DI) at month 24. Secondary endpoints included adverse events, Health and Labour Questionnaire score, physician and patient global assessments of disease activity, ≥75% Psoriasis Area and Severity Index (PASI-75) improvement, Psoriatic Arthritis Response Criteria (PsARC) response, and Fatigue Severity Scale (FSS) score. Month 12 interim efficacy data are reported here, calculated using last observation carried forward imputation.

Results: This intent to treat interim analysis was on 110 adults (mean±SD age: 48.4±10.9 years) with psoriasis (duration: 16.2±12.7 years) and PsA (duration: 8.9±8.4 years). At baseline, 109 of 110 patients had fair, poor, or very poor disease control on the Physician Global Assessment scale. Patients baseline HAQ-DI score was 1.50±0.56.

There were 27 (24.5%) discontinuations from the trial by month 12, most of which were due to adverse events (10%) or lack of efficacy (8.2%).

After 12 months of etanercept, patients' HAQ-DI score declined to 0.91±0.67, indicating improvement; in 57% (SD=5%) of patients, HAQ-DI score improved by ≥0.50 points. Seventy-eight percent (SD=8%) of patients were PsARC responders, and the PASI score improved (baseline: 4.8±7.8: month 12: 2.0±3.7), with 42% (SD=5%) of patients achieving a PASI-75. Patients also reported fewer days absent from work due to PsA (baseline: 0.8±2.5 days within past 2 weeks; month 12: 0.1±0.4 days) and reduced FSS scores (baseline: 6.36±2.19; month 12: 4.76±2.83).

Conclusion: This multicentre, open-label, single-arm longitudinal study is ongoing. Interim efficacy results suggest etanercept offers PsA patients long-term benefits in a real-world setting.

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A Meta-Analysis of Healing and Prevention of Digital Ulcers (DU) in Raynaud's Phenomenon (RP)

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Objective: Several trials have explored various drug therapies for digital ulcers (DU) in Raynaud's phenomenon (RP). The objective of this meta-analysis was to assess the efficacy of various treatments of DU.

Methods: All trials found in MEDLINE (January 1966 to present), EMBASE (1980 to present) for RP trials dealing with DU were found. Only randomised controlled trials comparing pharmacologic therapy with placebo or another agent were eligible. Trial quality was assessed with a quality score was based on randomisation, blinding, statistical methods, intention to treat analysis, and method of randomisation. Data from each trial were extracted and statistical analysis RevMan 5 software.

Results: Twenty-eight trials were found, and nine excluded. Main reasons for exclusion were non-randomisation, and no comparison agent. Quality score for trials was moderate (mean 2.9/5). Intravenous iloprost was associated with a significant increase in the healing of digital ulcers (relative risk 3.21; 95% CI 1.32 to 7.84). Nifedipine was associated with a small decrease in the number of patients developing new DU (relative risk 0.50; 95% CI 0.18 to 1.40). Bostentan was associated with a statistically significant reduction in the number of new DU (mean difference -1.30, CI -1.40 to -1.19) but not healing of DU. There was no significant difference in ulcer healing or prevention using dimethyl sulfoxide, anti-platelet medications, or prazosin. Only one single site trial with sildenafil showed a trend in ulcer healing but numbers with ulcers were small.

Conclusion: Small sample size, and limited data resulted very few proven treatments. The results suggest that there is some evidence to support use of intravenous iloprost in healing DU associated with RP. There may be some mild benefit in using the calcium channel blocker, nifedipine, to prevent DU. The evidence suggests bosentan decreases the number of new DU. More investigation is required, however, to further assess the suitability of these pharmacologic agents in treating and preventing DU in patients suffering with primary and secondary RP.

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Comparison of Canadian, British, and Swedish Patients Treated with Anti-TNF Therapies in a Real-life Clinical Setting

Janet Pope (University of Western Ontario); Carter Thorne (The Arthritis Program Research Group Inc., Newmarket, ON); Fotoula Psaradellis (JSS Medical Research Inc.); John Sampalis (JSS Medical Research Inc.) on behalf of investigators of the Optimization of Humira trial.

Objective: Use of anti-TNF therapy varies by country. Canadian rheumatologists, for example, may employ anti-TNF therapy less often than their US counterparts, because of issues related to access. We wanted to determine if real-world RA patients starting adalimumab therapy had similar disease severity vs. RA patients in registries.

Methods: The Optimization of Humira trial (OH) is an ongoing Canadian RCT comparing the effectiveness of intensive management targeting 0 swollen joints or minimal DAS28 score (DAS28<2.4) to routine care for RA patients receiving adalimumab in a real-life clinical setting. Baseline characteristics including DAS28, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), TJC, SJC, HAQ-DI, and patient's global assessment of disease activity (VAS) were compared withRA patient data in the British Society for Rheumatology Biologics Registry (BSRBR) and South Swedish Arthritis Treatment Group (SSATG) registry.

Results: 300 patients enrolled. Of these, 249 (83.0%) were naïve to anti-TNF therapy. Mean values (SD) in OH, BSRBR, and SSATG were DAS28: [OH: 5.8 (1.1) vs. BSRBR: 6.7 (1.0), p<0.001]; ESR: [OH: 30 (20) vs. BSRBR: 50 (28), p<0.001]; TJC: [OH: 12 (7) vs. BSRBR: 16 (7), p<0.001]; SJC: [OH: 11 (6) vs. BSRBR: 12 (6), p=0.01]; HAQ DI [1.5 (0.7) vs. BSRBR: 2.1 (0.5), p<0.001; and vs. SSATG: 1.3 (0.7), p<0.001]; VAS [OH: 62 (26) vs. BSRBR: 72 (20), p<0.001; and vs. SSATG: 54 (25), p<0.001]. Comparisons between patient baseline characteristics in OH indicated lower disease severity vs. the BSRBR, particularly for DAS28, ESR, TJC, SJC, HAQ-DI and VAS results. Moreover, patients in OH had a greater disease severity based on HAQ-DI and VAS vs. patients in the SSATG.

Conclusion: The results of this analysis suggest that, compared with British patients, Canadian patients begin anti-TNF therapies at lower disease severity but at greater disease severity vs. Swedish patients. Differences in access and other reasons may account for this.

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Comparison of Anti-TNF-Naïve and Anti-TNF-Experienced Patients with Rheumatoid Arthritis at Initiation of Treatment with Adalimumab: Baseline Results of the Optimization of Humira Trial

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Objective: RA patients experienced with anti-TNF therapy may be different than anti-TNF-naïve patients with respect to disease characteristics at onset of new anti-TNF treatment. Our objective was to compare baseline characteristics of anti-TNF-experienced patients with those of patients naïve to anti-TNF therapy at the time of initiation of adalimumab.

Methods: The aim of the Optimization of Humira study was to compare the effectiveness of intensive management targeting 0 swollen joints or minimal DAS28 score (DAS28<2.4) to routine care in RA patients who received adalimumab. As per the study protocol, a maximum of 20% anti-TNF experienced patients were included in the study. Baseline characteristics including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), TJC, SJC, DAS28, HAQ-DI, patient's global assessment of disease activity (PGA), age and sex were compared for anti-TNF-experienced, specifically those treated with etanercept or infliximab (EXP), and anti-TNF-naïve patients (NAÏVE).

Results: 300 patients enrolled. Their mean (SD) age was 54.8 (13.3) years and 81.0% were female. Of these, 237 (79.0%) were anti-TNF-naïve, and 51 (17.0%) patients were anti-TNF experienced (29 with etanercept, 16 with infliximab, and 6 for both etanercept and infliximab). 12 patients (4.0%) who had received other biologics were excluded. Mean values (SD) for the following parameters for EXP vs. NAÏVE patients, respectively, were CRP: [21.7 (32.9) vs. 17.5 (20.7)]; ESR: [28.7 (22.5) vs. 29.8 (20.4)]; SJC: [10.5 (6.0) vs. 10.7 (5.6)]; TJC: [12.8 (7.1) vs. 12.3 (7.3)]; and DAS28 [6.0 (1.2) vs. 5.8 (1.1)]. None of the between-group differences were statistically significant. However, the mean (SD) HAQ-DI for EXP patients of 1.7(0.6) was significantly greater vs. 1.5 (0.7) for NAÏVE patients (p=0.021). In addition, EXP patients had a greater patient assessment of disease activity vs. NAÏVE patients [71.3 (26.1) vs. 61.9 (26.2), p=0.021].

Conclusion: Although anti-TNF-naïve and anti-TNF-experienced patients who received adalimumab were similar with respect to several baseline parameters, significant differences in patient-reported measures (HAQ-DI and PGA) were observed, indicating more severe disease for anti-TNF-experienced patients.

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Inhibition of Progression of Structural Damage by Week 16 with Certolizumab Pegol: Results from the RAPID Trials

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Background: In the double-blind, placebo-controlled RAPID 1 (52 weeks) and 2 (24 weeks) trials, certolizumab pegol (CZP), the first, PEGylated, Fc-free TNF inhibitor, effectively reduced RA signs and symptoms and inhibited structural joint damage progression as add-on therapy to MTX. Patients who failed to achieve an ACR20 response at both Weeks 12 and 14 were withdrawn at Week 16. Previous studies reported that anti-TNF agents can inhibit radiographic progression independently of their ability to achieve an ACR20 response. A post-hoc analysis investigated whether inhibition of radiographic progression was evident at Week 16 in clinical non-responders treated with CZP + MTX.

Methods: Patients with active RA (N=982 RAPID 1 and N=619 RAPID 2) were randomized 2:2:1 to CZP (400 mg at Weeks 0, 2 and 4, followed by 200 or 400 mg every 2 weeks) or placebo (PBO), added to stable-dose MTX. Radiographs were taken at baseline (BL), Week 24 (both trials) and Week 52 (RAPID 1 only) or at withdrawal. Joint damage was assessed using the modified Total Sharp Score (mTSS) and erosion and joint space narrowing subscores (ES/JSN). Radiographic data at Week 16 from those patients who withdrew for ACR20 non-response were analyzed. Data from both CZP dose groups were combined for each study. An ANCOVA of the ranks was used, with treatment and region as factors and rank baseline mTSS as covariate.

Results: A total of 266 (RAPID 1) and 196 (RAPID 2) patients withdrew at Week 16 because they did not achieve an ACR20 response. Median DAS scores among these patients were similar at BL. BL mTSS, ES and JSN also were comparable in the CZP + MTX vs PBO+MTX arms. In both trials, changes from BL in mTSS, ES and JSN were significantly lower in the CZP + MTX arms than in the PBO + MTX arms among patient who withdrew at Week 16 (p≤0.05). Despite withdrawing at Week 16 due to lack of efficacy, a substantial % of patients treated with CZP + MTX in both trials had a ≥20% decrease from BL in the number of swollen and tender joints, respectively, at Weeks 12 and 14.

Conclusion: This analysis supports previous observations with TNF inhibitors that radiographic response is observed in patients not fulfilling the ACR20 response criteria. In these studies CZP + MTX rapidly retarded radiographic progression, with effects as early as 16 weeks.

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Long-Term Safety of Rituximab: 6-year Follow-up of the Rheumatoid Arthritis (RA) Clinical Trials and Re-treatment Population

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Purpose: To evaluate the long-term safety of rituximab (RTX) in RA patients.

Methods: Pooled analysis of safety data from a global clinical trial program for patients treated with RTX plus methotrexate (MTX). All patients were offered re-treatment with RTX as necessary.

Results: There were 5013 patient-years of RTX treatment for up to 6 years; 2578 RA patients received multiple courses (C) of RTX; 1890, 1043, 425, and 133 patients received ≥2, ≥3, ≥4, and ≥5 courses, respectively. Infusion-related reactions were the most frequent adverse events (AE), occurring in 35% of patients, though <1% were considered serious. Rates of AEs, serious AEs (SAEs), and overall infections remained stable following each course. The rate of serious infection events (SIEs) was stable for C1-C4, with a higher point estimate after C5 but with fewer patients (n=133) and a large confidence interval (Table). The number of infections, including SIEs/100 patient-years, was low when analyzed by exposure time from first dosing of RTX, and remained unchanged for each subsequent 6-month period. The overall SIE rate was 4.31/100 patient-years (95% CI: 3.77-4.92), and stable between periods at 4-6 events/100 patient-years. No tuberculosis reactivation was reported. IgG, M, and A decreased in some patients but in general was not sustained and not related to serious infections.

Conclusion: In this 6-year update of safety in RA patients, RTX remained well tolerated over multiple courses. Rates of overall AEs, SAEs, and infections remained stable over time and by treatment course, with the only exception being a higher point estimate for SIEs after C5.

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Certolizumab Pegol Inhibits Radiographic Progression at 16 Weeks of Treatment. Results from Two RCTs (RAPID 1 And 2)

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(University of Texas Southwestern Medical Center, Dallas, TX); RAPID 1 & 2 Investigators

Objective: In two RCTs: RAPID 1 (52 wks) and 2 (24 wks), certolizumab pegol (CZP), a PEGylated, Fc-free TNF inhibitor, reduced RA signs and symptoms and inhibited structural joint damage progression as add-on to MTX vs MTX alone. Those not achieving an ACR20 response at both Wks 12 and 14 were withdrawn at Wk 16. Previous studies reported that anti-TNFs can inhibit radiographic progression independently of their ability to achieve an ACR20. A post-hoc analysis at Wk 16 was done to determine if nonresponders treated with CZP+MTX had radiographic inhibition.

Methods: Active RA patients (N=982 RAPID 1 and N=619 RAPID 2) were randomized 2:2:1 to CZP (400 mg at Weeks 0, 2 and 4, followed by 200 or 400 mg every 2 wks) or placebo (PBO), added to stable-dose MTX. Radiographs were taken at baseline, and study end or withdrawal; using the modified Total Sharp Score (mTSS) and erosion and joint space narrowing sub-scores (ES and JSN). Radiographic nonresponder data from Wk 16 were analyzed, combining both CZP dose groups (200 and 400 mg).

Results: A total of 266 (RAPID 1) and 196 (RAPID 2) patients withdrew at Wk 16 because they did not achieve an ACR20. DAS scores among these patients were similar at baseline. Baseline mTSS, ES, and JSN also were comparable in the CZP + MTX vs. PBO + MTX arms. In both trials, changes from baseline in mTSS, ES, and JSN were significantly lower in the CZP + MTX arms than in PBO + MTX for patients who withdrew at Wk 16 (p 0.05). Despite withdrawing at Wk 16 due to lack of ACR 20, many patients with CZP + MTX had a ≥ 20% improvement in tender and swollen joints at Wks 12 and 14.

Conclusion: This analysis supports previous observations with TNF inhibitors that radiographic response is observed in patients not meeting an ACR20 response. However, the disconnect of clinical and radiologic response may be a problem of ACR criteria, where many non-respondents have improvements in joint counts but don't meet ACR20, or due to other biological reasons (of mechanism of antiTNFs). CZP + MTX showed radiographic inhibition as early as 16 wks.

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Assessment of Work Disability (WD) in Seronegative Spondyloarthropathies

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Background/Purpose: Seronegative spondyloarthropathies (SpA), including ankylosing spondylitis (AS), affect patients during their working years and may contribute to work disability (WD). In a recent meta-analysis of AS, figures for WD ranged from 3-50%, suggesting more research is needed [1]. We determined the prevalence of WD and limitations in work productivity in SpA using surveys, including the Work Limitations Questionnaire (WLQ).

Methods: After IRB approval, 260 patients with SpA received a mail questionnaire. The package contained the WLQ, HAQ, BASDAI, BASFI, BAS-G and Functional Comorbidity Index. The WLQ assesses work limitation on 4 scales: time demands, physical demands, mental-interpersonal demands and output demands. It measures on-the-job work limitations as well as loss of productivity at work. Relationships between WD, WLQ, demographics and disease activity were assessed through bivariate correlations and independent t-tests.

Results: Response rate was 31.2%; most had AS (64.2%). 46.9 % were male; mean age 45 years and disease duration of 10 years. The sex distribution of the respondents did differ from that of the original sample (60% male). 18.5% were WD in our assessment. Those with WD were older than non-WD (52.9 vs. 43.1 yrs, p<0.05), and also had higher scores on BASFI (6.8 vs 4.1), BAS-G (6.5 vs 4.6) and PGA of poor health (5.8 vs 4.0). WD also had significantly more comorbid diseases than non-WD (2.3 vs 4.0). WD was not associated with longer duration of disease, higher HAQ scores or higher BASDAI scores. Average decrease in work productivity due to health was 8.3%. Decreases in time management (37.3%), physical demands (28.5%), mental-interpersonal demands (23.0%) and output (33.1%) were noted. Reduced productivity was not associated with demographic factors. Productivity loss was highly correlated (r>0.6) with HAQ, BASFI, BASDAI,

and BAS-G scores. Decreased productivity also highly correlated with VAS fatigue, poor sleep, and overall health.

Conclusion: WD occurred in 18.5%, and work productivity was also reduced by 8.3%. WD was associated with older age and greater SpA disease activity. Losses in work productivity were highly correlated with currently used clinical outcome measures such as HAQ, BASFI, BASDAI and BAS-G. References:1.Boonen A et al. J Rheumatol 2001, 28:1056-1062.

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Role of TPMT Genotyping and Azathioprine Metabolites in Predicting Toxicity of Azathioprine in pSLE Patients

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Objective: To determine, if specific TPMT allelic variants or levels of the azathioprine metabolites, 6-TGN and 6-MMP, are associated with azathioprine toxicity in pSLE patients.

Methods: The cohort consisted of 56 pSLE patients treated with azathioprine who had TPMT polymorphisms G238C, G460A and A719G determined. In 38 of the patients levels of 6-TGN and 6-MMP were measured. Azathioprine toxicity was defined as leukopenia, white blood cell (WBC) count 100U/l. Sensitivity analysis of TPMT polymorphisms, metabolite levels and azathioprine toxicity was performed including positive (PPV) and negative predictive values (NPV).

Results: Four patients (7.1%) were heterozygous for TPMT A719G (allele frequency 3.6%) and one was also heterozygous for TPMT G460A. Two of the patients tolerated the regular dose of azathioprine while the other 2 developed significant leukopenia. Metabolites were measured in 3/4 and were elevated in only 1. However, this patient tolerated azathioprine well. Of the 52 patients with homozygous TPMT wildtype 36 patients (69%) tolerated full-dose azathioprine well while 16 patients (31%) developed toxicity. Leukopenia was seen in 4 patients (25%) and elevated LFTs in 12 patients (75%). Overall abnormal azathioprine metabolite levels were found in 9/35 patients (26%) with wildtype genotypes. Of the 9 patients with abnormal azathioprine metabolite levels, 3 had toxicity (1 leukopenia, 2 elevated LFTs) while 7 patients with normal metabolites had toxicity (3 leukopenia, 4 elevated LFTs). The sensitivity of TPMT polymorphisms for predicting azathioprine toxicity was 11% and specificity was 95% while the sensitivity of abnormal metabolites for predicting toxicity was 27% and specificity was 74%. Importantly the PPV of TPMT polymorphisms was good at 50% but the NPV was only 69%. Similarly the PPV of abnormal azathioprine metabolites was 30% and the NPV 71%.

Conclusion: Toxicity of azathioprine was common but abnormal TPMT polymorphisms were infrequently found. Testing for the TPMT genotyping and azathioprine metabolites was found to be of little value. We suggest that routine monitoring of LFTs and CBC is superior to TMPT genotyping and monitoring of metabolites to detect azathioprine toxicity in pSLE.

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Vascular Events in Systemic Lupus Erythematosus (SLE): Evaluation of Thrombophilic Factors in a Multicentre Inception Cohort (Thrombofil).

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Objective: (1) To quantify thrombotic risk in persons with newly diagnosed SLE, (2) to test if thrombotic risk is increased with antiphospholipid antibody (aPL) positivity, (3) to determine the role of concomitant activated protein C resistance (APCR), high sensitivity C-reactive protein (hsCRP), and elevated factors VIII (FVIII) or von Willebrand (vWF) in augmenting this risk.

Methods: ThromboFIL is an ongoing multicentre inception cohort that fol-

lows persons with newly diagnosed systemic lupus erythematosus (SLE) for incident vascular events (VE). 359 patients, diagnosed with SLE according to ACR criteria within five years and without VE at one year prior to diagnosis, were recruited from lupus clinics in five hospitals and followed annually for VE. All VE were confirmed by physician review. Clinical data collected at baseline and annually included demographics, medication history, traditional risk factors for cardiovascular disease (CVD), and disease activity (SLEDAI) and damage (SLICC/DI=SDI). For this analysis, SDI was modified to exclude VE (mSDI). Assays performed on 274 available bloods obtained at baseline and one year included: IgG and IgM anticardiolipin (aCL), lupus anticoagulant (LA), APCR, hsCRP, FVIII and vWF. Univariate and multivariate logistic regressions were performed.

Results: Mean age was 36.3 (± 14.4), 90% were female, 56.6% Caucasian, 16.8% were smokers, 8% had hypertension, and 2.5% had diabetes mellitus. Forty VE (30 venous; 10 arterial) occurred in 27 patients: 7 in the year prior to diagnosis; and 11 in yr 1(first year after diagnosis), 2 in yr 2, 3 in yr 3, 2 in yr 4, 1 in yr 5 and 1 in yr 8. Nine cases had multiple events. FVIII was the only laboratory variable significant in univariate analyses (OR=1.8; 95%CI=1.2, 2.9). Multivariate analyses showed gender (female; OR=0.13, 95%CI 0.04-0.50), SLEDAI (OR=1.11, 95%CI 1.4-1.20) and mSDI (OR=1.87, 95%CI 1.24-2.80) to be associated with VE. No laboratory tests were retained although the CI interval for FVIII was inconclusive.

Conclusion: Early VE in SLE was associated with higher disease activity and damage, and female gender was protective. We also show that FVIII may prove a useful marker for risk of VE.

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Group Visits for Rheumatoid Arthritis Patients: a Pilot Study

Kam Shojania (University of British Columbia); Matthew Ratzlaff (University of British Columbia)

Objective: A pilot study was conducted to explore the feasibility of a group visit model for patients with rheumatoid arthritis (RA) and for medical staff at a private practice.

Methods: RA patients deemed suitable for group discussion were invited to attend group visits in the meeting room of an outpatient hospital wellness centre. Six 3.5 hour long sessions were held monthly from July to December, 2007. Each session followed a pre-specified protocol and included time for group discussion, individual patient examinations, interactive question and answer periods, and topic-specific presentations from various health professionals. Participants completed a satisfaction questionnaire at the end of the last session.

Results: Nineteen of the 24 RA patients invited to the group visits agreed to attend, and approximately 13 to 15 were present at any given session. Participants expressed a high level of satisfaction in evaluation forms completed after the last session, reporting that they benefited from openly sharing experiences and coping strategies with other participants, and gained knowledge about RA and various treatments. Group visits allowed the rheumatologist to spend more time providing advice for various health issues and eliminated the need to repeat advice about common issues. The rheumatologist's overall time commitment and financial gain from the group visits were comparable to doing individual visits.

Conclusion: This group visit model is feasible for motivated RA patients who can meet the time commitment involved. Future research should explore correlations between the group visit model and patient compliance and disease outcomes.

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Development and Early Evaluation of an Interdisciplinary Post-graduate Academic and Clinical Education Program in Arthritis Care

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Objective: To present performance outcome data for the 2005-2008 (n=19) cohorts of ACPAC (Advanced Clinician Practitioner in Arthritis Care) Program graduates

To report quantitative and qualitative changes in clinical practice roles for the 2005-2007 cohorts identified at 6 and 12 months following graduation as new models of arthritis care develop in academic, non academic and remote community healthcare settings across Ontario.

Methods: Measurement of change in skills and knowledge of the 2005-2008 ACPAC program graduates involved a rigorous baseline and end-program theory and practical skills examination. Traditional and retrospective surveys were issued to the ACPAC trainee at baseline, mid-point and end program, as well as at 6 and 12 months following graduation to capture self-reported change in practice patterns across and subsequent to the training program. An externally conducted (arms length) structured interview of the ACPAC trained graduates and relevant stakeholders, including physicians and administrators, was undertaken at 12 months following graduation to identify barriers and enablers to the implementation of these new practice roles in arthritis care. The ACPAC education program was assessed using Dixon's levels of evaluation criteria [levels 2 (competency) and 3 (clinical practice)] in health education outcome.

Results: Evaluation of participants' learning and competency (Dixon's Level 2) for the 2005-2008 cohorts (n=19) showed significant change from baseline performance compared with the results of knowledge (p<.001) and skills (p<.001) exams at program completion. Change in clinical practice (Dixon's Level 3) was shown by quantitative analysis of responses from surveys issued at baseline, mid, end (2005-2008 cohort and 6 and 12 months post program (2005-2007 cohort) revealing an increase in frequency of certain advanced tasks and responsibilities across the training program. These are maintained at 12 months following graduation (2005-2007).

Triangulation of responses from the structured interview of physicians, administrators, and graduates identified five areas of emerging change in clinical role and responsibilities that were common to academic, non-academic and remote community healthcare facilities at 12 months following graduation. Changes in models of care appear directly related to the *enhanced triage* role of the ACPAC trained practitioner at 12 months post-program.

Conclusion: Extensive evaluation of the ACPAC trainees and program is integral to measuring the health education outcome process. Current research effort aims to determine the extent to which participants' clinical practices change in their advanced practice roles and the impact of the practitioner model on development of new models of care and interprofessional relationships.

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Case Report: 49-year-old Male with Psoriatic Arthritis Receiving Etanercept Who Contracted Neurosyphilis

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Objective: We report a potential infection with the use of biologic agents in an inflammatory arthritis patient.

Case: 49-year-old Caucasian male was diagnosed with Psoriatic Arthritis 5 years ago with involvement of his hands and feet with poor response with DMARDs and prompt response to Etanercept. He presented with visual blurring, dizziness, hearing loss and headache, which has been worsening over 6-week period. Four months prior, he reports of a painful ulcer on the penis and mouth that lasted two months for which medical attention was not sought. He had unprotected sex with several sexual partners prior to the development of the current symptoms. On examination, ulceration on the buccal mucosa of the lower lip and tongue. He also had exfoliation of the palms. Loss of vision on the right eye with limited eyesight in his left eye. No joint swelling or tenderness was noted. Initial laboratory evaluation revealed positive VDRL and FTA-ABS antibodies. Lumbar puncture confirmed the presence of lymphocytic pleocytosis and elevated protein. Cranial MRI with patchy white matter changes were noted. Patient was diagnosed with neurosyphilis with otitic involvement and uveitis. His treatment included penicillin and corticosteroid. His etanercept was discontinued and recovered with improvement of his neurologic symptoms but with decreased vision in the left eye with vision loss on the right.

Conclusion: Syphilis is an infection by Treponema pallidum that is con-

tracted sexually, with many different clinical presentations. Neurosyphilis is a rare infection in the antibiotic era but may pose a significant concern to patient on anti-TNF. Thus, immuno-compromised patients on biologic agents are at increased risk of infections. Patients often have no recollection of a primary chancre, as it is painless. Syphilis can be co-transmitted with other sexually transmitted diseases (e.g. Hepatitis, HIV). After the primary stage with the primary chancre at the site of inoculation (patient did not seek medical help for this), secondary syphilis produces a stage of generalised symmetrical rash, condylomata lata, painless generalised lymphadenopathy and constitutional symptoms.1 Many years later tertiary syphilis may develop manifesting itself as neurosyphilis (meningovascular syphilis) or as the cardiovascular form. Cardiovascular syphilis mostly manifests itself 10 to 25 years following the original inoculation. Non-specific iritis and iridocyclitis are the most commonly associated forms of uveitis and may be the predominant finding in secondary syphilis. Untreated syphilis leads to neurosyphilis and poses a great challenge in an immuno-compromised individual. Biologics have brought great relief and hope in the practice of Rheumatology. However, they are also associated with the development of serious life threatening infections and many other adverse effects (e.g. hematologic, cardiovascular, etc.). Thus, along with hope and relief of biologics comes extreme caution during selection of candidates, close observation, and emphasis on the importance of patient education.

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Increasing Use of ILAR Nomenclature and Classification System for Juvenile Idiopathic Arthritis (JIA) since 2004

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Objective: The ILAR classification system (ILAR-class), published 2004, collectively describing the childhood chronic arthritides as juvenile idiopathic arthritis (JIA), aimed to establish a single internationally accepted standard and nomenclature to facilitate interpretation and comparison of research. To determine if there has been increasing use of the ILAR-class in the medical literature between the years 2004 and 2007, both in North America and Europe; and secondarily to determine if ILAR-class has been used as intended.

Methods: We searched Medline and EMBASE core journal sets for the years 2004 and 2007 for all articles which reported original data and studied children or samples from children with chronic arthritis. Studies that described using ILAR criteria, or used the term JIA, were considered as using ILAR nomenclature. Geographic region was assigned by the primary affiliations of cited authors. Articles were scored as to correct use of the ILAR-class. A deviation from intended use was considered if the article used terminology or inclusion criteria inconsistent with published criteria or failed to consider exclusion criteria. Articles where intention of use could not be determined were excluded from this part of the analysis.

Results: Of 642 citations, 76 from 2004 and 92 from 2007 were eligible for inclusion. There was a significant increase in the usage of ILAR nomenclature from 2004 (61.8%) to 2007 (87.9 %), chi-square = 15.45, p < 0.05. This increase was significant in North America (42.1% to 78.9%, chi-square = 5.40, p < 0.05) and Europe (81.3 % to 92.5 %, chi-square = 6.62, p < 0.05). The analysis of usage of the ILAR criteria as intended was impeded by the lack of information specifying usage. Assuming that articles simply citing an ILAR publication were using ILAR -class correctly, there was not a significant change in use as intended: 85.7 % (2004) vs. 78.5 % (2007), chi-square =0.78, p = 0.38.

Conclusion: There has been significant uptake of nomenclature of ILAR-class internationally, although it was difficult to determine if criteria had been used as intended, particularly where reclassification of long term patients was not described. Improvement and evolution of classification should build on this internationally accepted base.

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How Sleepy Are Our Patients? An Assessment Utilizing Epworth

Sleepiness Scores in Rheumatology Clinic Patients

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Objective: To evaluate prevalence of sleepiness by utilizing the Epworth Sleepiness Scoring (ESS) system in a rheumatology clinic patient population. Secondly to compare pain, fatigue, global functioning, and modified Health Assessment Questionnaire scores in patients with and without abnormal ESS results.

Methods: Consecutive Rheumatology clinic patients were invited to participate in a self-administered questionnaire study. The questionnaire included: visual analogue scale measures for patient perceived pain, fatigue, and global functioning, the modified Health Assessment Questionnaire (mHAQ), the SF-36 quality of life measures, as well as the Epworth Sleepiness Score (ESS) questionnaire. An ESS of > 10 is considered abnormal and consistent with heavy sleep debt.

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. The diagnostic categories included: RA (n = 98) 35 %, seronegative arthritis (n =79) 28.2%, osteoarthritis and crystalline arthropathies (n = 47) 16.8 %, connective tissue diseases (n = 33) 11.8 % and soft tissue musculoskeletal disorders (n = 23) 8.2%. The mean age was 52.6 years (range 18-87). 25.9% were male. A previous medical evaluation for a sleep disorder was reported by 10% of patients. Pre-existing diagnoses of sleep disorders were reported by 13 % of patients (6% with OSA, 4 % with insomnia, 2 % with RLS, and 1 % with 'other' sleep disorders). Of the 280 study participants, 274 correctly completed the ESS instrument. The proportion of these patients with abnormal (> 10) ESS scores was .277 (95% CI ± .0530). There are statistically significant relationships observed between the abnormal ESS and patient symptoms of pain and fatigue, global functioning, depression scores, and quality of life summary measures. There were no significant differences perceived between normal and abnormal ESS groups on the basis of age, gender, marital status, or BMI.

Conclusion: 27.7% of all participating Rheumatology Clinic patients had abnormal Epworth Sleepiness Scores in this questionnaire study. Abnormal ESS scores were associated with poorer global function, mHAQ, fatigue and pain score results.

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Restless Legs Syndrome in a Rheumatology Clinic Patient Population

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Objective: To utilize the 2003 International Restless Legs Syndrome Study Group (IRLSSG) diagnostic criteria in evaluation of the prevalence of Restless Legs Syndrome (RLS) in a rheumatology clinic patient population. Secondly, to compare pain, fatigue, global functioning, modified Health Assessment Questionnaire (mHAQ), depression scores and sleep assessment instrument scores between patients who met RLS criteria and those who did not.

Methods: Consecutive Rheumatology Clinic patients were invited to participate in a self-administered questionnaire study. The questionnaire included: visual analogue scale (VAS) measures for patient perceived pain, fatigue, and global functioning, the mHAQ, the Center for Epidemiologic Studies Depression score (CES-D), the Epworth Sleepiness Score (ESS), as well as the Pittsburgh global sleep quality index (PSQI) and the IRLSSG diagnostic criteria for RLS. To make a diagnosis of RLS, all four diagnostic criteria must be positive.

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. The diagnostic categories included: RA (n = 98) 35 %, seronegative arthritis (n =79) 28.2%, osteoarthritis and crystalline arthropathies (n = 47) 16.8 %, connective tissue diseases (n = 33) 11.8 % and soft tissue musculoskeletal disorders (n = 23) 8.2%. The mean age was 52.6 years (range 18-87). 25.9% were male. A previous medical evaluation for a sleep disorder was reported by 10% of patients. Pre-existing diagnoses of sleep disorders were reported by 13 % of patients (6% with

OSA, 4 % with insomnia, 2 % with RLS, and 1 % with 'other' sleep disorders). The IRLSSG diagnostic criteria component of the questionnaire was correctly completed by 271 of the 280 participants. In this study population, the proportion who met all four criteria for RLS was .251 (95 % CI: ± .0516). Those who met RLS criteria are observed to have significantly higher levels of sleepiness by ESS, poorer PSQI scores and higher CES-D and mHAQ scores than those who did not. There are also a higher percentage of those with high risk for obstructive sleep apnea by Berlin score in the RLS group. There were no significant differences observed between groups in terms of fatigue, pain, global function, age, gender or BMI.

Conclusion: A quarter of all rheumatology clinic patients meet criteria for RLS. Those patients who met RLS criteria had poorer sleep quality and higher ESS results. However, they did not have higher pain scores, supporting a separation from articular discomfort as an underlying causal factor.

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Does an Abnormal Sleep Score Predict a Worse Quality of Life?

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Objective: To compare Quality of Life (QOL) scores between Rheumatology Clinic patients with and without abnormal sleep instrument scores.

Methods: Consecutive Rheumatology Clinic patients were invited to participate in self-administered questionnaire study. The questionnaire included the SF-36 QOL instrument, the Epworth Sleepiness Score (ESS), the Berlin sleep score, the Pittsburgh global sleep quality index (PSQI) and diagnostic criteria for restless legs syndrome (RLS).

Results: Of 341 consecutive rheumatology clinic patients invited to participate in this questionnaire study, 280 agreed. The diagnostic categories included: RA (n = 98) 35 %, seronegative arthritis (n =79) 28.2%, osteoarthritis and crystalline arthropathies (n = 47) 16.8 %, connective tissue diseases (n = 33) 11.8 % and soft tissue musculoskeletal disorders (n = 23) 8.2%. The mean age was 52.6 years (range 18-87). 25.9% were male. A previous medical evaluation for a sleep disorder was reported by 10% of patients. Pre-existing diagnoses of sleep disorders were reported by 13 % of patients (6% with OSA, 4 % with insomnia, 2 % with RLS, and 1 % with 'other' sleep disorders). In this study population, 28% had abnormal ESS, 67% had abnormal PSQI, 40% had high risk Berlin scores for OSA, and 25% met RLS diagnostic criteria. Comparison of SF-36 physical and mental summary component scores between those with abnormal sleep assessments and those without revealed significantly poorer QOL scores in those with high risk Berlin scores for OSA compared to low risk, as well as in those with abnormal ESS and PSQI scores compared to normal. Comparison of those meeting RLS criteria and those who did not revealed significant differences in mental summary scores, but not physical summary component scores.

Conclusion: Patients with abnormal sleep scores and meeting criteria for RLS were observed to have significant differences in SF-36 QOL measures compared to those with no such abnormalities.

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A Cross-Sectional Study on the Relation Between Clinical Characteristics and MRI Findings in the Hands of Rheumatoid Arthritis Patients — Preliminary Results

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Objective: To assess the correlation between magnetic resonance imaging (MRI) findings and each of clinical joint count and disease symptoms in the metacarpophalangeal (MCP) joints of rheumatoid arthritis (RA) patients as assessed by a 1T peripheral MRI (pMRI) scanner. Comparisons between a 1T pMRI scanner and a 3.0T full-body MRI scanner will be conducted.

Methods: In a cross-sectional study, the 2nd to 5th MCP joints of the hand most affected by RA are scanned in 150 RA patients with varying degrees of disease activity using a1T pMRI scanner. MR images are evaluated using the OMERACT RAMRIS scoring system, providing a semi-quantitative measure of bone erosions. A second analysis will quantify bone erosion volume using a semi-automated software algorithm, which can detect erosions as small as 4mm in diameter with sufficient short-term reproducibility. Clinical (DAS28), laboratory (RA biomarkers), health assessment (HAQ) and radiographic (SHARP and number of erosions) data are collected, and each correlated with MRI findings using a linear-regression analysis. RAMRIS scores for bone erosions, synovitis and bone edema will further be compared between the 1.0T and 3.0T MRI scanners in 30 participants using a Wilcoxon test. Significance for all tests will be assessed at the 95% confidence level.

Results: Enrollment began in July 2008 and will be completed by spring of 2009. Data were collected on 17 participants, who were 57.9±16.39 years of age, had 3.69±4.12 years of symptom duration, 2.63±4.71 swollen joints and 3.15±5.63 tender joints. Upon inspection, 1T pMRI appeared to detect a greater number of erosive and pre-erosive damage compared to radiography, including number of erosions and pre-cortical ruptures. While results are inconclusive, data is still being collected and statistical analyses will be performed when a sufficient sample is obtained.

Conclusion: It is anticipated that MRI findings will detect a greater number of erosions than X-ray. We expect that MRI findings will more strongly correlate with disease symptoms and activity than would joint count, thus providing a more reliable indication of disease status. The study will also validate the use of 1T pMRI as a tool for assessing characteristic features of disease activity in RA.

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The Effects of Nabilone on Sleep in Fibromyalgia: Results of a Randomized Controlled Trial

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Objective: Fibromyalgia (FM) is a chronic pain syndrome associated with dysregulation of central nervous system pain processing. Insomnia affects over 75% of patients, and tricyclic antidepressants are the mainstay of treatment. Cannabis is used by some patients with FM to help sleep. We evaluated the safety and efficacy of nabilone, a synthetic cannabinoid, on sleep disturbance in FM.

Methods: We conducted a randomized double-blind active control equivalency crossover trial to compare nabilone (0.5-1.0mg before bedtime) to amitriptyline (10-20mg before bedtime) in FM patients with chronic insomnia. Subjects received each drug for two weeks with a two-week washout period. The primary outcome was sleep quality, measured by the Insomnia Severity Index (ISI) and the Leeds Sleep Evaluation Questionnaire (LSEQ). Secondary outcomes included pain, mood, quality of life and adverse events (AEs).

Results: Thirty-one subjects were enrolled and 29 completed the trial (26 female, mean age 49.5 years). While sleep was improved by both amitriptyline and nabilone, nabilone was superior to amitriptyline (ISI difference=3.2, 95% CI 1.2-5.3). Nabilone was marginally better on the restfulness (LSEQ difference=0.5 (0.0-1.0) but not on wakefulness (difference=0.3 (-0.2, 0.8)). Adverse events (AEs) were mostly mild to moderate and were more frequent with nabilone. Most common AEs for nabilone were dizziness, nausea and dry mouth.

Conclusion: Nabilone is effective in improving sleep in patients with FM and is well tolerated. Low dose nabilone given once daily at bedtime may be considered as an alternative to amitriptyline. Longer trials are needed to determine the duration of effect and to characterize long-term safety.

The trial was conducted following Good Clinical Practice guidelines and was registered at www.clinicaltrials.gov (registration number NCT00381199).

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Is Isolated Angiitis Of The Vasa Vasorum A Precursor To Clinical GCA?

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Objective: To describe 4 cases of isolated angiitis of the vasa vasorum (IAVV) and examine its relation to the pathogenesis of GCA.

Methods: Case series and literature review.

Results: Patient 1 presented with acute monocular vision loss. The ESR was 31 mm/hr and CRP was normal. Temporal artery biopsy revealed mononuclear infiltrates in the adventitial layers surrounding a spared temporal artery. History, physical and immunologic markers were unremarkable. Patient 2 presented with a suspected anterior ischemic optic neuropathy of the right eye. No symptoms of GCA were reported. The ESR and CRP were 39 mm/hr and 10.8 mg/L, respectively. Biopsy revealed mononuclear inflammatory cells in the vasa vasorum of the temporal artery. No signs or symptoms of a systemic vasculitis were encountered. All immunologic markers were negative. Patient 3 was admitted to hospital with severe polyarthralgia of the large joints, headaches, jaw claudication and myalgia. The ESR and CRP were both markedly elevated. Temporal artery biopsy showed small caliber vessels cuffed by lymphocytes at the adventitial-perivascular junction. Rheumatologic review revealed muscle pain and weakness of the shoulder and pelvic girdle indicative of PMR. Patient 4 presented with symptoms thought to be consistent with PMR. TA/GCA was suspected after failure to respond to prednisone therapy. A temporal artery biopsy revealed light, patchy chronic inflammatory infiltrates associated with several vasa vasora with no inflammation or fibrinoid necrosis within the wall of the artery.

Conclusion: This series demonstrates that patients with IAVV are at risk for serious complications. IAVV can present without classic clinical symptoms of GCA and only slightly abnormal or even normal inflammatory makers. Treatment should be initiated immediately, as in biopsy-proven GCA. Recent evidence indicates that the inflammatory process of vasculitides begins at the level of the vasa vasorum. Thus, it is possible that IAVV is the precursor to GCA. The prognostic benefits of treating this vasculitis in its early stage are as yet unknown and further study may be warranted.

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Classification Criteria for Early Inflammatory Arthritis

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Objective: To establish classification criteria (CC) for early inflammatory arthritis (EIA).

Methods: Initial rheumatology presentation summaries for a sample of 30 prevalent inflammatory arthritis cases from a general rheumatology clinic and EIA clinic were assessed by a convenience sample of 18 rheumatologists. These cases, representing characteristics: age, gender, symptom and morning stiffness duration (AMS), joint counts, acute phase reactant levels, rheumatoid factor status, and others, where translated into paper cases. Rheumatologists classified each case as either EIA or not. Responses were compared with three CC: 1)Emery et al. (2002) referral recommendation for newly diagnosed RA (Emery: ≥3 swollen joints, OR ≥30 minutes AMS, OR MTP, OR MCP involvement); 2)criteria derived from a Delphi process incorporating feedback from 29 EIA rheumatology experts (Bell: ≥2 swollen joints AND six to 52 weeks symptom duration); and, 3a)fulfillment of either the 1987 American College of Rheumatology CC for RA OR 3b)European Spondyloarthropathy Study Group CC for spondyloarthropathy (ACR/ESSG). Common odds ratios (OR) and Breslow-Day (BD) heterogeneity tests for the association between rheumatologists' and criteria classification were calculated. The multiple rater kappa association was determined.

Results: Mean±SD age was 43±17 years. Eighty percent of cases were female. Median (interquartile range) symptom duration was 40 (24,104) weeks, AMS, 60 (18,120) minutes; swollen joint count, 6 (1,13); erythrocyte sedimentation rate, 25 (10,51) mm/h; and, C-reactive protein, 5 (1,14) mg/L. Rheumatologists, 50% female, were from Europe (43%), North America (40%), and Australia (17%), and 56% were academics. The majority was from an urban setting (94%), at mid-career stage (83%), or had an institutional prac-

tice (83%). The OR (95% CI; BD p value) for the associations between rheumatologist and criteria classification were: 10.3 (4.6,23.2;0.17) for Emery et al. (2002); 4.4 (2.5,7.7;0.28) for Bell; and, 0.7 (0.4,1.1;0.90) for ACR/ESSG; multiple rater kappa was 0.13±0.01 (p<0.001). Across rheumatologist demographic strata, the relative strength of associations was maintained.

Conclusion: Rheumatologists' classification of EIA was most strongly associated with the Emery et al. (2002) criteria.

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Baseline Predictors of RA-Associated Antibodies Seroconversion and Seroreversion Over 30 Months in Patients with Early Inflammatory Polyarthritis (EPA)

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Objective: To define the baseline predictors to develop (seroconversion) in initially seronegative patients, and to loose (seroreversion) in initially seropositive patients any of 3 RA-associated antibodies, over the first 30 months following onset of polyarthritis (EPA).

Methods: A set of demographic, clinical, genetic and environmental factors were assessed at inclusion in a cohort of consecutive adult patients with EPA. RA-associated antibodies (RF, anti-Cyclic Citrullinated Peptide (CCP) and anti-Sa) were measured at inclusion, at 18 and at 30 months. HLA-DR alleles were classified as encoding the Shared Epitope (SE), the DERAA epitope (DERAA), or non-SE and non-DERAA alleles (X, including HLA-DR3).

Results: An analysis of the first 208 patients is presented. At baseline vs 30 months, 89 (43%) vs 71 (34%), 75 (36%) vs 81 (39%), and 48 (23%) vs 25 (12%) patients were positive for RF, anti-CCP and anti-Sa, respectively. Four courses were determined for each antibody: remain positive, remain negative, become positive and become negative. Anti-Sa fluctuated more than anti-CCP (p=0.007), but stability was not significantly different between RF and anti-CCP nor between RF and anti-Sa.

In initially anti-CCP negative patients, double dose SE was associated with a trend towards conversion for anti-CCP (2/7 (28%) vs 9/125 (7%), p=0.10), but not for RF and anti-Sa. DERAA and HLA DR3 were not associated with antibody stability.

Age had an antibody-specific influence. Patients under 50 were more likely to loose RF (12/32 (37%) vs 9/57 (16 %) p=0.021), while anti-Sa negative patients under 50 were more likely to develop anti-Sa (5/52 (10%) vs 0/108 (0%) p=0.003); mean age of seroconverters 43.5 vs 59 y.o., p=0.0001. Anti-Sa seroconversion was more frequent in women under 45 than in women above 55 y.o. (2/24 (8%) vs 0/56 (0%) p=0.087). Age and gender had no influence on anti-CCP stability. Tobacco use was not associated with the stability of any RA antibody.

Conclusion: Our data support antibody-specific associations for genetic and demographic characteristics during the first years of EPA. Younger age (especially in premenopausal women) had divergent influences on the stability of RA antibodies. Our data add to the differences between anti-CCP and anti-Sa, although both target citrullinated antigens.

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Safety and Efficacy of Abatacept Over 4 Years of Treatment in Patients with Rheumatoid Arthritis and an Inadequate Response to Methotrexate in the AIM Trial

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Objective: To present the safety and efficacy of abatacept over 4 years in the AIM trial.

Methods: AIM was a randomized, double-blind (DB), placebo-controlled trial of 12 months' duration. Patients received a fixed dose of abatacept (~10 mg/kg) or placebo, plus methotrexate (MTX). Patients completing the DB period were eligible to enroll in the open-label long-term extension (LTE) period (fixed dose of abatacept ~10 mg/kg every 4 weeks plus MTX). Safety was assessed for all patients who received ≥1 dose of abatacept; incidence rates per 100 patient-years (pt-yrs) were calculated. Efficacy analyses included ACR 20, 50 and 70 responses, and are presented for all patients with data available at the visit of interest (as-observed analysis).

Results: A total of 433 and 219 patients were randomized and treated with abatacept or placebo, respectively; 378 and 161 of these patients entered the LTE period. In total, 414/539 (76.8%) patients who entered the LTE remained on treatment at the end of the 4 year study period. The types and incidence of adverse events (AEs) and serious adverse events (SAEs) were similar between the DB versus cumulative (combined DB + LTE) periods (303.4 vs 244.2/100 pt-yrs and 17.7 vs 14.7/100 pt-yrs, respectively). Incidence rates of infections and serious infections were 90.5 versus 69.0/100 pt-yrs and 4.2 versus 3.1/100 pt-yrs, in the DB versus cumulative periods, respectively. Malignancies, autoimmune events and tuberculosis (TB) were reported in 28 (4.7%), 45 (7.6%) and 3 (0.7%) patients, respectively, over 4 years. In the cumulative study period, 62 (10.4%) and 40 (6.7%) patients discontinued due to AEs and SAEs, respectively. The proportion of abatacept-treated patients who were ACR responders increased over 4 years; with no overlap of 95% CIs at 6 months and 4 years.

Conclusion: In the LTE period of the AIM trial, the safety of abatacept remained consistent with the DB period, with no unique or unexpected events observed over 4 years. Retention rates remained high and abatacept provided durable improvements in ACR responses over 4 years of treatment.

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The Frequency of Autoantibodies in the Canadian Scleroderma Research Group Cohort

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Objective: The serological hallmark of systemic sclerosis (SSc) is the presence of circulating autoantibodies directed to a variety of nuclear and cytoplasmic antigens. There have been few studies that have simultaneously analyzed the frequency of a wide range of these autoantibodies in a large SSc cohort using state of the art diagnostic technologies. The goals of this study were to determine the frequency of autoantibodies in a cohort.

Methods: Sera from 814 patients enrolled in the Canadian Scleroderma Research Group (CSRG) were evaluated for autoantibodies to an array of autoantigens. The assays included indirect immunofluorescence (IIF) on HEp-2 cells (ImmunoConcepts, Sacramento, CA) at a screening serum dilution of 1/160, addressable laser bead immunoassay (ALBIA: chromatin, Sm, U1RNP, Rib P, topoisomerase I (topo I), Jo-1, SS-A/Ro60, Ro52, SSB/La: QuantaPlex8, INOVA Diagnostics), line immunoassay (centromere (CENP), PM/Scl, fibrillarin) and ELISA (RNA polymerase III (RNAP), PM/Scl).

Results: By IIF 36 (4.4%) had a negative ANA. The frequency of specific autoantibodies was 14% (topo I), 33% (CENP), 4% U1RNP, 15% (RNAP), 9% PM/Scl, 20% Ro52, 7% SSA/Ro60, 4% chromatin, 3% SSB/La and 0.6% (Jo-1). In a subset of the SSc cohort the frequency of anti-fibrillarin was 4% and not all anti-CENP antibodies were identified by IIF. Antibodies to mitochondria, considered a marker for primary biliary cirrhosis were identified in 2% and were commonly associated with anti-CENP.

Conclusion: At a frequency of 33%, autoantibodies to CENP are the most common in the CSRG cohort. Of interest antibodies to Ro52 (20%) are the second most common autoantibody followed by RNAP and Topo I.

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Neurological Adverse Events on Anti-TNF Therapy

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Objective: We present a series of seven patients who developed neurological manifestations while on anti-TNF treatment.

Methods: All patients attended a rheumatology clinic in a teaching hospital, with 150 patients currently on anti-TNF therapy. In the past three years seven patients developed various neurological adverse effects. Data was collected by chart review.

Results: Five patients had AS while 2 had RA. The median (range) age was 49 (31-67) yrs. The median (range) disease duration was 14 (4-41) years. Two patients had family history of autoimmunity. Five patients were on infliximab (3-5 mg/Kg Q8Wk) and 1 each was on adalimumab (40 mg weekly) and etanercept (50 mg weekly). Three patients were on methotrexate ± HCQ before the event. The median (range) duration of anti-TNF therapy at the time of onset of neurological events was 24 (4-60) months. All patients had good control of their rheumatic disease at the time of the neurological event. The adverse events were (i) peripheral numbness and pareasthesiae (3 patients) (ii) diplopia with trochlear nerve palsy (iii) memory loss (iv) intention tremor (v) recurrent falls (one patient each). NCV revealed axonal ulnar neuropathy in one patient and was normal in one patient. Brain MRI was performed in 3 patients and was normal in all. ANA developed in 3/5 AS patients and one RA patient. Anti-TNF was stopped in 6 patients and all patients recovered neurologically over a median (range) duration of 6 (4-8) months. The serial autoantibody (ANA ± dsDNA) titer decreased after stopping anti-TNF medication in all patients. One patient was restarted on infliximab with resultant worsening of symptoms. The respective biological agent was changed to an alternative anti-TNF agent in 2 patients with no recurrence of the neurological symptoms.

Conclusion: Anti-TNF therapy can be associated with significant, but reversible neurological adverse events. In our experience a switch to an alternative anti-TNF agent was safe in such patients.

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Frequency of Bone Marrow Edema in Knee Osteoarthritis and Association with Pain Severity: Results from a Population-Based Study

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Objective: To evaluate the prevalence of bone marrow edema (BME) in a population-based study of early knee osteoarthritis (OA) and to determine the association between BME and pain severity.

Methods: Subjects, age 40-79 years, with knee pain were assembled, stratified by age decade and gender, in a cross-sectional population-based study and evaluated using clinical, x-ray, and magnetic resonance imaging (MRI) assessments. BME (0-3; none, mild, moderate, severe) was scored on MRI in 6 knee regions. BME severity was defined as BMEsum = sum of 6 BME scores and BMEmax = worst score at any region. Pain was assessed by Western Ontario and McMaster Universities (WOMAC) OA Index. Stage of OA was defined by x-ray Kellgren-Lawrence (KL) 0-4 and MR cartilage (MRC) 0-4 grading: No OA (NOA) (KL<2 and MRC=0), Pre-Radiographic OA (PROA) (KL<2 and MRC≥1), and Radiographic OA (ROA) (KL≥2 and MRC≥1). To assess the association of BME with pain severity, linear regression analysis was performed using Total WOMAC Pain as the primary outcome. Secondary outcomes were WOMAC Pain on Walking (Pain1) and WOMAC Pain on Climbing Stairs (Pain2). All analyses were adjusted for age, gender, body mass index, with or without OA stage, and incorporated stratum sampling weights.

Results: Of 255 subjects, 23 had NOA, 134 had PROA, and 98 had ROA. BME (BMEmax>0) was present in 8%, 37% and 74% of NOA, PROA, and

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ROA subjects respectively (p<0.01). Median BMEmax and BMEsum increased with OA severity (p<0.01 for both). No significant association was seen for BMEsum with Total WOMAC Pain (Regression Coefficient (RC)=0.06, 95% Confidence Interval (CI) [-0.03, 0.15]). BMEsum, however, was significantly associated with Pain1 (RC=0.12, 95% CI [0.00, 0.23]) and Pain2 (RC=0.27, 95% CI [0.08, 0.46]). For BMEmax, a significant association was seen only with Pain2 with the strongest association for severe BME compared to no BME (RC=0.61, 95% CI [0.05, 1.17]).

Conclusion: More than one third of pre-radiographic and the vast majority of radiographic knee OA have BME. Worse BME scores were associated with increased pain on walking and climbing stairs. In this population-based cohort of symptomatic subjects consisting mostly of PROA, BME severity is an important contributor to knee pain.

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Comparison of the Clinical Manifestations and Disease Severity of Systemic Lupus Erythematosus (SLE) Among Vancouver Residents Of Asian And Caucasian Origin.

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Objective: To compare Caucasian and Asian SLE patients followed by selected rheumatologists in the Greater Vancouver area for: 1) clinical manifestations and pattern of organ involvement; 2) Disease severity using the SLICC damage index.

Methods: A retrospective medical chart review was conducted for the period 1999-2005 of rheumatology practices selected for large numbers of lupus patients of Asian origin. To be included patients had to meet 1982 ACR criteria for SLE and be Caucasian or Asian. Ethnicity was determined by chart review or by asking the treating rheumatologist if missing from chart. Asian ethnicity included Chinese, Japanese, Philippino, and Vietnamese. East Indians were not considered as Asians. Data were extracted using a standard form that included: demographics, SLE duration, 1982 ACR criteria, SLE treatment, SLICC, and involvement of the following systems, using predefined criteria derived from the SLAM: skin, myositis, arthritis, haematological, renal, cardiovascular, pulmonary, gastrointestinal, and neuropsychiatric manifestations.

Results: Our sample included 165 Caucasians and 102 Asians (Mean age: 41.1 vs 44.9 years, resp. and 88.6% vs. 95% were female, resp). Asian patients had more frequent renal involvement than Caucasians: proteinuria (41% vs 17%, resp.), biopsy proven glomerulonephritis (39% vs 13%), renal insufficiency (15% vs 4%) & end-stage renal failure (8% vs. 2%); as well as haematological manifestations: lymphopenia (80% vs. 60%) and thrombocytopenia (37% vs 22%) (all p < 0.05). Caucasian patients had more frequent skin disease compared to Asians: discoid rash (15% vs 7%) and photosensivity (48% vs 30%), as well as neuropsychiatric manifestations, mainly cognitive impairment, anxiety, mood disorders and migraine headaches, but severe CNS involvement, such as vasculitis, CVA, seizures or psychosis, were not more frequent. Other SLE manifestations did not differ between grps. SLICC scores were not different between the 2 grps (median = 1.0 in both).

Conclusion: In our sample of Vancouver residents, people of Asian origin had a different pattern of SLE manifestations, with more renal and haematological, but less CNS disease, compared to Caucasians. There was no significant difference in disease severity between the two groups using the SLICC damage index.

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Tocilizumab Combined with Methotrexate Induces a Rapid and Sustained Decrease of Bone and Cartilage Degradation in Patients with Rheumatoid Arthritis

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Objective: Investigate the time and dose-dependent effects of tocilizumab (TCZ) plus methotrexate (MTX) on bone and cartilage turnover markers in patients with moderate to severe rheumatoid arthritis (RA) from the randomized, placebo-controlled, phase 3 OPTION study.

Methods: 416 of the initial 623 patients randomized in OPTION with an inadequate response to MTX were included (80% female, mean age: 52 yr, mean disease duration 7.5 yr, mean DAS 28, 6.82 units), based on providing consent for biochemical specimen analysis. They were randomized to receive one of three infusions every 4 weeks for 20 weeks with final follow-up at week 24: TCZ at 8 mg/kg +MTX, 4 mg/kg +MTX, or placebo +MTX (10 to 25 mg weekly). At baseline and after 4, 16 and 24 weeks, serum markers of bone formation (type I collagen N-propeptide, PINP), bone resorption (ICTP), cartilage turnover (type IIA collagen N-propeptide, PIIANP), cartilage degradation (type II collagen helical peptide, Helix-II) and matrix-metalloprotease-3 (MMP-3) were measured.

Results: TCZ + MTX induced a decrease of ICTP versus placebo + MTX which was significant at week 16 in the 8 mg/kg dose (-12.0%, p<0.05), with a similar reduction at week 24 (-12.0%, p<0.001). As early as 4 weeks, TCZ 8 mg/kg + MTX decreased cartilage turnover markers PIIANP and Helix-II, and MMP-3 which was significant, with further reduction at week 16 and week 24. Both doses of TCZ+MTX modestly increased bone formation marker PINP, which was significant at week 4. Patients receiving TCZ + MTX with clinical remission at week 24 (DAS 28 <2.6) had a significantly larger decrease in ICTP (median: -25.6% vs -8.4%, p <0.01), Helix-II (-68.8% vs -36.7%, p<0.0001) and MMP-3 (-60.6% vs -50.0 p<0.05) than non-responders.

Conclusion: Combined with MTX, TCZ at 8 mg/kg rapidly and markedly reduced biochemical markers of bone resorption, cartilage turnover and MMP-3. This biochemical marker data suggests that this therapeutic combination may have structural effects that need to be confirmed by radiological data.

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Severity of Hip Disease Is Coupled with Severity of Spinal Disease in Ankylosing Spondylitis

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Objective: In ankylosing spondylitis (AS) chronic inflammation in the sacroiliac joint and spine is followed by ankylosis. In the hip, it is followed by cartilage erosion and joint destruction. The frequency and predictors of hip disease in AS have not been fully elucidated. We address these issues in the current study.

Methods: Patients attending the spondylitis clinic in a large teaching hospital are seen according to a standard protocol in which clinical, demographic, laboratory and radiographic data are recorded at regular intervals. All patients met the modified New York criteria for AS. All patients had Xrays of the cervical and lumbar spine and pelvis as part of their clinical assessment. The AS cohort was then divided into the presence (HIP+) or absence (HIP-) of hip disease by radiographic evidence of joint space narrowing or by total hip replacement (THR). Means and standard deviations (SD) were calculated for various clinical variables and compared using the students t-test.

Results: Amongst 220 AS patients, 47 (21.4%) had radiographic evidence of hip disease and of these, 15 patients (6.7% of the cohort) had had THR (8 bilateral, 7 unilateral). Mean current age in years (±SD) was 42.8 (±14.7) in the HIP+ and 38.9 (±12.9) in the HIP- groups (p=0.08). Mean disease duration in years (±SD) was 19.3 (±11.6) in the HIP+ and 15.6 (±11.3) in the HIP- groups (p=0.05).

There was no difference in proportion of HLA-B27 positive patients, 75.7% (HIP+) and 82.3% (HIP-), or in the proportion with juvenile onset AS, 25.5% (HIP+) and 24.9% (HIP-). There was a trend towards greater number of males in the HIP+ group (89.4% versus 78.6%) (p=0.10). There was no statistical difference in BASDAI, ESR or CRP between the 2 groups.

There was a significant difference in the radiographic and clinical severity of spinal disease between the 2 groups. Mean mSASSS (±SD) was 32.4 (±27.7) in the HIP+ and 16.1 (±22.0) in the HIP- groups (p<0.001). Mean BASMI (±SD) was 4.9 (±2.7) in the HIP+ and 2.7 (±2.4) in the HIP- groups (p<0.001). We analyzed a modified BASMI in which the intermalleolar distance score was excluded (BASMI - IMD), and this too was significantly different between the HIP+ (3.9 ±2.5) and HIP- (2.2 ±2.1) groups (p<0.001).

Conclusion: Hip disease is a frequent finding in AS and is associated with clinically and radiographically more severe spinal disease. Although the pathological consequences in these sites differ, the occurrence and severity seem to be linked and suggest common pathogenic mechanisms.

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The Minimally Important Difference (MID) for Patient Reported Outcomes in Systemic Lupus Erythematosus (SLE) Including Pain, Fatigue and SF36

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Objective: Patient reported outcomes are widely used in clinical practice and trials for systemic lupus erythematosus (SLE). We studied a large clinical practice, as well as patients enrolled in the 1000 Canadian Faces of Lupus database, to determine the minimally important difference (MID) for pain, fatigue, sleep, HAQ-DI, SF-36 PCS and SF-36 MCS using a patient-reported overall health status anchor.

Methods: SLE patients who had consecutive clinic visits at one SLE clinic with a completed HAQ-DI as well as a pain, fatigue, and sleep VAS (0-100), and an overall health status question: "How would you describe your overall status since your last visit?": much better, better, the same, worse, or much worse were included. If rated as better or worse, they were defined as the minimally changed subgroups. Also, SLE patients at multiple centers with at least two consecutive annual visits in the 1000 Canadian Faces of Lupus database who completed the SF-36 and the health transition question were eligible.

Results: There were 202 patients in London, of whom 94% were women, mean age 50 years, and mean disease duration 10 years. The mean baseline scores were between 39 and 50 for outcomes of interest on a VAS (0-100) where a positive change meant worsening. MIDs for better and worse respectively were: pain (-15.8, 8.5), fatigue (-13.9, 9.1), and sleep problems (-8.6, 7.6). The baseline and follow-up HAQ-DI (scale 0 to 3) was 0.639 (0.610) and 0.644 (0.653) with MID for HAQ being quite small; MID for better -0.08 and worse 0.14. The MID for SF-36 was 2.1 (better) and -2.2 (worse) for the Physical Component Score and 2.4 for better and -1.2 for worse in the Mental Component Score.

Conclusion: The MID in SLE patients may be different bi-directionally depending on the measured outcome. The mean change observed for those reporting better than worse in pain and fatigue was greater compared to mean change in HAQ. These are important for the interpretation of clinical trials and patient care.

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The Process of Revising Scleroderma Classification Criteria: Part I Delphi Consensus

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Objective: Systemic sclerosis (Scleroderma; SSc) is a CTD of variable disease subsets and severity. In the Canadian Scleroderma Research Group (CSRG), 12% do not meet criteria for SSc but are identified as having SSc. The 1980 SSc classification criteria are outdated and fail to identify a subset of patients with limited SSc. Also, clinical and biological measures can be added to increase sensitivity and specificity. Several newer criteria have been developed, however none have achieved acceptance and validation. For instance, if adding dilated nailbed capillaries and anticentromere Ab > 98% of CSRG patients can be re-classified as SSc. Validated criteria can allow for consistency across studies.

Methods: A revised list of classification criteria have been developed with a literature review consisting of 25 items. Using a Delphi consensus exercise of 3 rounds among an international team of >70 rheumatologists, we will develop a short list of items that should be tested for final criteria. The order of the items was randomized. During each round, the participants will complete a survey to determine which items should be included in the revised criteria. At each of 3 rounds, items that do not achieve 70% 'yes' consensus will be excluded. Then, the proposed list of criteria will be reviewed to ensure face validity. Part II: The revised criteria will then be tested in the CSRG database to determine how many patients would fit criteria and what item combination performs best. Part III: We will develop cases of real SSc patients and other patients that may mimic SSc and will send to participating rheumatologists to then develop further consensus, over sampling from patients who do not meet the former 1980 criteria, to refine the criteria and; (Part IV) test the new criteria through non SSc databases (such as the 1000 Faces of Lupus database), to establish sensitivity and specificity; and lastly, (Part V) by prospective application to serial SSc and other patients to ensure criteria validity.

Results: We will report on Parts I and II which are currently underway.

Conclusion: We anticipate that there will be 6 to 8 criteria including autoantibodies and nailbed dilated capillaries that will be added to current SSc criteria.

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Association Between Nonfasting Triglycerides and Coronary Artery Disease in SLE

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Objective: Historically, triglycerides (TG) have been measured in the fasting state. However, postprandial hypertriglyceridemia and the presence of remnant lipoproteins may play a role in atherosclerosis.

To determine whether nonfasting and fasting TG levels differ in individual patients and to assess whether nonfasting TG levels are associated with an increased risk of future coronary artery disease (CAD) in lupus patients.

Methods: Patients are followed at regular 2-6 month intervals according to a standard protocol which includes: complete history and physical exam, SLE Activity Index (SLEDAI-2K), and Systemic Lupus International Collaborative Clinics Damage Index (SDI). Fasting lipid profile was measured once yearly and nonfasting was determined at all other visits.

To determine the variability of fasting and nonfasting TG levels within patient, we selected patients with 2 visits within 4 months, one which had fasting TG and one with nonfasting TG. Furthermore, their lipid lowering therapy and steroid doses had to remain unchanged. We compared the fasting and nonfasting levels of TG using a paired t test and then dichotomized the values as normal/abnormal.

To assess whether the level of nonfasting TG predict the risk of future coronary artery disease (CAD), we selected inception patients (seen in clinic within 1 year of SLE diagnosis) with no previous history of CAD. The first available nonfasting TG was used. CAD was defined as angina or myocardial infarction. T-test and chi-square test were used to determine the association between nonfasting TG and CAD.

Results: 514 patients were identified with fasting and nonfasting TG levels. The mean fasting TG (1.37 ± 0.78) was statistically different from the mean nonfasting TG (1.54 ± 1.06) (difference=-0.16±0.75, p<0.001) but this is of questionable clinical significance. Examining dichotomized TG values as normal / abnormal there was concordance between fasting and nonfasting TG in 92% of the cases; only 40/514 (8%) were discordant.

604 inception lupus patients were identified with first available nonfasting TG and no previous CAD. 484 had normal TG values and 120 had elevated values. Forty nine patients went on to develop CAD. The mean nonfasting TG of patients with no CAD (1.78 ± 1.23) was not statistically different from that of patients with CAD (1.84 ± 1.05), p=0.74. CAD was documented in 35 / 484 (7.2%) patients with normal TG compared to 14 / 120 (11.7%) with abnormal TG (p=0.11).

Conclusion: The level of nonfasting TG was not clinically significantly dif-

ferent from fasting TG. Nonfasting TG did not predict the new CAD events in lupus patients.

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Dietary Energy Intake and Corticosteroids in Children with Systemic Lupus Erythematosus

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Objective: Patients with pediatric Systemic Lupus Erythematosus (pSLE) are at increased risk of premature atherosclerosis. Obesity is likely to accentuate this risk as well as reduce health-related quality of life, functional capacity, and increase pain and fatigue. The goals of this study were: 1) to describe the dietary energy intake (DEI) level and pattern in a cohort of children with pSLE and 2) to examine the association between DEI levels, disease activity and corticosteroid treatment.

Methods: Pediatric SLE patients enrolled into a prospective study completed a 3 day diet diary and an activity questionnaire. Corticosteroid therapy and disease activity (SLEDAI) were recorded and a fasting lipid profile was performed. Comparisons were made using t-tests, chi-square, or correlations where appropriate. Multivariable models were explored using general linear regression.

Results: There were 39 patients (mean age: 15.7 ± .2 years, 79% female) who participated in our study with a mean disease duration of 2.9 ±2.8 years, a mean BMI of 24.4 ±5.7 kg/m^2, and a median SLEDAI score of 4.0 (0-13). The average DEI intake was found to be 1666 ±423 kcal. The mean estimated energy requirement was calculated to be 2090 ±424 kcal resulting in a 20% difference (potential under-reporting) of the DEI which is typical for this diet questionnaire methodology. The mean percentages of DEI from fat (28%), protein (18%), and carbohydrate (54%) were all found to be in a healthy range. Most patients in our study were overweight (21%) or obese (23%) and patients were found to be mainly "Moderately active" (46%) or "Sedentary" (41%), with few patients "Active" (13%). The median change in body weight for the 3 months preceding DEI measure was 0.2 kg (-6.7-22.8) with a concurrent median cumulative dose corticosteroid dose of 1.4 g (0-5.1). The median corticosteroid dose at the time of DEI measure was 15 mg per day (0-60). A multivariable analysis model (R^2=37% p=0.003) showed that DEI decreased with increasing corticosteroid dose at the time of DEI measure when adjusting for gender, BMI, and age.

Conclusion: Many patients were overweight or obese, yet appeared to have healthy and balanced levels of dietary energy intake. Higher levels of corticosteroid may be associated with reduced dietary intake yet an increase in body weight.