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 ($P \leq 0.0001$ 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 ($P \leq 0.0003$ 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