Rheumatoid arthritis – biological DMARDs

SAT0120

COMPARATIVE EFFECTIVENESS OF TOFACITINIB AND TNF INHIBITORS SINCE 2014. IMPACT OF COMBINATION WITH METHOTREXATE

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Background: Tofacitinib (TOFA), a targeted synthetic DMARD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is also indicated for the treatment of PsA and UC since October 2018. Clinical experience with this molecule has been increasing, and questions relating to its efficacy and long-term safety are of interest. Data collection through RHUMADATA[®], a Quebec based clinical database and registry, allows comparison of newer options with more traditional agents such as tumor necrosis factor inhibitors (TNFi).

Objectives: The current analysis compares TOFA to TNFi used with and without methotrexate (MTX) among patients with RA.

Methods: Data collected since January 1, 2014 (when TOFA became available in Canada) at the Institut de Recherche en Rhumatologie de Montréal (IRRM) and the Centre de l'Ostéoporose et de Rhumatologie de Québec (CORQ) was extracted from Rhumadata[®] on January 7, 2019. Patients initiated on TOFA or a TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab) without or with MTX were selected. Data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (lab results, patient and physician-reported outcomes, and disease activity measures) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and Cox methods.

Results: A total of 480 patients were prescribed TOFA (n=162) or a TNFi (n=318) since January 1, 2014. Of those, 57% (n=92) and 70% (n=224) were treated with MTX in the TOFA and TNFi group respectively and mean disease duration was 12.1 (standard deviation=11.0) and 7.2 (8.1) years. TOFA and TNFi represent the first treatment following csDMARD-IR for 33%(TOFA) and 62%(TNFi). In the TOFA group, 84% were women, 15% were smokers and the mean age at treatment initiation was 57.7 (11.5) years. In the TNFi group, 77% were women, 12% were smokers and the mean age at treatment initiation was 54.2 (13.7) years. At treatment initiation, patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.6 (2.5), 5.9 (2.7) and 5.7 (2.9) in the TOFA group and 5.0 (2.9), 5.5 (3.0) and 5.1 (3.1) in the TNFi group. Baseline disease activity was assessed as moderate or high/severe in 85.9% and 76.7% of TOFA (?) patients (DAS28(4)-ESR criteria). Among the 56 (35%) TOFA and 146 (46%) TNFi patients ceasing therapy, reasons for cessation were "inefficacy" (TOFA: 64% vs TNFi: 56%) and "adverse events" (TOFA: 16% vs TNFi: 11%). Patients remaining on TOFA and TNFi therapy at last follow-up had an average treatment duration of 1.7 (1.1) and 2.7 (1.5) years and no difference in retention was observed between TOFA and TNFi treated patients (log-rank p=0.41). Patients treated with a TNFi in combination with MTX had better treatment retention than those treated without MTX (log-rank p=0.04) while patients treated with TOFA+/-MTX had similar retention (log-rank p=0.96). These results remain unchanged when adjusted for gender, age at treatment initiation, disease duration, and comorbidities.

Conclusion: In our real-world data registry, treatment with TNFi and TOFA yielded similar retention over time. Subjects treated with TNFi and MTX remained on treatment longer than those treated without MTX while subjects treated with tofacitinib with or without MTX had similar retention.

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SAT0121

EFFECT OF SARILUMAB ON GLYCOSYLATED HEMOGLOBIN IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DIABETES

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Background: Sarilumab is a human mAb blocking the IL-6R α , approved for adult patients with moderately to severely active RA. The incidence of Type 2 diabetes is increased in patients with RA, and elevated IL-6 may be an independent risk factor.

Objectives: We conducted a post hoc analysis into the effect of sarilumab treatment on glycosylated hemoglobin (HbA1c) levels.

Methods: TARGET (NCT01709578) was a 24-week study of sarilumab 150/200 mg q2w vs placebo (all +csDMARD) in TNFi-inadequate response/intolerant (IR/INT) patients. MONARCH (NCT02332590) was a 24-week monotherapy study of sarilumab 200 mg q2w vs adalimumab 40 mg q2w in MTX-IR/INT, bDMARD-naïve patients. There were 78/546 (14.3%) and 28/369 (7.6%) diabetic patients per ADA criteria (baseline fasting glucose ≥ 7 mmol/L or baseline HbA1c $\geq 6.5\%$) in TARGET and MONARCH, respectively.

Results: In patients with RA and diabetes, the decrease in HbA1c at Week 24 was greater in sarilumab-treated groups than placebo (TARGET; in combination with csDMARDs) or adalimumab (MONARCH; monotherapy) groups (Figure). There was no interaction between change in HbA1c and corticosteroid use nor were changes in HbA1c correlated with changes in CRP, DAS28-CRP, or hemoglobin level. Among sarilumab-treated patients, those with baseline IL-6 >37.5 pg/mL ($>3\times$ upper limit of normal) had greater reductions in HbA1c (least squares mean change -0.27) than those with baseline IL-6 levels ≤ 37.5 pg/mL (least squares mean change -0.11). Sarilumab safety profile was similar in diabetic vs non-diabetic patients with RA.

Figure. Reduction in HbA1c in patients with RA and diabetes (per ADA criteria) in A) TARGET and B) MONARCH

Conclusion: Patients with RA and diabetes treated with sarilumab had greater improvements in HbA1c than those treated with adalimumab or placebo. With monotherapy, differences between sarilumab and

adalimumab were more pronounced among patients with higher baseline serum IL-6 levels.

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SAT0122

COMPARISON OF REAL-WORLD PERSISTENCE OF SUBCUTANEOUSLY ADMINISTERED BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG (DMARD) THERAPIES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA) SWITCHING FROM ANOTHER BIOLOGIC

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Background: The EULAR and ACR clinical guidelines recommend switching to a different disease-modifying antirheumatic drug (DMARD) when biologic-treated patients experience treatment failure or toxicity. Lack of efficacy and adverse events are among the most commonly reported reasons for switching biologic therapies. Limited information is available regarding biologic therapy persistence across subcutaneously administered (SC) biologic agents in the real-world setting, as well as for comparative information on biologic persistence for SC biologics among patients with rheumatoid arthritis (RA) who are not naive to biologic treatment.

Objectives: To compare persistence of SC biologic DMARDs (bDMARDs) in patients with RA as subsequent-line therapy following a failure of first line bDMARDs.

Methods: US administrative claims data were used to create a longitudinal cohort of adult patients with RA initiating SC biologic between 1/1/2012 and 6/30/2017 (initiation date = index). Patients were required to have failed 1st bDMARD to enter study (but could later switch therapy) and to have 6 and at least 3 months of continuous enrollment pre- and post-index (date of prescription for bDMARD). Those with other autoimmune conditions were excluded from the study. Outcomes were biologic persistence, defined as number of days between initiation date and last supplied day of last fill. Parametric survival models with exponential distribution with robust variance estimator were used to compare outcomes for tocilizumab versus other biologics, adjusting for differences in baseline characteristics, accounting for correlation among different bDMARD episodes.

Results: There were 10,301 patients with 12,704 bDMARD episodes: abatacept (n=2,988), adalimumab (n=3,599), certolizumab (n=982), etanercept (n=2,760), golimumab (n=745), or tocilizumab (n=1,630). Mean age was 51.0-53.3. Mean [SD] Elixhauser comorbidity scores were significantly higher ($p < 0.001$) for tocilizumab (2.8 [2.3]) compared to abatacept (2.5 [2.2]), adalimumab (2.5 [2.1]), certolizumab (2.4 [2.0]), etanercept (2.4 [2.0]), or golimumab (2.4 [2.2]). Adjusted median days (95% CI) of persistence were: abatacept 320 (305, 335); adalimumab 280 (268, 293); certolizumab 262 (241, 284); etanercept 289 (274, 304); golimumab 304 (274, 333); and tocilizumab 333 (311, 356). Tocilizumab had significantly ($p < 0.05$) higher persistence compared to adalimumab, certolizumab, and etanercept (Figure 1). Of patients who were observed for 12 months, 45% of patients initiated tocilizumab bi-weekly and 55% initiated weekly. Of the 347 patients initiating bi-weekly tocilizumab, 33% switched to weekly over 12-month follow up; the mean time to switch was 177 days. After 12 months of follow-up, approximately 68% of patients finished on weekly dosing and 32% on biweekly dosing.

Conclusion: Among patients with RA who previously used ≥ 1 other biologic, tocilizumab-treated patients had similar or statistically significantly better biologic persistence compared with other biologics.

Adjusted Persistence (with 95% CI) of Biologic DMARDs Among Patients with RA

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SAT0123

RISK FOR TUBERCULOSIS DURING TREATMENT WITH BIOLOGICAL THERAPY: IS IT TIME FOR REVIEWING SCREENING PROTOCOL? – RESULTS FROM BRAZILIAN REGISTRY OF BIOLOGICAL THERAPIES IN RHEUMATIC DISEASES (BIOBADABRASIL)

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Background: As Brazil is accountable for 33% of the tuberculosis (TB) burden in Americas, with an annual incidence of 33.5/100,000 in 2017[1], the occurrence of tuberculosis infection in patients with rheumatic diseases in use of biological therapy is a recurrent concern.

Objectives: To assess incident TB among patients with rheumatic disease in use of biological therapy in a country with high incidence of TB.

Methods: BiobadaBrasil is a multicentric prospective cohort study involving patients with rheumatic diseases who started the first biologic or a synthetic disease modifying anti-rheumatic drug (DMARD)[6]. This analysis includes patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) recruited from Jan 2009 to Aug 2018 and followed-up for one or multiple courses of treatment until censoring or incident TB. The primary outcome was the incidence of tuberculosis (in any organ site). The history of exposure to tuberculosis, chest Rx, screening and treatment for latent tuberculosis infection (LTBI), and use of prophylactic isoniazid were evaluated before each course of treatment. Multivariate Cox proportional hazards models (with DMARDs included as time-varying covariates) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI); analyses were performed with the Survival package of R.

Results: Sample: 2858 patients (female =70.2%; RA = 72%, AS=20%, and PsA = 8%). A total of 31 (1.1%) patients developed tuberculosis during treatment. One patient on abatacept and one on tocilizumab developed TB while all the others were on TNF-inhibitors(29). The median (interquartile range) exposure to the current DAMRD course was 11.1 (5.9-20) months. TB patients did not significantly differ from others regarding disease duration, sex or age. Almost half (n=14,45%) of TB patients did not present evidence of previous exposure or any screening positive test for TB; 9 (29%) TB patients had received adequate LTBI treatment (isoniazid) recently or in the past. Furthermore, 8(26%) had incomplete/inconsistent screening. The overall incidence of TB was 1.9/1000 patients/year, and was not significantly different among the diseases (1.63 for RA, 2.06, for AS, and 3.79/1000/year for PsA). In univariate analysis, exposure to anti-TNF monoclonal antibodies (HR 3.1, 95%CI 1.18-8.15, $P=0.02$) and presence of any marker of previous contact with TB (positive history of TB, known contact with TB, positive TST, or abnormal chest X-ray: HR 4.2 (2.1-8.5, $p < 0.001$)) were positively associated with the risk of TB. Including simultaneously these variables in the Cox model, they were independent risk factor for TB ($p < 0.05$).

Conclusion: Monoclonal anti-TNF antibodies and previous exposure/diagnosis of TB are independent risk factors for developing TB in Brazil. TB