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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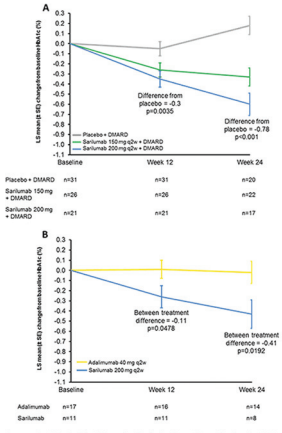
Background: Sarilumab is a human mAb blocking the IL-6Rα, approved for adult patients with moderately to severely active RA. The incidence of Type 2 diabetes is increased in patients with RA, and elevated IL-6 may be an independent risk factor.
Objectives: We conducted a post hoc analysis into the effect 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 ≥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× 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



Retrospective ADA criteria for diabetes: baseline fasting glucose ≥7 mmol/L or baseline HbA1c ≥6.5% (American Diabetes Association, Diabetes Care 2018;41(Suppl.1):S13–S27)

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