

## **Impact of Concomitant Use of Disease Modifying Antirheumatic Drugs and Methotrexate Administration Route on Durability of Biologic Treatment: Results from the Ontario Best Practice Research Initiative (OBRI) Cohort**

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**Objectives:** Prior controlled clinical trials and observational studies have suggested that concurrent DMARD therapy enhances the efficacy of TNF inhibitors. Furthermore, differences in the effectiveness and survival of subcutaneous vs. oral methotrexate have been previously shown. We aimed to assess the impact of concomitant DMARD use and methotrexate route of administration on time to biologic discontinuation in RA patients initiating biologic treatment in a large Canadian observational cohort.

**Methods:** Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) that initiated biologic therapy and had at least one follow-up assessment were included in the primary analysis. Patients using combination therapy with biologics and MTX were also included for the subgroup analysis. The impact on biologic discontinuation due to (i) any reason, (ii) inefficacy, and (iii) safety, was assessed with multivariate Cox regression using concomitant DMARD use (primary analysis) and MTX route of administration (secondary analysis) as time-dependent covariates.

**Results:** Among the 748 patients included in the primary analysis, 116 (15.5%) received biologic monotherapy and 632 (84.5%) were on combination therapy. Mean (SD) age and disease duration were 55.5 (12.7) years and 9.5 (9.9) years, respectively, while the majority were females (79.1%), without any significant differences between groups. Over a mean (SD) follow-up of 1.8 (1.6) years biologic discontinuation was reported for 38.6% of patients. Upon adjusting for potential confounders (socio-demographics, health insurance information, disease parameters, prior and concomitant medications), no significant differences were observed between combination therapy with DMARDs vs. biologic monotherapy in discontinuation due to any reason [HR (95%CI): 0.90 (0.68-1.20)], inefficacy and safety reasons [0.95 (0.66-1.38)], or inefficacy [1.45 (0.89-2.39), 0.14]. However, patients on combination therapy had significantly lower hazard of discontinuation due to safety reasons as compared to patients on monotherapy [0.47 (0.28-0.78), 0.004].

In the subgroup analysis, upon adjusting for potential confounders and taking into consideration MTX dose, no statistical association between route of MTX administration and biologic durability was observed.

**Conclusions:** This analysis showed that, unlike registries from other countries, concomitant use of DMARDs is not associated with durability of biologic treatment in Canadian routine clinical practice. However, a lower hazard for discontinuation due to safety reasons was observed in patients on combination therapy suggesting potential survivor bias. Furthermore, neither route of administration nor dose of MTX were significant predictors of biologic durability despite the fact that previous studies have shown differences in efficacy when a biologic was used as monotherapy, with suboptimal doses of concurrent MTX.