

## **Concomitant use of Oral vs. Subcutaneous Methotrexate at Biologic Initiation: a Comparison of Biologic Treatment Survival in the Ontario Best Practice Research Initiative (OBRI) Cohort**

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**Objectives:** Previous studies have shown differences in the effectiveness and survival of subcutaneous vs. oral methotrexate. Furthermore, concurrent methotrexate therapy has been shown to enhance the efficacy of anti-TNFs. The purpose of this study was to describe the pattern of methotrexate utilization in RA patients initiating biologic treatment in a large observational cohort and to compare the impact of methotrexate route of administration and dose on biologic durability in real-life.

**Methods:** Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) initiating combination therapy with a biologic and methotrexate were included. Analysis was primarily descriptive. Cox regression was used to examine the impact of methotrexate route of administration and dose at baseline on biologic durability. Methotrexate dose was classified as low ( $\leq 15$  mg/week), moderate (15-20 mg/week), and high ( $>20$  mg/week).

**Results:** Among 2,585 RA patients enrolled in OBRI, 885 initiated biologic therapy. Of the latter, 517 (58.4%) were treated concomitantly with methotrexate and were included in the analysis. Mean (SD) age and disease duration were 55.8 (13.1) years and 9.2 (9.8) years, respectively, while the majority were females (78.9%) and treated with an anti-TNF agent (83.0%). Overall, 271 (52.4%) were treated with oral methotrexate and 236 (45.6%) with subcutaneous without any significant differences between biologic types.

The predominant dose was 15-20 mg/week for oral methotrexate (43.2% of patients) and  $>20$  mg/week for subcutaneous use (47.0%).

Mean (SD) disease parameters at baseline were: DAS28 = 4.6 (1.4); swollen joint account = 6.3 (4.9); tender joint count = 6.9 (6.4); physician global = 5.1 (2.4); patient global = 5.3 (2.7).

Over a mean (SD) follow-up of 1.8 (1.5) years biologic discontinuation was reported for 39.5% of patients. Neither route of administration [ $HR_{SC-Oral}$  (95%CI) = 1.2 (0.9-1.6)] nor dose [ $HR_{Moderate-Low}$  (95%CI) = 1.05 (0.74-1.49);  $HR_{High\ vs.\ Low}$  (95%CI) = 1.08 (0.76-1.53)] of methotrexate at baseline were significantly associated with biologic discontinuation. Similar results were observed upon adjusting for gender, baseline age, disease duration, and DAS28.

**Conclusions:** This analysis has shown that subcutaneous methotrexate is used in Canadian routine care in a significant proportion of patients which is higher than that in other international registries. Neither route of administration nor dose of methotrexate were significant predictors of biologic durability despite the fact that previous studies have shown differences in efficacy when methotrexate is used without a biologic. Additional analyses considering changes over time in the mode of methotrexate administration are required to further validate these findings.