Time to Discontinuation of Biologic Therapy by Mechanism of Action in Rheumatoid Arthritis: Results from The Ontario Best Practice Research Initiative (OBRI) Cohort

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Background: Patients with rheumatoid arthritis (RA) may discontinue their biologic disease modifying antirheumatic drug (bDMARDs) due to non-response, loss of response or adverse events. However, time to discontinuation may be related to mechanism of action. We aimed to compare drug survival of tumor necrosis factor inhibitors (TNFi) versus non-TNFi in patients initiating bDMARD treatment in a Canadian (Ontario) observational cohort.

Methods: Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) who started their first bDMARD therapy within 30 days before or any time after OBRI enrolment were included. Patients were excluded if they had less than 2 visits during this period of time. Patients were followed from bDMARD start until discontinuation/switching, death, lost to follow-up, or last visit, whichever came first. Time to discontinuation of bDMARD due to (1) any reason, (2) non-response, physician, and patient decision, (3) non-response, and (4) adverse events (AEs) were assessed using Kaplan-Meier survival analysis for TNFi versus Non-TNFi/Tofa users. Cox proportional hazards regression model was also used to compare TNFi versus Non-TNFi/Tofa users adjusting for the effect of potential confounders. To deal with missing data, multiple imputation by chained equations was performed.

Results: A total of 796 patients were included of whom 130 (16.3%) received non-TNFi and 756 (83.7%) received TNFi (Table 1). TNFi included: Etanercept, Adalimumab, Certolizumab, Golimumab, and Infliximab. Non-TNFi and Tofa included: Abatacept, Rituximab, Tocilizumab, and small molecule Tofacitinib. Mean (SD) age and disease duration were 56.2 (12.8) years and 8.3 (9.0) years, respectively, and the majority were females (79.8%).

Over a mean (SD) follow-up of 2.4 (2.0) years, bDMARD discontinuation was reported for 291 (36.6%) due to any reason, 229 (28.8%) due to non-response, AEs, physician, and patient decision, 110 (13.8%) due to non-response, and 81 (10.2%) due to AEs, respectively.

There was a significant difference in time to discontinuation due to any reason (Logrank p=0.0002); non-response, AEs, physician, and patient decision (Logrank p=0.04) between TNFi and non-TNFi/Tofa users. However, there was no significant difference in bDMARD discontinuation due to non-response (Logrank p=0.36) and AEs (Logrank p=0.06).

After adjusting for potential confounders, difference in discontinuation remained significant between the TNFi and non-TNFi/Tofa group for any reason [HR: 0.62 (0.46-0.84)] and non-response, AEs, physician, and patient decision [HR: 0.67 (0.47-0.94)].

Conclusions: The analysis demonstrates that patients initially started on non-TNFi/Tofa therapy are significantly more likely to discontinue their therapy earlier for any reason and due to non-response,

AEs, physician and patient decision compared to TNFi therapy. Lack of response is likely not driving this, however AEs and, to an even greater degree, patient and physician preference likely influenced the results.

Keywords: biologic discontinuation, drug survival, mechanism of action, TNFi, rheumatoid arthritis, registry

Word count: 430
Character: 2,601