

Time to Discontinuation of Biologic Therapy by Mechanism of Action in Rheumatoid Arthritis Patients: Results From The Ontario Best Practices Research Initiative (OBRI)

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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 of bDMARDs.

OBJECTIVES

- 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 registry.

METHODS

- The Ontario Best Practices Research Initiative (OBRI) includes a clinical registry of RA patients (OBRI-RA registry) followed in routine care in Ontario, Canada.
- RA patients enrolled in the OBRI initiating their bDMARD within 30 days prior to or anytime following enrolment were included in the analysis.
- Patients were excluded if they had less than 2 visits during this period of time.
- Patients were followed from bDMARD start until discontinuation, death, lost to follow-up, or last visit, whichever came first.
- Time to discontinuation of bDMARD due to (i) any reason, (ii) non-response or loss of response, and (iii) adverse events (AEs), were assessed using Kaplan-Meier survival analysis for TNFi versus non-TNFi users.

RESULTS

- A total of 943 patients were included of whom 187 (19.8%) received non-TNFi and 756 (80.2%) received TNFi (Table 1).
- TNFi** included: Etanercept, Adalimumab, Certolizumab, Golimumab, and Infliximab and **Non-TNFi** included: Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

- Mean (SD) age and disease duration were 56.4 (12.7) years and 9.6 (9.8) years, respectively, and the majority were females (79.1%) and biologic naïve (84.4%).
- Patients in the non-TNFi group had significantly longer disease duration, higher swollen joint count, higher HAQ-DI, higher number of comorbidities, and were more likely to use csDMARDs and bDMARDs prior to enrolment compared to patients in TNFi group (Table 1).
- Over a mean (SD) follow-up of 2.4 (2.0) years, bDMARD discontinuation was reported for 37.6% of patients, with a significant difference in time to discontinuation between TNFi and non-TNFi users (Logrank p=0.0085) (Figure 1a).
- There was no significant difference in bDMARD discontinuation due to non-response or loss of response (Logrank p=0.67) between the two groups (Figure 1b).
- At 2 years, more patients remained on TNFi (71.0%) compared to non-TNFi (57.0%).
- At 5 years, 51.0% and 44.0% of patients still remained on TNFi and non-TNFi, respectively.

Figure 1: Kaplan-Meier Survival Curves for Time to bDMARD Discontinuation Based on Mechanism of Action

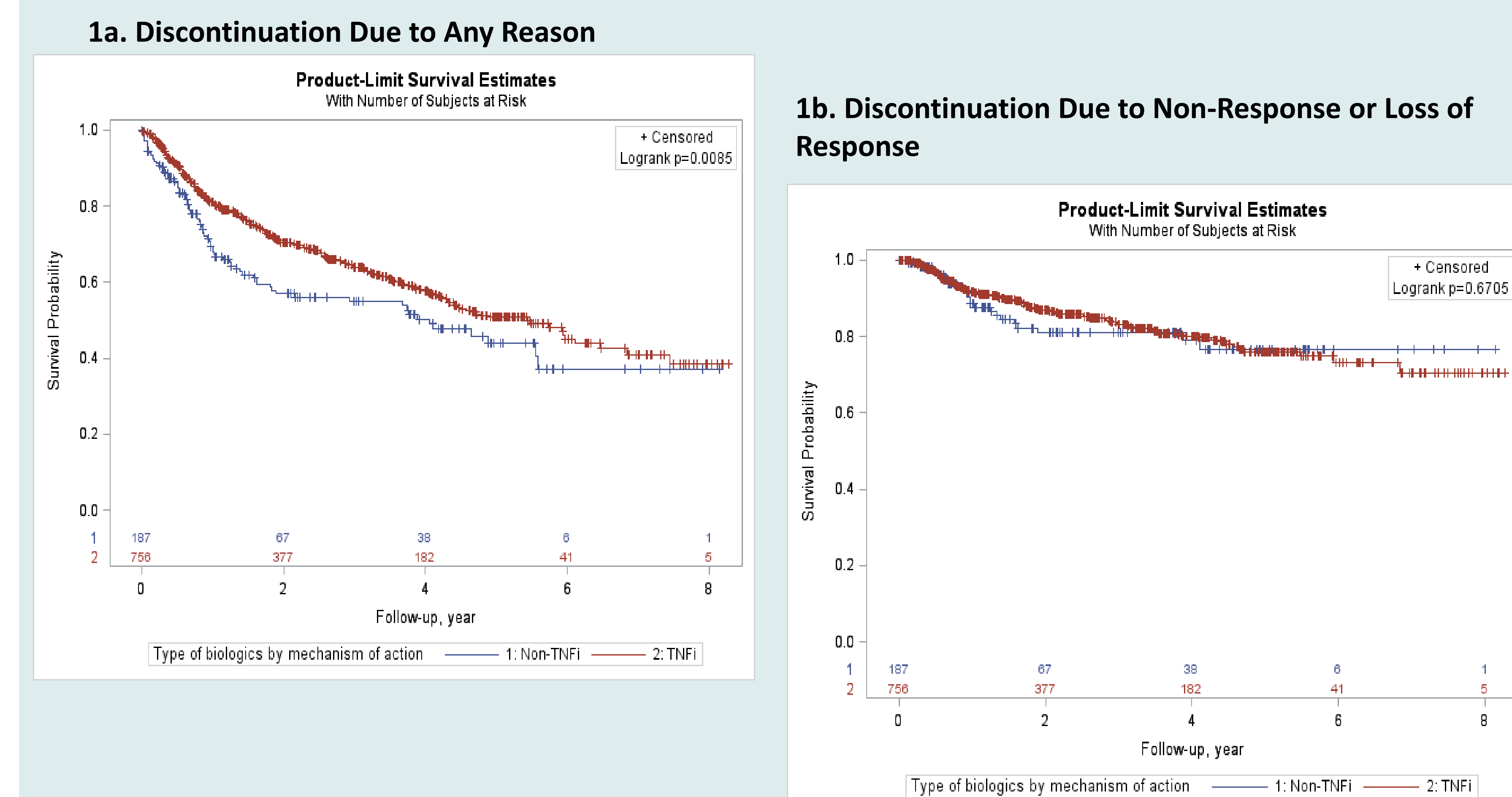


Table 1: Baseline Characteristics of RA Patients With Biologic Therapy Overall and by Mechanism of Action

| | TOTAL (N=943) | BY MECHANISM OF ACTION | | p-value |
|---|------------------|------------------------|-----------------|---------|
| | | Non-TNFi (n=187) | TNFi (n=756) | |
| Sociodemographic Factors | | | | |
| - Age, mean (sd) | 56.4 (12.7) | 58.0 (12.3) | 56.0 (12.8) | 0.06 |
| - Sex, Female, n (%) | 746 (79.1) | 151 (80.7) | 595 (78.7) | 0.54 |
| - Residential area, rural, n (%) | 151 (16.0) | 30 (16.0) | 121 (16.0) | 0.99 |
| - Education status, post-secondary, n (%) | 529 (56.1) | 116 (62.0) | 413 (54.6) | 0.05 |
| - Annual income class (≥ 50,000 CD), n (%) | 358 (38.0) | 73 (39.0) | 285 (37.7) | 0.85 |
| - Smoking history, n (%) | | | | |
| Never smoking | 426 (45.2) | 83 (44.4) | 343 (45.4) | 0.02 |
| Former smoking | 318 (33.7) | 73 (39.0) | 245 (32.4) | |
| Current smoking | 156 (16.5) | 23 (12.3) | 133 (17.6) | |
| Disease Factors | | | | |
| - Disease duration, mean (sd) | 9.6 (9.8) | 12.6 (11.2) | 8.8 (9.3) | < 0.001 |
| - Disease early onset, n (%) | 132 (14.0) | 19 (10.2) | 113 (14.9) | 0.09 |
| - RF positive, n (%) | 654 (69.3) | 123 (65.4) | 531 (70.2) | 0.81 |
| - Swollen joint count (0-28), mean (sd) | 7.0 (5.1) | 8.2 (5.8) | 6.7 (4.8) | 0.01 |
| - Tender joint count (0-28), mean (sd) | 7.2 (6.4) | 7.7 (6.9) | 7.1 (6.3) | 0.31 |
| - Physician Global Assessment (0-10), mean (sd) | 5.1 (2.3) | 5.1 (2.5) | 5.1 (2.2) | 0.78 |
| - Patient Global Assessment (0-10), mean (sd) | 5.5 (2.7) | 5.7 (2.7) | 5.5 (2.7) | 0.39 |
| - DAS28-ESR (0-9.4), mean (sd) | 4.7 (1.4) | 4.8 (1.5) | 4.7 (1.4) | 0.24 |
| - CDAI (0-76), mean (sd) | 25.0 (12.9) | 27.1 (14.5) | 24.6 (12.5) | 0.08 |
| - HAQ-DI (0-3), mean (sd) | 1.4 (0.8) | 1.5 (0.8) | 1.3 (0.7) | 0.005 |
| - Number of comorbidities, mean (sd) | 3.5 (2.9) | 4.2 (3.2) | 3.3 (2.8) | 0.001 |
| Medication Factors | | | | |
| - Prior use of csDMARDs, n (%) | 848 (89.9) | 178 (95.2) | 670 (88.6) | 0.03 |
| - Prior use of bDMARDs, n (%) | 147 (15.6) | 57 (30.3) | 90 (11.9) | < 0.001 |
| - Concurrent use of csDMARDs, n (%) | 788 (83.6) | 142 (75.9) | 646 (85.4) | 0.002 |
| - Concurrent use of steroid, n (%) | 208 (22.0) | 50 (26.6) | 158 (20.9) | 0.08 |
| - Concurrent use of NSAIDs, n (%) | 181 (19.2) | 27 (14.4) | 154 (20.4) | 0.07 |

- The overall retention rate for biologics was comparable to findings in European registries.
- We found that patients stay on TNFi longer compared to non-TNFi. However, there was no difference in discontinuation due to non-response or loss of response.
- Further analyses are required to adjust for the effect of potential confounders (e.g. age, sex, disease activity, and other treatment regimens) on biologic discontinuation.

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