

What is the Rate of Primary and Secondary Failure of Anti-TNF in RA Patients? Data from a Rheumatoid Arthritis Cohort

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Objectives: Although most RA patients respond to anti-TNF treatment, some present with refractory disease (primary failure) while others show some initial clinical response and eventually lose responsiveness (secondary failure). Assessing primary/secondary failure is complex due to the use of different definitions and variations in the timing of patient assessment in real-life.

Methods: Patients from the Ontario Best Practices Research Initiative (OBRI) initiating anti-TNF treatment <30 days prior to or at any point post-OBRI enrolment were included. Those discontinuing anti-TNF due to primary failure or secondary failure, as per the judgment of the treating physician, were re-classified based on: (i) time of failure (<6 months, 6-12 months, >12 months); (ii) prior achievement of DAS28 low disease activity (LDA) or moderate/good EULAR response. Interruptions of <6 months, where patients restarted the same anti-TNF were counted as continuous drug use. Time to treatment discontinuation was assessed with Kaplan-Meier survival analysis.

Results: 9 patients (78.7% female) were included with a mean (SD) age 56.4 (12.8) years and disease duration of 9.6 (9.5) years at anti-TNF initiation. Mean (SD) disease parameters were: DAS28: 4.7 (1.4); SJC: 7.0 (4.8); TJC: 7.4 (6.6); physician global (0-10 NRS): 5.2 (2.3); patient global (0-10 NRS): 5.6 (2.7). After a mean (SD) follow-up of 13.1 (11.3) months, 124 (19.0%) patients were discontinued due to failure as per the treating physician [57 (46%) and 67 (54%) due primary and secondary failure, respectively]; with mean (SD) Kaplan-Meier-based time to failure of 59.4 (1.6) months. Re-classification based on the failure time showed that, among patients discontinued due to failure as per the treating physician, 32.3% were discontinued in <6 months of treatment, 28.2% at 6-12 months, and 39.5% after 12 months. In terms of treatment response, 32.8% achieved DAS28 LDA or moderate/good EULAR response prior to discontinuation due to failure by the treating physician (19.6% and 41.1% among patients discontinued due to primary and secondary failure, respectively; $\kappa=0.22$). Among patients discontinued within 6 months due to failure as per the treating physician, only 11.4% had previously shown response.

Conclusion: This analysis has shown that, among patients discontinuing anti-TNF treatment due to failure, the rate of secondary failure may range from 33% to 54% depending on the definition used, highlighting the need for standardization. Overall, there was good agreement between the physician assessment of early (<6 months) failure and prior (non)achievement of response but lower agreement in the assessment of secondary failure.