# Discontinuation of Tumor Necrosis Factor Inhibitors in Psoriatic Arthritis and Psoriasis

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## INTRODUCTION

- Tumor necrosis factor-α inhibitors (TNFi), including adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab, are first-line therapy for the treatment of psoriatic arthritis and moderate-to-severe psoriasis.[1]
- Treatment discontinuation is usually followed by disease relapse, and persistence of biologic therapy is a surrogate for efficacy and safety of treatment.[1]
- Previous studies on TNFi discontinuation rates in psoriatic arthritis patients are varied.[1,2,3]

## OBJECTIVE

This study aims to compare discontinuation rates across the five TNFis and associations with patient characteristics, as well as identify reasons for discontinuation of TNFi in patients with psoriasis and/or psoriatic arthritis.

## METHODS

Study design: A retrospective analysis of the Program to Understand the Longterm Outcomes in SpondyloARthritis (PULSAR) cohort was performed. PULSAR is a prospective, longitudinal registry and biorepository with medical and demographic data for over 1200 rheumatology patients at Veterans Affairs Medical Centers (VAMC).

Participants: Subjects with psoriatic arthritis and/or psoriasis, who received a TNFi from the VAMC from 2007-2017, were included for analysis.

Statistical methods: Univariate and multivariate analyses of the characteristics of patients who discontinued a TNFi at 12 months were conducted using Stata. Stata was also used to conduct a time to event analysis of drug persistence over 3 years. Discontinuation of a biologic course was defined as the length between the usual dose of the TNFi plus 90 days without treatment. Course was defined as the difference between the date the prescription was first filled and the date of discontinuation without a gap in treatment > 90 days.

## RESULTS

320 individuals with 927 TNFi courses, including adalimumab (N = 378), certolizumab (N = 24), etanercept (N = 396), golimumab (N = 42), and infliximab (N = 87), were available for analysis. 243 of these patients also had both psoriasis and psoriatic arthritis. 16.2% of subjects discontinued at least one TNFi course at one year, and 35.6% discontinued at two years.

**Figure 1**: TNFi Persistence in Psoriasis and Psoriatic Arthritis (Adjusted for Course Order)

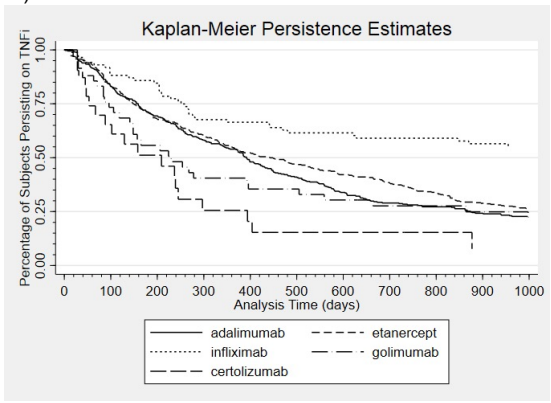



**Table 1**: Characteristics of TNFi Discontinuation

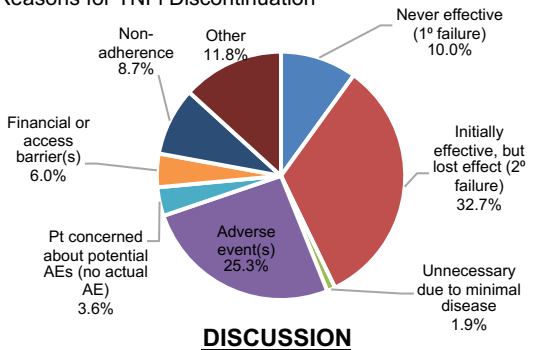
| | Initial Multivariate Regression | | | | Final Multivariate Regression | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | Haz. Ratio | p value | [95% Conf | Interval] | Haz. Ratio | p value | [95% Conf | Interval] |
| Age (years) | 0.967 | 0.612 | 0.849 | 1.101 | | | | |
| Gender, % male | 0.958 | 0.838 | 0.633 | 1.449 | | | | |
| Caucasian, % | 0.772 | 0.574 | 0.313 | 1.905 | | | | |
| African American, % | 0.450 | 0.181 | 0.139 | 1.450 | | | | |
| Hispanic, % | 1.472 | 0.421 | 0.573 | 3.779 | | | | |
| Asian, % | 1.006 | 0.989 | 0.415 | 2.438 | | | | |
| American Indian, % | 0.596 | 0.332 | 0.209 | 1.695 | | | | |
| Other Race, % | 1.000 | omitted | | | | | | |
| Former Smoker | 0.852 | 0.364 | 0.602 | 1.204 | | | | |
| Current Smoker | 1.600 | 0.050 | 1.001 | 2.558 | | | | |
| Never Smoker | 1.000 | referent | | | | | | |
| Education, years | 1.045 | 0.329 | 0.957 | 1.141 | | | | |
| Presence of PsA | 0.998 | 0.706 | 0.986 | 1.010 | | | | |
| Duration Ps (years) | 0.996 | 0.525 | 0.985 | 1.008 | | | | |
| HLA-B27 Positive, % | 0.959 | 0.807 | 0.684 | 1.344 | | | | |
| Mean CRP (mg/L) | 1.007 | 0.568 | 0.983 | 1.031 | | | | |
| Mean ESR (mm/hr) | 0.992 | 0.236 | 0.980 | 1.005 | | | | |
| Course | 1.113 | 0.003 | 1.037 | 1.195 | 1.100 | 0.000 | 1.067 | 1.133 |
| Charlson Comorbidity Index | 0.983 | 0.669 | 0.907 | 1.065 | | | | |

Ps = Psoriasis; PsA = Psoriatic Arthritis; CRP = C-reactive Protein; ESR = Erythrocyte Sedimentation Rate

**Table 2**: Discontinuation of Tumor Necrosis Factor Inhibitor (TNFi) Compared to Infliximab

| | Initial Multivariate Regression | | | | Final Multivariate Regression | | | |
|---|---|---|---|---|---|---|---|---|
| Biologic | Haz. Ratio | p value | [95% Conf | Interval] | Haz. Ratio | p value | [95% Conf | Interval] |
| Infliximab | 1.000 | referent | | | 1.000 | referent | | |
| Adalimumab | 1.348 | 0.418 | 0.654 | 2.779 | 2.678 | <0.001 | 1.857 | 3.863 |
| Etanercept | 2.169 | 0.043 | 1.024 | 4.591 | 2.667 | <0.001 | 1.856 | 3.831 |
| Golimumab | 0.657 | 0.558 | 0.162 | 2.671 | 2.405 | 0.001 | 1.465 | 3.949 |
| Certolizumab | 3.308 | 0.027 | 1.145 | 9.554 | 3.097 | <0.001 | 1.729 | 5.546 |

**Figure 2**: Reasons for TNFi Discontinuation




## DISCUSSION

- The majority of patients continued at least one TNFi course at 1 and 2 years.
- On average, the probability of discontinuing a TNFi increased by 10.0% for each additional TNFi course (p<0.001).
- Compared to infliximab, the other TNFi had higher rates of discontinuation (p≤0.001 for all TNFi).
- Secondary failure was the most prevalent reason for discontinuation followed by adverse events.
- Limitations: lack of demographic diversity and secondary failure based on clinical data without anti-drug antibodies.
- Strengths: robust number of subjects with multiple comorbidities and observed length of follow-up.

## REFERENCES

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