

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

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## INTRODUCTION

- Tumor necrosis factor- $\alpha$  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.<sup>1</sup>
- Treatment discontinuation is usually followed by disease relapse, and persistence of biologic therapy is a surrogate for efficacy and safety of treatment.<sup>1</sup>
- Previous studies on TNFi discontinuation rates in psoriatic arthritis patients are varied.<sup>1,2,3</sup>

## 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).

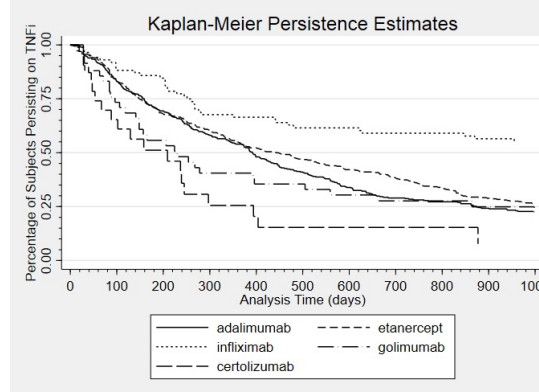
**Participants:** Subjects with psoriatic arthritis and/or psoriasis, who received a TNFi from the VAMC from 2007-2017, were included for analysis.

**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

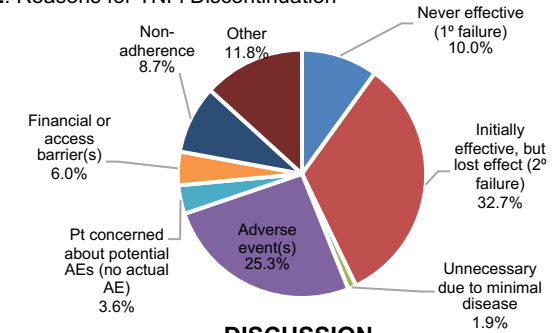
Variable	Initial Multivariate Regression				Final Multivariate Regression			
	Haz. Ratio	p value	[95% Conf. Interval]		Haz. Ratio	p value	[95% Conf. Interval]	
Age (years)	0.967	0.612	0.849	1.101				
Gender, % male	0.958	0.838	0.633	1.449				
Caucasian, %	0.772	0.574	0.313	1.905				
African American, %	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

Biologic	Initial Multivariate Regression				Final Multivariate Regression			
	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.

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