

ORIGINAL ARTICLE

Discontinuation and switching patterns of tumour necrosis factor inhibitors (TNFis) in TNFi-naive and TNFi-experienced patients with psoriatic arthritis: an observational study from the US-based Corrona registry

Philip J Mease,¹ Chitra Karki,² Mei Liu,² YouFu Li,³ Bernice Gershenson,³ Hua Feng,² Peter Hur,⁴ Jeffrey D Greenberg⁵

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For numbered affiliations see end of article.

Correspondence to
Professor Philip J Mease;
pmease@philipmease.com

ABSTRACT

Objective To examine patterns of tumour necrosis factor inhibitor (TNFi) use in TNFi-naive and TNFi-experienced patients with psoriatic arthritis (PsA) in the USA.

Methods All patients aged ≥ 18 years with PsA enrolled in the Corrona Psoriatic Arthritis/Spondyloarthritis Registry who initiated a TNFi (index therapy) between March 2013 and January 2017 and had ≥ 1 follow-up visit were included. Times to and rates of discontinuation/switch of the index TNFi were compared between TNFi-naive and TNFi-experienced cohorts. Patient demographics and disease characteristics at the time of TNFi initiation (baseline) were compared between cohorts and between patients who continued versus discontinued their index TNFi by the first follow-up visit within each cohort.

Results This study included 171 TNFi-naive and 147 TNFi-experienced patients (total follow-up, 579.2 person-years). Overall, 75 of 171 TNFi-naive (43.9%) and 80 of 147 TNFi-experienced (54.4%) patients discontinued their index TNFi; 33 of 171 (19.3%) and 48 of 147 (32.7%), respectively, switched to a new biologic. TNFi-experienced patients had a shorter time to discontinuation (median, 20 vs 27 months) and were more likely to discontinue ($p=0.03$) or switch ($p<0.01$) compared with TNFi-naive patients. Among those who discontinued, 49 of 75 TNFi-naive (65.3%) and 59 of 80 TNFi-experienced (73.8%) patients discontinued by the first follow-up visit; such patients showed a trend towards higher baseline disease activity compared with those who continued.

Conclusions The results of this real-world study can help inform treatment decisions when selecting later lines of therapy for patients with PsA.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic, immune-mediated rheumatic disease that affects the musculoskeletal system, skin and

Key messages

What is already known about this subject?

- Patients with psoriatic arthritis (PsA) often cycle among tumour necrosis factor inhibitors (TNFis), although data regarding the effectiveness of TNFi cycling in clinical practice are inconclusive.
- As biologics with alternative mechanisms of action become available, it is important to understand the persistence of TNFi use among TNFi-naive versus TNFi-experienced patients and to characterise those who continue versus discontinue their TNFis in order to better inform treatment decisions for patients with PsA.

What does this study add?

- In this real-world analysis of US patients with PsA, TNFi-experienced patients were more likely to discontinue or switch their index TNFi and had a shorter time to discontinuation compared with TNFi-naive patients.
- Patients who discontinued their index TNFi by the first follow-up visit were more likely to be female and showed a trend toward higher disease activity and worse patient-reported outcomes compared with those who continued.

How might this impact on clinical practice?

- These results may help inform treatment decisions when selecting later lines of therapy for patients with PsA.

nails.^{1 2} The symptoms of PsA are diverse and may include axial skeletal disorders, nail and skin changes, peripheral joint inflammation, enthesitis and/or dactylitis.¹⁻³ Patients with PsA also have increased risk of developing a number of comorbidities, including hypertension, hyperlipidaemia, cardiovascular disease,

type 2 diabetes mellitus, Crohn's disease, chronic obstructive pulmonary disease and depression, compared with the general population.³⁻⁵ PsA is frequently associated with psoriasis; an estimated 6%–42% of patients with psoriasis have or will develop PsA,^{1 6 7} while studies suggest that 10%–40% of patients with psoriasis may have undiagnosed PsA.^{8 9} The clinical heterogeneity of symptoms and potential burden of comorbidities can complicate the diagnosis and treatment of PsA.^{3 10}

Symptomatic treatment of PsA typically includes non-steroidal anti-inflammatory drugs and corticosteroids.^{11 12} For patients with active PsA, disease-modifying antirheumatic drugs, such as methotrexate or biologics, may be necessary for disease control.^{11 12} Tumour necrosis factor inhibitors (TNFis) have traditionally been the first choice of biologic agent for patients with refractory PsA.¹²⁻¹⁴ The efficacy and safety of TNFis for the treatment of PsA have been demonstrated in clinical trials.¹⁵⁻¹⁹ However, previous real-world studies have shown that approximately 20%–40% of patients with PsA who initiate a TNFi may discontinue due to primary or secondary loss of efficacy, adverse effects or other reasons.^{20 21} For patients who do not respond to a particular TNFi, switching to another TNFi may be effective and is a treatment option based on the published literature and experience in clinical practice.^{12-14 21}

European registry studies have shown mixed outcomes with respect to the effectiveness and persistence of TNFis in patients with PsA who received first-line versus second-line TNFis, with some studies showing better outcomes in patients who switched TNFis and others showing no difference between treatment lines or poorer response and persistence in patients who initiated a second-line versus first-line TNFi.²⁰⁻²⁵ A prospective, observational study of patients with PsA in southern Sweden showed moderate improvement in disease activity following the first switch of TNFi, but poorer response in patients who switched a second time.²⁶ A previous study using US claims data showed that patients who initiated a first-line TNFi had longer persistence compared with those who initiated a second-line TNFi; however, this study did not assess patient factors that may be associated with persistence, such as disease activity and patient-reported outcomes (PROs) at initiation, or reasons for discontinuation.²⁷

Few studies have characterised patients with PsA who continue versus discontinue a TNFi based on line of TNFi therapy in real-world settings in the USA. A previous study of patients with PsA enrolled in the US-based Corrona Registry observed greater persistence with TNFi therapy among biologic-naïve patients compared with biologic-experienced patients; baseline patient characteristics associated with non-persistence included high disease activity and longer disease duration in both patient populations as well as prior non-biologic disease-modifying antirheumatic drug use and greater skin involvement among biologic-experienced patients.²⁸ However, this study was

conducted in patients enrolled in the Corrona Registry who initiated a TNFi between October 2002 and March 2013, prior to the approval of biologics with alternative mechanisms of action (MOAs) for the treatment of PsA and before the launch of the Corrona Psoriatic Arthritis/Spondyloarthritis (PsA/SpA) Registry (March 2013), which focuses on a unique cohort of patients with PsA/SpA. The introduction of newer biologics with alternative MOAs has provided additional treatment options for first-line biologic therapy and for patients who have an inadequate response to a TNFi. The availability of these biologics with new MOAs may change biologic prescribing patterns and patient preferences in clinical practice; thus, reassessment of treatment patterns is needed as the therapeutic landscape continues to expand.

To better inform decisions regarding choice of biologic therapy for patients with PsA in clinical practice, it is important to understand the persistence of TNFi use among TNFi-naïve patients compared with those who cycle among multiple TNFis and to characterise those who continue versus discontinue a first versus second or later line of TNFi therapy. Therefore, the objective of this study was to examine patient characteristics and patterns of TNFi use in TNFi-naïve versus TNFi-experienced patients with PsA enrolled in the US Corrona PsA/SpA Registry.

METHODS

Study population

The Corrona PsA/SpA Registry (NCT02530268) is a large, independent, prospective, observational cohort of patients diagnosed with PsA or SpA by a rheumatologist. The registry includes patients recruited by 43 participating rheumatologists from 35 private and academic practice sites across 22 states in the USA. Follow-up data collection occurs approximately every 6 months using questionnaires completed by patients and their treating rheumatologists. As of December 2017, data on 2526 patients with PsA/SpA had been collected. The Corrona PsA/SpA Registry includes information on 10 767 patient visits and approximately 5928 patient-years of follow-up observation time, with a mean duration of follow-up of 3.0 years (median, 3.3 years).

This study included all patients aged ≥ 18 years enrolled in the Corrona PsA/SpA Registry who were diagnosed with PsA, initiated a TNFi (index therapy) between March 2013 and January 2017 and had ≥ 1 follow-up visit after TNFi initiation. Patients were assigned to a cohort based on prior biologic use (TNFi naïve: no prior TNFi or other biologic; TNFi experienced: ≥ 1 prior TNFi without use of a prior non-TNFi biologic) and followed until discontinuation of the index biologic or the end of the study period. Patients within the TNFi-naïve and TNFi-experienced cohorts were stratified by continuation or discontinuation of the index TNFi by the first follow-up visit. Patients in the continued group were those who were still receiving

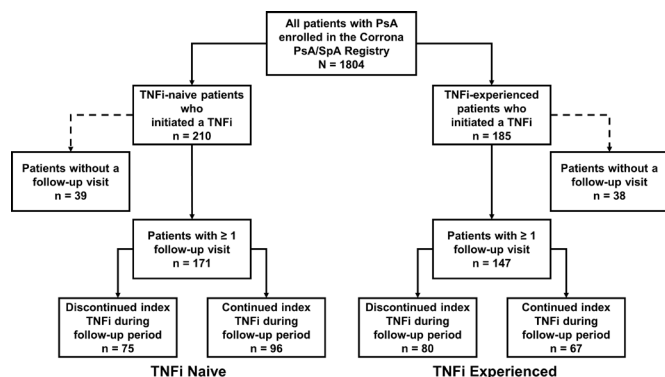


Figure 1 Patient disposition. The total follow-up period included 579.2 person-years, with a mean (SD) follow-up of 21.9 (9.6) months and median (IQR) follow-up of 23.0 (15.0) months. Patients included in the discontinued groups were those who switched to a new biologic (TNFi naive, n=33; TNFi experienced, n=48) or who discontinued without switching (TNFi naive, n=42; TNFi experienced, n=32). PsA, psoriatic arthritis; SpA, spondyloarthritis; TNFi, tumour necrosis factor inhibitor.

the index TNFi at the first follow-up visit; patients in the discontinued group were those who switched from the index TNFi to a different TNFi or who discontinued the index TNFi without switching by the first follow-up visit. For patients who switched TNFis during follow-up, only the first TNFi initiation was included in the analysis.

All participating investigators were required to obtain full board approval for conducting non-interventional research involving human subjects with a limited data set. All research was conducted in compliance with the Helsinki Declaration of 1964 and all later amendments. All registry subjects were required to provide written informed consent and authorisation prior to participating.

Outcomes and assessments

Data were collected using questionnaires completed by patients and their treating rheumatologists at office visits. Data collected at the time of TNFi initiation (baseline) included patient demographics, clinical characteristics, laboratory measurements, disease activity measures and PROs; baseline characteristics were compared between TNFi-naive and TNFi-experienced patients and between those who continued versus discontinued their index TNFi by the first follow-up visit.

Time to discontinuation (with or without switching) and time to switch to a new biologic over the total follow-up period were reported for patients who discontinued their index TNFi in the overall population and in the TNFi-naive and TNFi-experienced cohorts. Provider-reported reasons for discontinuation or switch of the index TNFi were collected for patients who discontinued at any point during follow-up and for those who discontinued by the first follow-up visit in the overall population and in the TNFi-naive and TNFi-experienced cohorts. Potential reasons for discontinuation or switch included lack of effect (inadequate response or failure to maintain response), side effects

(serious, minor or fear of side effects), social reasons (cost, patient preference or frequency of administration), doing well (remission or similar events) and other reasons.

Statistical analysis

Baseline patient demographics, clinical characteristics, disease activity measures and PROs were compared between TNFi-naive and TNFi-experienced patients and between those who continued versus discontinued their index TNFi by the first follow-up visit within each cohort using the χ^2 or Fisher exact test for categorical variables and the two-sample t-test or Wilcoxon rank-sum test for continuous variables. Categorical variables were summarised using frequency counts and percentages; continuous variables were summarised by the number of observations, mean, SD, median and IQR. Reasons for discontinuation or switch of the index TNFi were summarised descriptively. Time to discontinuation (with or without switching) and time to switch of the index TNFi were assessed by Kaplan-Meier analysis for the overall population and in the TNFi-naive and TNFi-experienced cohorts. Log-rank tests were performed to test the equality of survivor functions between the TNFi-naive and TNFi-experienced cohorts. Statistical analyses were performed using Stata V.14.

RESULTS

Patient population and baseline characteristics

Of the 1804 patients with PsA enrolled in the Corrona PsA/SpA Registry, 395 initiated a TNFi during the study period (March 2013–January 2017); 318 had ≥ 1 follow-up visit and were included in the analyses (TNFi naive, n=171 (53.8%); TNFi experienced, n=147 (46.2%)) (figure 1). Overall, the mean (SD) age was 53.6 (13.7) years, 56.8% of patients were female and the majority of patients (90.6%) were white (table 1). TNFi-experienced patients had significantly longer PsA disease duration (mean (SD), 13.3 (10.0) vs 9.5 (9.7) years; $p < 0.01$) and a higher proportion had a history of prednisone use (27.9% vs 17.5%; $p = 0.03$) compared with TNFi-naive patients (table 1).

TNFi-naive patients had lower average lateral lumbar flexion (mean (SD), 13.5 (5.0) vs 21.8 (16.9) cm; $p = 0.04$), lower baseline patient global assessment scores (mean (SD), 41.1 (28.0) vs 52.2 (29.2); $p < 0.01$) and higher EQ-5D scores (mean (SD), 0.74 (0.21) vs 0.70 (0.21); $p = 0.02$) compared with TNFi-experienced patients; a higher proportion of TNFi-naive patients had minimal disease activity compared with TNFi-experienced patients (39.3% vs 27.4%; $p = 0.04$) (table 2). TNFi-experienced patients had greater Spondyloarthritis Research Consortium of Canada Enthesitis Index scores among those with enthesitis (mean (SD), 4.6 (3.9) vs 2.9 (2.3)), higher pain (mean (SD), 47.3 (29.5) vs 40.9 (29.6)) and Health Assessment Questionnaire for the Spondyloarthropathies (mean (SD), 0.73 (0.66) vs 0.85 (0.68) scores, and a higher percentage of work

Table 1 Baseline demographics and clinical characteristics of TNFi-naive and TNFi-experienced patients with PsA overall and in those who continued versus discontinued their index TNFi by the first follow-up visit

Characteristic	Total population (N=318)	TNFi naive			TNFi experienced		
		Overall (n=171)	Continued (n=122)	Discontinued (n=49)	Overall (n=147)	Continued (n=88)	Discontinued (n=59)
Age, mean (SD), years	53.6 (13.7)	53.0 (15.2)	53.6 (16.2)	51.5 (12.2)	54.3 (11.6)	54.0 (11.8)	54.9 (11.4)
Female, n (%)	179 (56.8)	94 (55.3)	64 (52.5)	30 (62.5)	85 (58.6)	45 (51.7)	40 (69.0)*
White, n (%)	288 (90.6)	159 (93.0)	112 (91.8)	47 (95.9)	129 (87.8)	78 (88.6)	51 (86.4)
BMI, mean (SD), kg/m ²	32.4 (7.6)	32.1 (8.0)	32.1 (8.1)	32.1 (8.0)	32.7 (7.1)	32.0 (7.3)	33.6 (6.8)
BMI (in kg/m ²) classification, n (%)							
Normal/underweight (<25.0)	41 (13.8)	27 (17.2)	20 (17.9)	7 (15.6)	14 (9.9)	11 (13.1)	3 (5.3)
Overweight (25.0 to <30.0)	83 (27.9)	40 (25.5)	24 (21.4)	16 (35.6)	43 (30.5)	29 (34.5)	14 (24.6)
Obese (≥30.0)	174 (58.4)	90 (57.3)	68 (60.7)	22 (48.9)	84 (59.6)	44 (52.4)	40 (70.2)
Insurance type, n (%)							
Private	249 (78.5)	136 (79.5)	93 (76.2)	43 (87.8)	113 (77.4)	70 (80.5)	43 (72.9)
Medicare	21 (6.6)	12 (7.0)	11 (9.0)	1 (2.0)	9 (6.2)	3 (3.5)	6 (10.2)
Medicaid	21 (6.6)	12 (7.0)	9 (7.4)	3 (6.1)	9 (6.2)	6 (6.9)	3 (5.1)
Medicare+private	21 (6.6)	8 (4.7)	7 (5.7)	1 (2.0)	13 (8.9)	8 (9.2)	5 (8.5)
None	5 (1.6)	3 (1.8)	2 (1.6)	1 (2.0)	2 (1.4)	0	2 (3.4)
Disease duration, mean (SD), years	11.2 (10.0)	9.5 (9.7)	9.7 (9.8)	8.8 (9.6)	13.3 (10.0)†	14.1 (9.4)	12.1 (10.9)
History of comorbid conditions, n (%)							
Diabetes mellitus	43 (13.5)	21 (12.3)	15 (12.3)	6 (12.2)	22 (15.0)†	13 (14.8)	9 (15.3)
Cardiovascular disease‡	45 (14.2)	18 (10.5)	15 (12.3)	3 (6.1)	27 (18.4)	17 (19.3)	10 (17.0)
Any cancer§	25 (7.9)	13 (7.6)	10 (8.2)	3 (6.1)	12 (8.2)	7 (8.0)	5 (8.5)
Serious infection¶	25 (7.9)	12 (7.0)	8 (6.6)	4 (8.2)	13 (8.8)	8 (9.1)	5 (8.5)
Current MTX use, n (%)	157 (49.4)	92 (53.8)	63 (51.6)	29 (59.2)	65 (44.2)	40 (45.5)	25 (42.4)
History of prednisone use, n (%)	71 (22.3)	30 (17.5)	22 (18.0)	8 (16.3)	41 (27.9)†	30 (34.1)	11 (18.6)
Current prednisone use, n (%)	27 (8.5)	12 (7.0)	8 (6.6)	4 (8.2)	15 (10.2)	8 (9.1)	7 (11.9)

*P<0.05 for the comparison between patients who continued versus discontinued their index TNFi within the TNFi-naive or TNFi-experienced cohort.

†P<0.05 for the comparison between the overall populations of TNFi-naive and TNFi-experienced patients.

‡Combined histories of myocardial infarction, acute coronary syndrome, coronary artery disease, congestive heart failure, peripheral artery disease, cardiac revascularisation procedure, ventricular arrhythmia, cardiac arrest, unstable angina, stroke, transient ischaemic attack, pulmonary embolism, carotid artery disease, deep venous thrombosis or other cardiovascular event.

§Excludes non-melanoma of the skin.

¶Includes infections that led to hospitalisation or intravenous antibiotics: joint/bursa, cellulitis, sinusitis, diverticulitis, sepsis, pneumonia, bronchitis, gastroenteritis, meningitis, urinary tract, upper respiratory tract or infection of other specified site.

BMI, body mass index; MTX, methotrexate; PsA, psoriatic arthritis; TNFi, tumour necrosis factor inhibitor.

time missed (mean (SD), 9.8% (24.0%) vs 2.6% (7.8%); p=0.03) compared with TNFi-naive patients, although only the difference in percentage of work time missed reached statistical significance (table 2).

Time to discontinuation/switch of index TNFi during total follow-up

The total follow-up was 579.2 person-years; the mean (SD) and median (IQR) total follow-up were 21.9 (9.6)

Table 2 Baseline disease activity and patient-reported outcomes in TNFi-naive and TNFi-experienced patients with PsA overall and in those who continued versus discontinued their index TNFi by the first follow-up visit

Characteristic*	Total population (N=318)	TNFi naive		TNFi experienced			
		Overall (n=171)	Continued (n=122)	Discontinued (n=49)	Overall (n=147)	Continued (n=88)	Discontinued (n=59)
Enthesitis, n (%)	73 (23.0)	35 (20.5)	24 (19.7)	11 (22.5)	38 (25.9)	19 (21.6)	19 (32.2)
SPARCC Enthesitis Index (1–16)†	3.8 (3.3)	2.9 (2.3)	2.5 (1.5)	3.8 (3.4)	4.6 (3.9)	4.2 (3.9)	5.0 (3.9)
Dactylitis, n (%)	37 (11.6)	21 (12.3)	13 (10.7)	8 (16.3)	16 (10.9)	9 (10.2)	7 (11.9)
Dactylitis count (1–20)‡	2.5 (2.1)	2.3 (2.3)	1.8 (1.7)	3.1 (3.0)	2.6 (1.9)	2.8 (2.3)	2.4 (1.5)
Tender joint count (0–68)	4.9 (9.2)	4.2 (8.4)	3.0 (4.9)	7.3 (13.4)	5.7 (10.0)	5.5 (10.9)	6.1 (8.7)
Swollen joint count (0–66)	2.2 (3.8)	2.2 (3.7)	1.8 (2.8)	3.2 (5.1)	2.2 (4.0)	2.1 (4.3)	2.2 (3.6)
Spinal mobility measures, cm							
Occiput-to-wall distance	2.1 (4.6)	0.6 (2.0)	0.8 (2.3)	0.2 (0.5)	3.2 (5.6)	3.6 (7.1)	2.8 (4.2)
Lateral lumbar flexion (average of right and left)	18.4 (13.9)	13.5 (5.0)	14.7 (4.9)	9.8 (3.4)	21.8 (16.9)§	21.1 (16.2)	22.3 (18.0)
MDA, n (%)¶	93 (33.9)	59 (39.3)	45 (42.1)	14 (32.6)	34 (27.4)§	23 (30.3)	11 (23.0)
ASDAS-CRP	2.0 (0.8)	2.1 (0.9)	2.0 (0.9)	2.3 (1.0)	1.9 (0.7)	1.9 (0.7)	1.9 (0.8)
BASDAI (0–10)	4.3 (2.7)	4.1 (2.8)	4.0 (2.7)	4.5 (2.8)	4.5 (2.6)	4.2 (2.5)	4.9 (2.7)
BASFI (0–10)	3.3 (2.7)	3.1 (2.8)	3.0 (2.7)	3.4 (2.9)	3.6 (2.6)	3.3 (2.4)	4.0 (2.8)
CDAI	11.2 (9.7)	10.7 (10.0)	9.2 (7.6)	14.1 (13.6)**	11.9 (9.2)	10.5 (8.3)	13.5 (10.1)
DAS28-CRP	2.7 (1.2)	2.7 (1.3)	2.4 (1.0)	3.5 (1.7)**	2.8 (1.1)	2.7 (1.0)	2.8 (1.2)
CRP, mg/L	2.7 (6.9)	3.8 (9.0)	3.0 (7.2)	6.0 (12.8)	1.5 (3.2)	1.5 (3.1)	1.5 (3.4)
ESR, mm/hour	17.1 (15.6)	17.6 (15.8)	17.6 (16.6)	17.4 (13.3)	16.7 (15.6)	16.5 (17.3)	17.1 (12.2)
Physician global assessment of psoriasis	21.4 (21.5)	21.9 (21.9)	20.4 (21.3)	25.4 (23.2)	20.8 (21.1)	16.4 (16.9)	27.2 (24.6)**
BSA, % affected	4.9 (9.6)	4.9 (8.7)	5.3 (9.6)	3.8 (5.7)	4.9 (10.6)	5.0 (11.3)	4.6 (9.2)
Patient global assessment	46.3 (29.1)	41.1 (28.0)	38.2 (27.8)	48.2 (27.6)**	52.2 (29.2)§	50.5 (30.5)	54.7 (27.3)
Patient-reported pain (VAS 0–100)	43.9 (29.7)	40.9 (29.6)	37.6 (28.9)	49.5 (29.8)**	47.3 (29.5)	46.4 (29.8)	48.7 (29.4)
Patient-reported fatigue (VAS 0–100)	45.6 (28.5)	43.9 (28.4)	42.5 (28.3)	47.3 (28.6)	47.6 (28.7)	43.8 (26.5)	53.0 (31.0)**
Morning stiffness, n (%)							
Yes	283 (89.0)	151 (88.3)	105 (86.1)	46 (95.8)	132 (89.8)	81 (92.0)	51 (86.4)
<30 min	69 (24.4)	40 (26.5)	32 (30.5)	8 (17.4)	29 (22.0)	19 (23.5)	10 (19.6)
≥30 min	214 (75.6)	111 (73.5)	73 (69.5)	38 (82.6)	103 (78.0)	62 (76.5)	41 (80.4)
HAQ-S (0–3)	0.78 (0.67)	0.73 (0.66)	0.67 (0.63)	0.87 (0.73)	0.85 (0.68)	0.79 (0.66)	0.94 (0.70)
EQ-5D (0–1)	0.72 (0.21)	0.74 (0.21)	0.76 (0.19)	0.70 (0.24)	0.70 (0.21)§	0.72 (0.20)	0.67 (0.22)
EQ VAS	70.6 (45.4)	70.9 (20.8)	73.1 (19.1)	65.6 (23.8)	70.2 (63.1)	75.7 (79.7)	62.0 (19.7)

Continued

Table 2 Continued

Characteristic*	Total population (N=318)	TNFi naive		TNFi experienced			
		Overall (n=171)	Continued (n=122)	Discontinued (n=49)	Overall (n=147)	Continued (n=88)	Discontinued (n=59)
Current employment, n (%)	188 (61.8)	101 (62.4)	74 (62.7)	27 (61.4)	87 (61.3)	55 (65.5)	32 (55.2)
WPAl domains, %							
Absenteeism (work time missed)	6.1 (17.9)	2.6 (7.8)	3.1 (8.3)	1.6 (6.8)	9.8 (24.0)§	4.5 (14.3)	17.8 (32.4)
Presenteeism (impairment at work/reduced on-the-job effectiveness)	24.3 (24.8)	21.9 (21.3)	22.1 (22.4)	21.5 (18.7)	27.0 (28.2)	25.5 (27.2)	29.3 (30.0)
Work productivity loss (overall work impairment/absenteeism plus presenteeism)	27.4 (27.8)	24.4 (23.2)	25.3 (24.4)	22.4 (20.3)	30.5 (31.8)	26.5 (28.5)	36.0 (35.8)
Activity impairment	35.5 (29.4)	33.2 (29.2)	31.1 (28.3)	38.4 (31.1)	38.1 (29.5)	35.6 (28.1)	41.7 (31.3)

*All values were calculated based on available data and are presented as mean (SD) unless otherwise stated and had <20% missing data except for spinal mobility measures, ESR, CRP, DAS28-CRP, ASDAS-CRP and MDA.

†SPARCC Enthesitis Index among patients with enthesitis.

‡Dactylitis count among patients with dactylitis.

§P<0.05 for the comparison between the overall populations of TNFi-naive and TNFi-experienced patients.

¶MDA was defined as 'yes' if a patient met ≥5 of the following seven criteria: tender joint count ≤1, swollen joint count ≤1, BSA ≤3%, patient-reported pain VAS ≤15, patient global activity VAS ≤20, HAQ-S ≤0.5 and tender enthesesal points ≤1.

**P<0.05 for the comparison between patients who continued versus discontinued their index TNFi within the TNFi-naive or TNFi-experienced cohort.

ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BSA, body surface area; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28-CRP, Disease Activity Score in 28 joints with C-reactive protein; EQ-5D, EuroQol-five dimension; ESR, erythrocyte sedimentation rate; HAQ-S, Health Assessment Questionnaire for the Spondyloarthritis; MDA, minimal disease activity; PsA, psoriatic arthritis; SPARCC, Spondyloarthritis Research Consortium of Canada; TNFi, tumour necrosis factor inhibitor; VAS, visual analogue scale; WPAl, Work Productivity and Activity Impairment questionnaire.

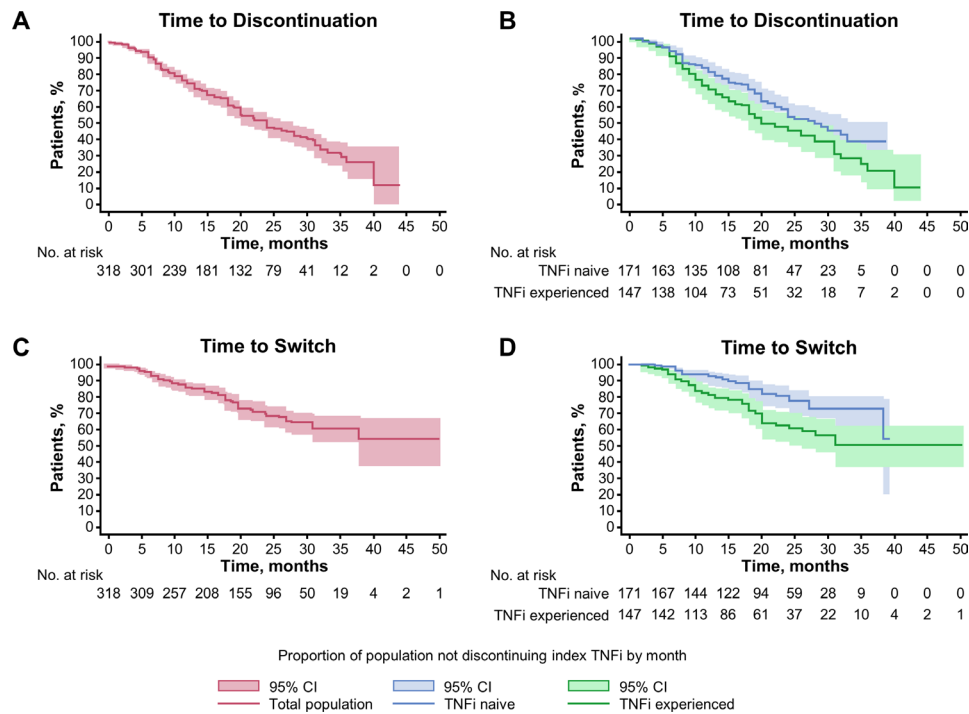


Figure 2 Time to discontinuation of the index TNFi in (A) the overall population and (B) TNFi-naive versus TNFi-experienced patients and time to switch in (C) the overall population and (D) TNFi-naive versus TNFi-experienced patients. TNFi, tumour necrosis factor inhibitor.

months and 23.0 (15.0) months, respectively. During follow-up, 75 of 171 TNFi-naive (43.9%) and 80 of 147 TNFi-experienced (54.4%) patients discontinued their index TNFi, including 33 of 171 (29.3%) and 48 of 147 (32.7%), respectively, who switched to a new biologic. The overall median time to discontinuation (with or without switching) was 24 months (95% CI 20 to 28 months) (figure 2A). TNFi-naive patients had a significantly longer time to discontinuation (with or without switching) compared with TNFi-experienced patients (median, 27 months (95% CI 22 to 33 months) versus 20 months (95% CI 18 to 28 months); $p=0.03$) (figure 2B). Among those who discontinued or switched their index TNFi, the mean (SD) time to discontinuation or switch was 14.5 (8.0) months in TNFi-naive patients compared with 14.0 (8.9) months in TNFi-experienced patients.

Due to the low number of switching events ($n=81$), the median (95% CI) time to switch to a new biologic could not be estimated (figure 2C). However, a long-rank test of the equality of survivor functions between TNFi-naive and TNFi-experienced patients showed that TNFi-naive patients had a significantly lower rate of switch compared with TNFi-experienced patients ($p<0.01$) (figure 2D). Among those who switched to a new biologic, the mean (SD) time to switch was 16.0 (8.1) months in TNFi-naive patients compared with 13.5 (7.5) months in TNFi-experienced patients.

Of the 155 patients who discontinued or switched their index TNFi, 97 had ≥ 1 provider-reported reason for discontinuation or switch (TNFi naive, $n=41$; TNFi experienced, $n=56$). The most commonly reported

reasons for discontinuation or switch of the index TNFi in both the TNFi-naive and TNFi-experienced cohorts were lack of efficacy (37/41 (90.2%) and 41/56 (73.2%), respectively) and side effects (5/41 (12.2%) and 15/56 (26.8%), respectively) (figure 3A).

Characteristics of patients who continued versus discontinued index TNFi by first follow-up visit

The mean (SD) time to the first follow-up visit was 11.5 (6.7) months (median (IQR), 10.0 (7.0) months). Of the 155 patients who discontinued or switched their index TNFi, 108 (69.7%) did so by the first follow-up visit, including 49 of 75 TNFi-naive (65.3%) and 59 of 80 TNFi-experienced (73.8%) patients. In both the TNFi-naive and TNFi experienced cohorts, a higher proportion of patients who discontinued their index TNFi were female compared with those who continued (62.5% vs 52.5% and 69.0% vs 51.7%, respectively), although this difference was only statistically significant in the TNFi-experienced cohort ($p=0.04$) (table 1).

TNFi-naive patients who discontinued their index TNFi by the first follow-up visit had significantly higher baseline Clinical Disease Activity Index (CDAI; mean (SD), 14.1 (13.6) vs 9.2 (7.6); $p=0.03$) and Disease Activity Score in 28 joints with C-reactive protein (DAS28-CRP; mean (SD), 3.5 (1.7) vs 2.4 (1.0); $p=0.01$) scores compared with those who continued (table 2). TNFi-naive patients who discontinued their index TNFi by the first follow-up visit also had a higher tender joint count (mean (SD), 7.3 (13.4) vs 3.0 (4.9)) and lower average lateral lumbar flexion (mean (SD), 9.8 (13.4) vs 14.7 (4.9) cm) at baseline compared

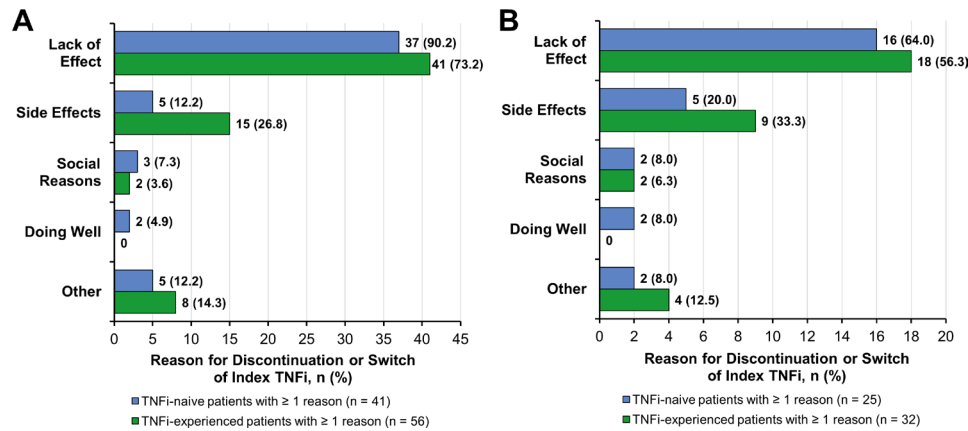


Figure 3 Provider-reported reasons for discontinuation or switch of the index TNFi in (A) the overall population and (B) patients who discontinued by the first follow-up visit. Potential reasons for discontinuation or switch included lack of effect (inadequate response or failure to maintain response), side effects (serious, minor or fear of side effects), social reasons (cost, patient preference or frequency of administration), doing well (remission or similar events) and other reasons. Patients may have had more than one reason for discontinuation. TNFi, tumour necrosis factor inhibitor.

with those who continued; however, these differences did not reach statistical significance (table 2). Differences in baseline PROs were also observed: TNFi-naive patients who discontinued their index TNFi by the first follow-up visit had higher baseline pain (mean (SD), 49.5 (29.8) vs 37.6 (28.9); $p=0.02$) and patient global assessment (mean (SD), 48.2 (27.8) vs 38.2 (27.6); $p=0.04$) scores compared with those who continued (table 2).

Among TNFi-experienced patients, those who discontinued their index TNFi by the first follow-up visit had higher baseline physician global assessment (mean (SD), 27.2 (24.6) vs 16.4 (16.9); $p=0.01$) and fatigue (mean (SD), 53.0 (31.0) vs 43.8 (26.5); $p=0.05$) scores compared with those who continued (table 2). Additionally, TNFi-experienced patients who discontinued their index TNFi by the first follow-up visit had reported a greater percentage of work time missed (mean (SD), 17.8% (32.4%) vs 4.5% (14.3%)) and work productivity loss (mean (SD), 36.0% (35.8%) vs 26.5% (28.5%)) compared with those who continued, although these differences did not reach statistical significance (table 2).

Of the 108 patients who discontinued or switched their index TNFi by the first follow-up visit, 57 had ≥ 1 provider-reported reason for discontinuation or switch (TNFi naive, $n=25$; TNFi experienced, $n=32$). The most commonly reported reasons for discontinuation or switch in both the TNFi-naive and TNFi-experienced cohorts were lack of efficacy (16/25 (64.0%) and 18/32 (56.3%), respectively) and side effects (5/25 (20.0%) and 9/32 (33.3%), respectively) (figure 3B).

DISCUSSION

This real-world study using data from the US-based Corrona PsA/SpA Registry provides insight into the persistence and switching of TNFi therapy among TNFi-naive versus TNFi-experienced patients with PsA. Patients who initiated their first TNFi had a longer time to discontinuation and were less likely to switch TNFis compared

with those who had previously received ≥ 1 TNFi. Of those who discontinued their index TNFi, the majority discontinued by the first follow-up visit. There was a trend towards higher baseline disease activity and worse PROs among patients who discontinued their index TNFi by the first follow-up visit compared with those who continued in both the TNFi-naive and TNFi-experienced cohorts; however, most differences did not reach statistical significance. In both the TNFi-naive and TNFi-experienced groups, the primary provider-reported reasons for discontinuation or switch of the index TNFi were lack of effect and side effects, both overall and among patients who discontinued by the first follow-up visit.

A prior study of patients with PsA enrolled in the Corrona Registry showed that a higher proportion of biologic-naive patients were persistent on their TNFi over 4 years of follow-up compared with biologic-experienced patients and that biologic-naive patients had a longer time to non-persistence compared with biologic-experienced patients (median, 32 vs 23 months).²⁸ Consistent with the results of the prior study, TNFi-naive patients in our study had a longer time to discontinuation (median, 27 vs 20 months) and were less likely to discontinue or switch biologics compared with TNFi-experienced patients. However, the median time to TNFi discontinuation was shorter in our study compared with the previous study. This difference may be due, in part, to differences between patient populations, including longer disease duration (mean, 11.2 vs 8.3 years) and higher prevalence of comorbidities (cardiovascular disease, 14.2% vs 5.4%; cancer, 7.9% vs 4.3%; diabetes mellitus, 13.5% vs 10.6%) in our study population compared with the previous study²⁸; a previous study in the DANBIO registry showed that a greater burden of comorbidities was associated with shorter TNFi persistence.²⁹ Additionally, the previous study was conducted prior to the approval of biologics with alternative MOAs for the treatment of PsA; the approval of new therapies with alternative MOAs has

provided physicians and patients with a greater number of treatment options, and recently updated US and European guidelines for the management of PsA reflect the availability, efficacy and safety of these new biologics.^{13 14} Current treatment guidelines also recommend using a treat-to-target-like strategy, when feasible, for the management of PsA, including regular monitoring and adjustment of therapy to achieve disease control.^{13 14} Together, these factors may lead to faster cycling of therapies in patients with an initial inadequate response to a TNFi in current clinical practice, possibly contributing to the shorter time to discontinuation observed in our study. Of note, the current Corrona PsA/SpA Registry collects data on a number of PsA/SpA-specific disease activity assessments that were not available at the time of the previous Corrona study. Our results therefore help address a knowledge gap regarding PsA-specific characteristics of patients who continue versus discontinue TNFis.

In both the TNFi-naïve and TNFi-experienced cohorts in our study, a higher proportion of patients who discontinued their index TNFi were female compared with those who continued. Previous studies support the association of female sex with likelihood of TNFi discontinuation. Real-world studies in Europe and the USA have shown that women with PsA are more likely to discontinue TNFi therapy and have shorter drug survival compared with men.^{27 30–32} Additional factors previously found to be associated with shorter TNFi persistence and increased likelihood of TNFi discontinuation and switch include longer disease duration, the presence of other comorbidities, low CRP levels (≤ 10 mg/L), higher disease activity as assessed by the CDAI, greater skin involvement and higher patient global assessment score.^{28–30 33} In our study population, there were no significant differences in disease duration or presence of comorbidities between patients who continued versus discontinued their index TNFi in the TNFi-naïve or TNFi-experienced cohort. Additionally, there were no significant differences in baseline CRP levels; however, the overall CRP levels in all groups were < 10 mg/L at baseline. TNFi-naïve patients who discontinued their index TNFi by the first follow-up visit had significantly higher baseline CDAI and DAS28-CRP scores compared with those who continued. There was a trend towards higher CDAI and other disease activity measures at baseline among TNFi-experienced patients who discontinued their index TNFi compared with those who continued, although these differences did not reach statistical significance. Additionally, patients who discontinued their index TNFi had higher pain and patient global assessment scores at baseline compared with those who continued; these differences were statistically significant in the TNFi-naïve cohort. Differences in patient characteristics associated with TNFi discontinuation in our study versus previous studies may be due, in part, to differences among study populations with respect to age, disease duration, comorbidities and/or baseline disease activity.

This study is subject to the general limitations of real-world observational studies. A general concern is that patients enrolled in registries may not be representative of patients seen elsewhere in general practice. Patients in this study are routinely seen and treated by rheumatologists voluntarily participating in the Corrona PsA/SpA Registry and may not be representative of all patients with PsA in the USA. In addition, the small sample size may have limited the ability to detect statistically significant differences in baseline characteristics, disease activity measures and PROs between patients who continued versus discontinued their index TNFi by the first follow-up visit. Sample size considerations also necessitated the pooling of TNFis for analysis; thus, no conclusions can be drawn regarding the persistence or rate of switch of any specific TNFi among patients with PsA. Analyses of discontinuation and switching were not adjusted for differences in patient characteristics, and no conclusions can be drawn regarding characteristics predictive of TNFi discontinuation. Finally, only half of patients who discontinued their index TNFi by the first follow-up visit (57/108) and 60% of patients who discontinued overall had provider-reported reasons for discontinuation, which limits insight into the reasons for discontinuation or switch of TNFis in TNFi-naïve versus TNFi-experienced patients.

In this real-world analysis of US patients with PsA, TNFi-experienced patients were more likely to discontinue or switch their index TNFi and had a shorter time to discontinuation compared with TNFi-naïve patients. Patients who discontinued by the first follow-up visit were more likely to be female compared with those who continued, and there was a trend towards higher disease activity and worse pain and patient global assessment scores among patients who discontinued compared with those who continued. The most commonly reported reasons for discontinuation or switch of the index TNFi among both TNFi-naïve and TNFi-experienced patients were lack of effect and side effects. These results may help inform treatment decisions when selecting later lines of therapy for patients with PsA.

Author affiliations

¹Swedish Rheumatology Research Group, Swedish Medical Center and University of Washington, Seattle, Washington, USA

²Corrona, LLC, Waltham, Massachusetts, USA

³University of Massachusetts Medical School, Worcester, Massachusetts, USA

⁴Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA

⁵Department of Medicine, Division of Rheumatology, New York University School of Medicine, New York, New York, USA

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Patient consent for publication Not required.

Ethics approval All participating investigators were required to obtain full board approval for conducting non-interventional research involving human subjects with a limited data set. The Corrona PsA/SpA Registry and its investigators have been reviewed and approved by a central institutional review board (IRB; New England Independent Review Board, NEIRB No. 120160070). For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRB.

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