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ARTICLE

Characterization of insufficient responders to anti-tumor necrosis factor therapies in patients with moderate to severe psoriasis: real-world data from the US Corrona Psoriasis Registry

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ABSTRACT

Objective: Biologic therapies have dramatically changed the management of moderate to severe psoriasis; however, few US real-world studies characterize the unmet needs of patients who do not respond to biologic therapies. This study examined the characteristics at enrollment of patients with moderate to severe psoriasis who had insufficient responses to anti-tumor necrosis factor therapies (anti-TNFs).

Methods: Patients enrolled in the Corrona Psoriasis Registry from April 2015 to June 2018 who initiated an anti-TNF at enrollment were stratified on the basis of body surface area (BSA) improvement to <3% or a 75% improvement from enrollment to the 6-month follow-up visit (response versus insufficient response). Patient demographics and disease characteristics were described at enrollment, and changes in outcomes were assessed at 6-month follow-up for those who received anti-TNFs.

Results: Of 180 anti-TNF initiators who had ≥1 follow-up visit, 50.6% were classified as responders. Logistic regression modeling showed that female sex was significantly associated with a decreased likelihood of achieving a response (OR = 0.534, 95% CI = 0.289–0.988, $p = .046$).

Conclusion: Despite the small sample size and short follow-up period, these findings may help dermatologists to identify patients with moderate to severe psoriasis who have unmet treatment needs.

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Psoriasis; Corrona Psoriasis Registry; biologics; effectiveness

Introduction

Psoriasis is a common chronic inflammatory disorder that affects >7.4 million people in the USA, with an estimated prevalence of 2–4% (1). The physical, psychological, and social health of patients with psoriasis is impacted by the signs and symptoms associated with the skin lesions of psoriasis (2,3). The National Psoriasis Foundation (NPF) classifies the severity of psoriasis on the basis of the percentage of affected body surface area (BSA; mild, <3%; moderate, 3–10%; severe, >10%) (4,5).

Topical medications, phototherapy, and traditional systemic therapies continue to be mainstays for the treatment of psoriasis; however, the clinical management of patients with moderate to severe psoriasis has changed dramatically with the advent of biologic therapies (6). Patients and clinicians now have several options for biologic treatments, including anti-tumor necrosis factor inhibitors (anti-TNFs; adalimumab, certolizumab pegol, etanercept, and infliximab) (6–16); the interleukin (IL)-12/23 inhibitor ustekinumab (17–19); the IL-23 inhibitors guselkumab, tildrakizumab, and risankizumab (20–24); the IL-17A inhibitors secukinumab and ixekizumab (25–29); and the IL-17RA inhibitor brodalumab (30,31). The goals for treatment of psoriasis have described improvements in percentage of affected BSA, Psoriasis Area and Severity Index (PASI) score, and lesion severity using the Physician Global Assessment as measurable targets (32,33). Understanding the importance of selecting treatment targets that are feasible in clinical practice, the NPF conducted a study with US experts to identify their preferences for instruments and treatment targets (34). The panel described the most acceptable response at 3 months as either improvement in percentage of affected BSA to <3% or a 75% improvement in BSA from baseline, with achievement of affected BSA ≤1% as the ideal target response (34).

Anti-TNFs are often the first-line biologic treatment in patients with psoriasis and are considered the first-generation biologics (35). For patients who have an inadequate response to a first-line anti-TNF, switching to another anti-TNF as second-line treatment is common in routine clinical practice (36,37); however, some patients still may not achieve optimal treatment responses and may benefit from switching to a drug with a different mechanism of action. Switching or discontinuing anti-TNFs has significant implications for clinical and economic outcomes in patients with psoriasis (38,39); therefore, real-world studies that characterize patients on the basis of response to therapy would provide valuable information to help healthcare providers identify patients who may benefit from a different approach to care and/or a biologic therapy with a different mechanism of action. Consensus treatment targets are useful tools for clinicians to evaluate treatment response in clinical practice; however, there is limited

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evidence from real-world settings in the United States that describes outcomes with biologic therapies and characterizes patients with moderate to severe psoriasis on the basis of response to biologic therapies, such as anti-TNFs. The objective of this descriptive, retrospective analysis of the Corrona® Psoriasis Registry was to examine differences in characteristics at registry enrollment and change in outcomes between patients with moderate to severe psoriasis who responded and those who had an insufficient response to anti-TNFs.

Materials and methods

Study setting

The Corrona Psoriasis Registry is a prospective, multicenter, observational disease-based registry launched in April 2015 in collaboration with the NPF. Patients are recruited from 170 private and academic practice sites across 41 states in the United States, with 401 participating dermatologists (40). Patients are enrolled in the registry if they meet all the following inclusion criteria: diagnosed with psoriasis by a dermatologist, aged ≥18 years, and started or switched to and continued a US Food and Drug Administration-approved systemic or biologic treatment for psoriasis within the previous 12 months.

As of June 30, 2018, Corrona had enrolled 5302 patients, with data on 12,736 patient visits and 4345.1 patient-years of follow-up observation time. The mean time of patient follow-up was 1.40 years (median, 1.29 years). The Corrona Psoriasis Registry was approved by both local and central (IntegReview, Corrona-PSO-500) review boards at participating sites. All patients provided written informed consent.

Study population

This study included all patients aged ≥18 years with moderate to severe psoriasis (affected BSA ≥3%) enrolled in the Corrona Psoriasis Registry between April 2015 and June 2018 who initiated an anti–TNF (adalimumab, etanercept, or infliximab) at the enrollment visit (index therapy) and had ≥1 6-month follow-up visit during the observation period with nonmissing BSA data at the enrollment and 6-month visits. Patients were stratified on the basis of response to the index anti-TNF at the 6-month follow-up visit. Responders were defined as patients who achieved an improvement in percentage of affected BSA to <3% or a 75% improvement in BSA from enrollment to the 6-month follow-up visit. Insufficient responders were defined as patients who remained at moderate to severe disease activity (affected BSA ≥3%) or did not achieve a 75% improvement in BSA from enrollment to the 6-month follow-up visit. Patients who discontinued the index biologic or switched to another biologic for efficacy or safety reasons at the 6-month follow-up visit were also classified as insufficient responders.

Study variables and outcomes

Data were collected using questionnaires from patients and their treating dermatologists at office visits; data collected at the time of anti-TNF initiation at the enrollment visit included demographics (age, sex, race, ethnicity, and body mass index [BMI]); clinical characteristics (duration of psoriasis and psoriatic arthritis and history of comorbidities); disease characteristics (5-point Investigator's Global Assessment [IGA] [0–4], BSA [continuous and categorical], and PASI [0–72]); prior use of biologic therapies (adalimumab, alefacept, certolizumab pegol, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab, investigational drugs, and other biologics); and patient-reported outcomes (PROs; patient overall pain, itch, and fatigue [visual analog scale (VAS) 0–100]; Dermatology Life Quality Index [DLQI; 0–30]; EuroQol VAS [0–100]; and Work Productivity and Impairment [WPAI]).

Change in outcomes from enrollment to the 6-month follow-up visit was assessed in responders and insufficient responders to index anti-TNFs. Outcomes of interest included change from enrollment in disease activity measures (achievement of IGA 0/1 among those with IGA 2–4 at enrollment, PASI 75, and PASI 90) and PROs (mean [SD] change in patient pain and itch and achievement of DLQI score 0–5 among those with DLQI score 6–30 at enrollment).

Data analysis

Descriptive analyses of patient demographics, clinical characteristics, PROs, and treatment characteristics were conducted at time of enrollment in the Corrona Psoriasis Registry and were stratified by response/insufficient response to the index anti-TNF. Categorical variables were summarized using frequency counts and percentages. Continuous variables were summarized by the number of observations and the mean (SD).

Patient demographics, clinical characteristics, PROs, and treatment characteristics were compared at enrollment between anti-TNF responders and insufficient responders using standardized differences and 95% CIs to quantify the effect size independent of confounding sample sizes. A standardized difference of <0.1 indicates a negligible difference in the mean or prevalence of a covariate between treatment groups (41). For proportions and means, the standardized differences were calculated using the absolute differences divided by a pooled variation. For categorical variables, the standardized differences were calculated using a multivariate Mahalanobis distance method (42). For change in outcomes from enrollment to the 6-month follow-up visit, standardized differences (95% CI) were used to quantify differences in outcomes between anti-TNF responders and insufficient responders. Statistical significance was determined using paired *t* tests for continuous outcomes and Wilcoxon rank-sum tests for interval/ordinal outcomes. All analyses were 'as observed' based on available data.

An exploratory analysis was performed using logistic regression modeling to determine the association of baseline covariates with response to anti-TNFs at the 6-month follow-up visit. Characteristics measured at enrollment and included for the exploratory modeling were chosen *a priori* on the basis of clinical and statistical insights or were considered and selected when significantly different between responders and insufficient responders (i.e. standardized difference of >0.1). Parameters included female sex (reference: male), BMI (continuous), BSA (continuous), and EQ-5D-3L score (continuous). The final reported model was determined by the χ^2 goodness-of-fit significance tests. Associations were presented as odds ratios and 95% CIs.

Statistical analyses were performed using Stata (StataCorp. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP; 2015).

Results

Demographics and patient characteristics at enrollment

As of June 2018, of 5302 patients who were enrolled in the Corrona Psoriasis Registry, 2282 initiated systemic therapy at enrollment, including 545 who initiated anti-TNFs (Figure 1). Of the anti-TNF initiators, 180 met the study inclusion criteria; at

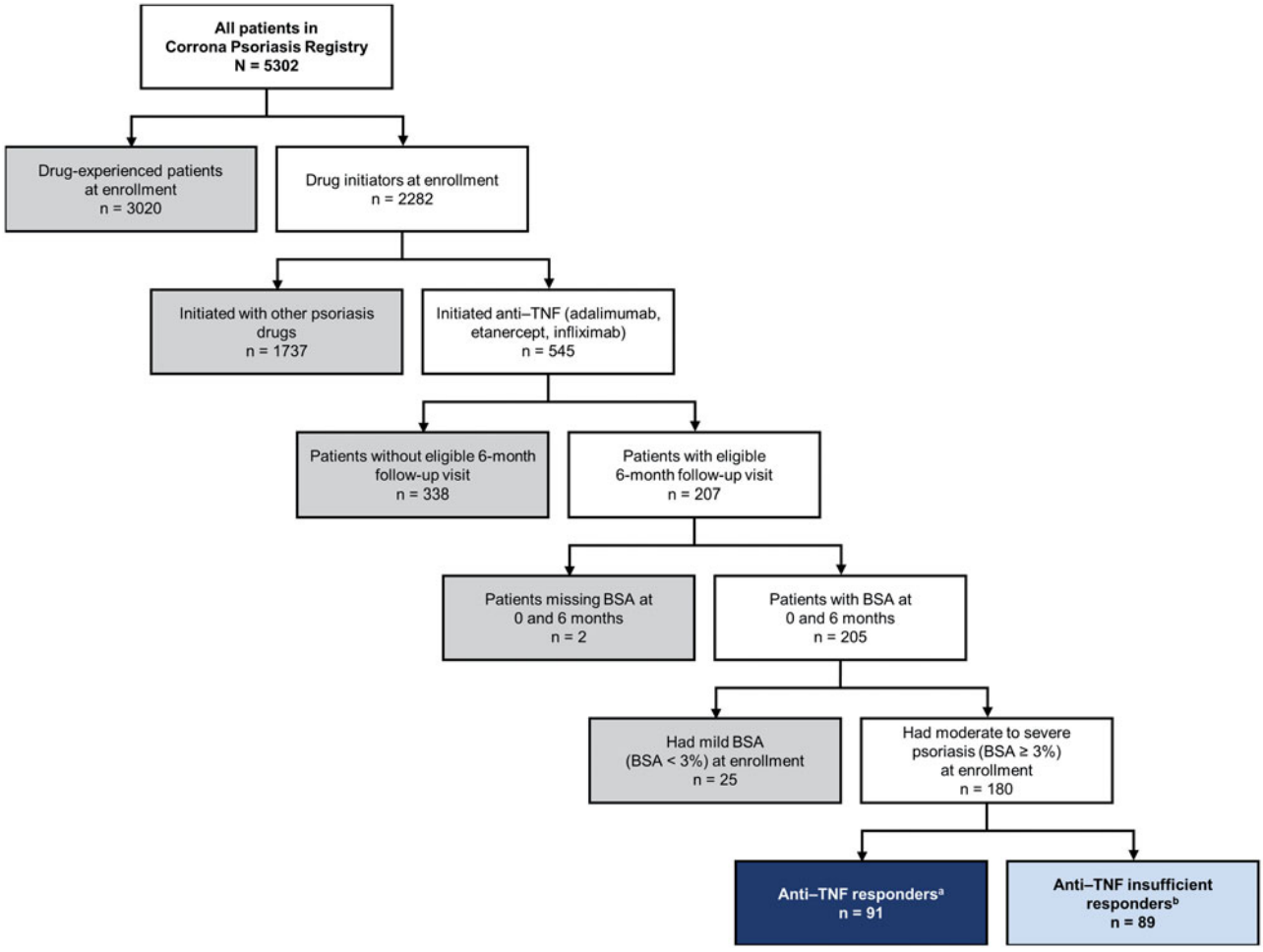

Figure 1. Patient disposition flow chart. Anti-TNF: anti-tumor necrosis factor therapy; BSA: body surface area. [a]Responders were defined as patients who achieved an improvement in percentage of affected BSA to <3% or a 75% improvement in BSA from enrollment to the 6-month follow-up visit. [b]Insufficient responders were defined as patients who remained at moderate to severe disease activity (affected BSA ≥3%) or did not achieve a 75% improvement in BSA from enrollment to the 6-month follow-up visit. Patients who discontinued their index biologic or switched to another biologic for efficacy or safety reasons were also classified as insufficient responders.

Table 1. Demographics of patients with moderate to severe psoriasis at enrollment stratified by response to index anti-TNFs at 6 months.

Characteristic	Anti-TNF responder ($n = 91$)	Anti-TNF insufficient responder ($n = 89$)	St diff (95% CI)
Age, mean (SD), years	48.6 (15.1)	48.1 (14.6)	0.03 (−0.26 to 0.33)
Female, *n* (%)	34 (37.4)	49 (55.1)	0.36 (0.07 to 0.66)
Race, *n* (%)			0.16 (−0.13 to 0.46)
White	69 (75.8)	72 (80.9)	
Black	6 (6.6)	3 (3.4)	
Asian	10 (11.0)	9 (10.1)	
Other[a]	6 (6.6)	5 (5.6)	
Ethnicity, *n* (%)			0.00 (−0.30 to 0.29)
Hispanic	5 (5.5)	5 (5.6)	
BMI, mean (SD), kg/m^2	29.9 (7.2)	32.8 (8.8)	−0.36 (−0.66 to −0.06)
BMI (kg/m^2) classifications, *n* (%)			0.40 (0.10 to 0.70)
Normal/underweight (<25.0)	24 (26.7)	16 (18.0)	
Overweight (25.0 to <30.0)	28 (31.1)	18 (20.2)	
Obese (≥30.0)	38 (42.2)	55 (61.8)	

Anti-TNF: anti-tumor necrosis factor therapy; BMI: body mass index; St Diff: standardized difference.
[a]Other includes Native American, Native Hawaiian, other Pacific Islander, or other.

the 6-month follow-up visit, 91 patients (50.6%; 83 adalimumab, 7 etanercept, 1 infliximab) and 89 patients (49.4%; 75 adalimumab, 14 etanercept) were classified as responders and insufficient responders, respectively.

Evaluation of demographics and patient characteristics showed imbalances between responders and insufficient responders at enrollment (Table 1). Anti-TNF responders were less likely to be female (37.4 versus 55.1%) or white (75.8 versus 80.9%), had a lower mean (SD) BMI (29.9 [7.2] versus 32.8 [8.8] kg/m^2), and were less likely to be obese (≥30 kg/m^2; 42.2 versus 61.8%) compared with anti-TNF insufficient responders.

Clinical and disease characteristics at enrollment

At enrollment, anti-TNF responders and insufficient responders had similar mean (SD) duration of psoriasis (13.8 [13.3] versus 13.4

Table 2. Clinical characteristics of patients with moderate to severe psoriasis at enrollment stratified by response to index anti-TNFs at 6 months.

Characteristic	Anti-TNF responder ($n = 91$)	Anti-TNF insufficient responder ($n = 89$)	St diff (95% CI)
Duration of psoriasis, mean (SD), years	13.8 (13.3)	13.4 (13.3)	0.04 (−0.26 to 0.33)
Psoriatic arthritis, *n* (%)	29 (31.9)	39 (43.8)	−0.25 (−0.54 to 0.05)
Duration, mean (SD), years	5.9 (9.6)	5.7 (8.8)	0.02 (−0.46 to 0.51)
IGA score (0–4), mean (SD)	3.1 (0.5)	3.1 (0.6)	0.11 (−0.18 to 0.41)
IGA score, *n* (%)			0.15 (−0.14 to 0.44)
0: Clear	0	0	
1: Almost clear	0	0	
2: Mild	8 (8.8)	12 (13.5)	
3: Moderate	63 (69.2)	59 (66.3)	
4: Severe	20 (22.0)	18 (20.2)	
Worst BSA ever, mean (SD), % involvement	17.7 (16.3)	22.3 (19.6)	−0.25 (−0.56 to 0.06)
BSA, mean (SD), % involvement	14.5 (14.8)	15.3 (13.3)	−0.05 (−0.34 to 0.24)
BSA (% involvement) categories, *n* (%)			0.15 (−0.14 to 0.44)
Mild (0–<3%)	0	0	
Moderate (3–10%)	54 (59.3)	50 (56.2)	
Severe (>10%)	37 (40.7)	39 (43.8)	
PASI score (0–72), mean (SD)	10.0 (8.1)	8.4 (5.6)	0.23 (−0.07 to 0.52)
PASI score > 10, *n* (%)	37 (40.7)	26 (29.2)	0.24 (−0.05 to 0.54)
History of comorbidities, *n* (%)			
Psoriatic arthritis	29 (31.9)	39 (43.8)	−0.25 (−0.54 to 0.05)
Hypertension	31 (34.1)	32 (36.0)	−0.04 (−0.33 to 0.25)
Hyperlipidemia	31 (34.1)	21 (23.6)	0.23 (−0.06 to 0.53)
Anxiety	18 (19.8)	25 (28.1)	−0.20 (−0.49 to 0.10)
Depression	17 (18.7)	19 (21.3)	−0.07 (−0.36 to 0.23)
Diabetes mellitus	12 (13.2)	17 (19.1)	−0.16 (−0.45 to 0.13)
Cardiovascular disease[a]	2 (2.2)	3 (3.4)	−0.07 (−0.36 to 0.22)
Lymphoma/malignancy[b]	2 (2.2)	3 (3.4)	−0.07 (−0.36 to 0.22)
Metabolic syndrome	0	0	0.00 (−0.29 to 0.29)

Anti-TNF: anti-tumor necrosis factor therapy; BSA: body surface area; IGA: Investigator's Global Assessment; PASI: Psoriasis Area and Severity Index; St Diff: standardized difference

[a]Cardiovascular disease includes revascularization procedures (coronary artery bypass graft, stent, angioplasty), ventricular arrhythmia, cardiac arrest, acute coronary syndrome, coronary artery disease, transient ischemic attack, hemorrhage with or without hospitalization (serious bleed), deep vein thrombosis, peripheral arterial disease, pulmonary embolism, and carotid artery disease.

[b]All malignancies excluding nonmelanoma skin cancer.

[13.3] years), five-point IGA scores (3.1 [0.5] versus 3.1 [0.6]), percentage of affected BSA (14.5% [14.8%] versus 15.3% [13.3%]), and PASI scores (10.0 [8.1] versus 8.4 [5.6]) (Table 2). A lower proportion of anti-TNF responders had psoriatic arthritis at enrollment than insufficient responders (31.9 versus 43.8%), although the mean (SD) duration of psoriatic arthritis in those affected was similar between the 2 groups (5.9 [9.6] versus 5.7 [8.8] years). Compared with anti-TNF insufficient responders, anti-TNF responders recorded a lower worst ever BSA mean (SD) value (17.7% [16.3%] versus 22.3% [19.6%]) and were less likely to have a history of anxiety (19.8 versus 28.1%). Anti-TNF responders had a numerically higher prevalence of a history of hyperlipidemia than insufficient responders (34.1 versus 23.6%).

Overall, anti-TNF responders were numerically more likely to be biologic naive than insufficient responders (Figure 2). The proportion of anti-TNF responders and insufficient responders who had prior biologic use was 20.9 and 27.0%, respectively. Of the biologic-experienced patients, a lower proportion of anti-TNF responders used ≥2 prior biologics than insufficient responders (5.5 versus 11.2%).

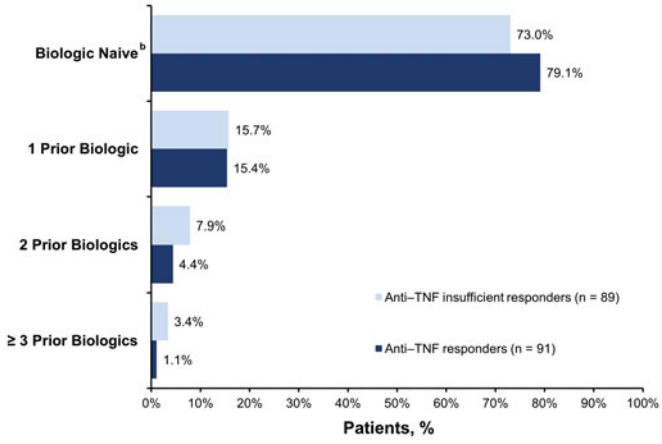

Figure 2. Treatment history of patients with moderate to severe psoriasis at enrollment stratified by response to index anti–TNFs at 6 months[a]. Anti-TNF, anti-tumor necrosis factor therapy. [a]Prior biologics included adalimumab, alefacept, certolizumab pegol, efalizumab, etanercept, golimumab, infliximab, ixekizumab, secukinumab, ustekinumab, investigational drugs, and other biologics. [b]Standardized difference (95% CI)=0.14 (−0.15 to 0.44).

Patient-reported outcome measures at enrollment

Compared with anti-TNF insufficient responders at enrollment, anti-TNF responders reported lower mean (SD) pain (34.4 [32.1] versus 40.7 [31.2]) and fatigue (36.3 [30.0] versus 46.9 [27.3]) scores (Table 3). Anti-TNF responders also reported better mean (SD) DLQI scores (7.6 [5.5] versus 9.3 [5.7]), better dermatology-related quality of life as indicated by the proportion of patients reporting a moderate to extremely large effect on life (53.3 versus 73.0%), and lower percentage of impairment across all WPAI questionnaire domains.

Change in clinical and patient-reported outcomes from enrollment at 6-month follow-up

As expected, anti-TNF responders achieved significant differences in improvements from enrollment in mean IGA, PASI, and DLQI scores and patient-reported pain and itch and achievement of IGA 0/1, PASI 75, PASI 90, and DLQI 0–5 among those with DLQI 6–30 at enrollment compared with insufficient responders at the 6-month follow-up visit (Table 4).

As an exploratory analysis, logistic regression modeling assessed the adjusted association of characteristics at enrollment with

Table 3. Patient-reported outcome measures of patients with moderate to severe psoriasis at enrollment stratified by response to index anti-TNFs at 6 months.

Characteristic	Anti-TNF responder ($n = 91$)	Anti-TNF insufficient responder ($n = 89$)	St diff (95% CI)
Patient overall pain (VAS 0–100), mean (SD)	34.4 (32.1)	40.7 (31.2)	−0.20 (−0.49 to 0.10)
Patient overall itch (VAS 0–100), mean (SD)	57.3 (31.6)	59.9 (31.4)	−0.08 (−0.38 to 0.21)
Patient overall fatigue (VAS 0–100), mean (SD)	36.3 (30.0)	46.9 (27.3)	−0.37 (−0.66 to −0.07)
DLQI score (0–30), mean (SD)	7.6 (5.5)	9.3 (5.7)	−0.30 (−0.59 to 0.00)
DLQI ('effect on life'), *n* (%)			0.50 (0.21 to 0.80)
0–1: None	5 (5.6)	5 (5.6)	
2–5: Small	37 (41.1)	19 (21.3)	
6–10: Moderate	19 (21.1)	34 (38.2)	
11–20: Very large	27 (30.0)	27 (30.3)	
21–30: Extremely large	2 (2.2)	4 (4.5)	
EuroQol VAS (0–100), mean (SD)	70.1 (22.4)	63.7 (22.1)	0.28 (−0.01 to 0.58)
Currently employed, *n* (%)	67 (73.6)	60 (67.4)	0.14 (−0.16 to 0.43)
WPAI summary scores, mean (SD) (*n*)			
% Work hours missed due to psoriasis	4.7 (12.9) [$n = 61$]	3.5 (8.8) [$n = 58$]	0.11 (−0.25 to 0.47)
% Impairment while working due to psoriasis	18.6 (23.3) [$n = 61$]	24.5 (26.8) [$n = 57$]	−0.24 (−0.60 to 0.13)
% Overall work hours affected by psoriasis	20.8 (25.7) [$n = 61$]	26.3 (28.3) [$n = 57$]	−0.20 (−0.57 to 0.16)
% Daily activities impaired by psoriasis	25.1 (29.1) [$n = 89$]	30.5 (26.6) [$n = 86$]	−0.19 (−0.49 to 0.11)

Anti-TNF: anti-tumor necrosis factor therapy; DLQI: Dermatology Life Quality Index; St diff: standardized difference; VAS: visual analog scale; WPAI: Work Productivity and Activity Impairment.

Table 4. Change in outcomes from enrollment to 6-month follow-up among responders and insufficient responders to index anti-TNFs.

Characteristic	Anti-TNF responder ($n = 91$)	Anti-TNF insufficient responder ($n = 89$)	St diff (95% CI)
Clinical outcomes			
Change in IGA score (0–4), mean (SD)	−2.1 (1.0)	−0.6 (0.9)	−1.64 (−1.97 to −1.30)[a]
Achievement of IGA 0/1 (among those with IGA 2–4 at enrollment), *n* (%)	63 (69.2)	12 (13.5)	1.37 (1.05 to 1.70)[a]
Change in PASI score (0–72), mean (SD)	−8.9 (7.3)	−2.7 (5.8)	−0.94 (−1.24 to −0.63)[a]
Achievement of PASI 75, *n* (%)	79 (86.8)	19 (21.3)	1.74 (1.40 to 2.09)[a]
Achievement of PASI 90, *n* (%)	52 (57.1)	4 (4.5)	1.39 (1.06 to 1.71)[a]
Patient-reported outcomes			
Change in patient pain (VAS 0–100), mean (SD)	−28.1 (32.7)	−9.0 (32.4)	−0.59 (−0.89 to −0.29)[a]
Change in patient itch (VAS 0–100), mean (SD)	−42.7 (34.4)	−13.3 (33.8)	−0.86 (−1.17 to −0.55)[a]
Change in DLQI score (0–30), mean (SD)	−5.9 (5.8)	−2.2 (6.7)	−0.60 (−0.90 to −0.30)[a]
Achievement of DLQI score 0–5 (among those with DLQI score 6–30 at enrollment), *n* (%)	43 (89.6)	27 (41.5)	1.17 (0.77 to 1.57)[a]

Anti-TNF: anti-tumor necrosis factor therapy; DLQI: Dermatology Life Quality Index; IGA: Investigator's Global Assessment; PASI: Psoriasis Area and Severity Disease; St diff: standardized difference.
[a]$p < .05$ for comparisons between responders and insufficient responders.

response to anti–TNFs at the 6-month follow-up visit and found that female sex was significantly associated with a decreased likelihood of achieving a response (OR = 0.534, 95% CI = 0.289–0.988, $p = .046$) (Table 5). Although there were imbalances in several patient characteristics based on unadjusted comparisons, there were no significant associations between anti-TNF response and BMI, BSA, or EQ-5D-3L score when adjusting for baseline covariates on the basis of clinical and statistical insights when covariates were significantly different between responders and insufficient responders.

Table 5. Exploratory analysis: logistic regression modeling of the adjusted association of characteristics at enrollment with response to anti–TNFs at the 6-month follow-up visit[a].

Parameter (at enrollment)	Odds ratio (95% CI)	*p* Value
Female sex (reference: male)	0.534 (0.289–0.988)	.046
BMI (continuous)	0.966 (0.928–1.006)	.097
BSA (continuous)	1.001 (0.980–1.024)	.898
EQ-5D-3L (continuous)	1.011 (0.997–1.025)	.133

Anti-TNF: anti-tumor necrosis factor therapy; BMI: body mass index; BSA: body surface area.
[a]Characteristics included for the exploratory modeling were chosen *a priori* based on clinical and statistical insights or were considered and selected when significantly different between responders and insufficient responders (i.e. standardized difference of >0.1).

Discussion

In this real-world analysis of US patients with moderate to severe psoriasis, 50.6% of patients who initiated anti-TNFs were classified as responders at the 6-month follow-up visit. In general, there were imbalances in patient characteristics at enrollment between responders and insufficient responders; however, only female sex was associated with decreased likelihood of achieving a response based on adjusted modeling. Few studies have investigated sex differences in responses to anti-TNFs in patients with psoriatic disease. One retroactive study of 199 patients found that male sex was associated with a better response to anti-TNFs (adalimumab, etanercept, and infliximab) (43). A study of patients with psoriatic arthritis from the DANIO register showed that male sex was strongly associated with greater anti-TNF effectiveness, including better odds of achieving responses at 3 and 6 months and improved overall persistence of response (44). The findings from our study suggest that the relationship between sex and anti-TNF effectiveness may require further exploration.

Response was based on a modified definition from the consensus expert survey conducted by the NPF, which described the most acceptable response at 3 months as either improvement in affected BSA to <3% or a 75% improvement in BSA from baseline (34); the modification extended the time to acceptable response from 3 to 6 months. Corrona follow-up visits take place

approximately every 6 months; therefore, the same BSA targets were used for response at the first follow-up visit, which helped the treating dermatologist make treatment decisions on the basis of the observed response. Although anti-TNF responders and insufficient responders were both significantly impacted by the disease at enrollment, there were numerous imbalances between groups in the distribution of patient demographics, clinical characteristics, and disease measures. Notably, anti-TNF responders reported better dermatology-related quality of life than insufficient responders at enrollment and were slightly less impaired by the disease as assessed by nearly all other PROs.

Previous studies suggest that efficacy and drug survival rates of anti-TNFs decrease with subsequent lines of therapy in patients with psoriasis (45,46). Differences in dermatologist prescribing patterns and prior biologic use may have influenced differences observed in other clinical and PRO measures at enrollment. In this analysis, responders were more likely to be biologic naive than insufficient responders. Most biologic-experienced anti-TNF insufficient responders had received $\geq$2 biologics before the anti-TNF initiation. The higher proportion of patients with prior biologic use and the initiation of later lines of anti-TNFs in anti-TNF insufficient responders may indicate that these patients had more refractory disease, which was reflected by worse PRO scores at enrollment than anti-TNF responders.

Compared with insufficient responders, anti-TNF responders demonstrated significant improvements in clinical outcomes at the 6-month follow-up visit as well as in patient-reported pain, itch, and dermatology-related quality of life. The NPF has observed that BSA is the preferred instrument for assessing psoriasis treatment response in US clinical practice (34). Although BSA is easy to use in a clinical setting, it may be subject to high interobserver variability and does not account for severity of lesions (34,47). Instruments that take into consideration clinical presentation of the disease, such as IGA or PASI, can provide a more detailed assessment of clinical disease activity and response to therapy (34,47,48). BSA, PASI, and IGA measures are closely correlated in patients with psoriasis in clinical settings; consistent with these observations, patients with BSA-defined response in our study had significant improvement from enrollment in IGA and PASI scores at 6 months compared with BSA-defined insufficient responders (48,49). Thus, BSA may serve as an easily implemented surrogate for disease activity when assessing treatment response. However, BSA does not account for psoriasis symptom severity, comorbidities, or effects of psoriasis on quality of life (34,47); in our analysis, 21% of anti–TNF insufficient responders achieved a PASI 75 response.

In addition to the symptoms of pain and itch, psoriasis has an impact on physical and mental health that is comparable to that of other chronic diseases (50). The social stigma associated with the appearance of psoriatic plaques can lead to anxiety, depression, and social isolation in patients with psoriasis (51,52). Consistent with these observations, approximately 20–25% of patients in our study reported a history of anxiety or depression, with a slightly lower prevalence of anxiety among anti-TNF responders than insufficient responders. Moderate to severe psoriasis is also associated with substantial work and activity impairment; lower income; and reduced employment opportunities, career prospects, and earning potential (4,53–55). In our study, employment was impacted by disease in both responders and insufficient responders, although a numerically higher proportion of anti-TNF responders were currently employed at enrollment and had less impairment in working and daily activities than anti-TNF insufficient responders. Importantly, the impact of psoriasis on patients' health-related quality of life does not always correlate with lesion severity, and even a small amount of skin involvement can impact quality of life. In a large, multinational, population-based survey, approximately 25% of patients with mild psoriasis (affected BSA $\leq$ 3%) reported a substantial negative impact on their health-related quality of life (56). Additionally, patient-reported disease severity has been observed to be higher than physician-assessed disease severity (57). PROs can contribute to a more holistic assessment of response to therapy in patients with psoriasis by providing information about the effectiveness of therapies from a patient perspective through measurement of improvement in health-related quality of life.

Limitations

This study has limitations that are shared by all real-world observational studies. Because our data source was a US registry, the results may not be generalizable to patients with psoriasis outside of the United States. Participation in the Corrona Psoriasis Registry by patients and their treating dermatologists is voluntary; therefore, selection bias may influence the results. These findings are only descriptive, although logistic regression modeling was performed to determine whether response to anti-TNFs was associated with key covariates at enrollment, with no adjustments made to control for potential confounding or any highly correlated characteristics. This study was limited by a small number of patients who initiated anti-TNFs and a short follow-up period ($\approx$ 6 months), which may preclude meaningful analysis of achievement of a response. Furthermore, loss of efficacy may not be completely seen 6 months after initiation of treatment. Lastly, approximately 90% of anti-TNF initiations were adalimumab; therefore, this study is largely driven by an analysis of adalimumab response versus insufficient response. Larger studies with more even distribution of biologic initiations and longer follow-up are needed to better characterize patients who achieve a sustained response with an index anti-TNF and to perform adjusted analyses.

Conclusions

These data from the Corrona Psoriasis Registry provide valuable insights into disease burden and outcomes in patients with moderate to severe psoriasis who respond or do not respond to an anti-TNF in US clinical practice. Switching or discontinuing biologic treatment, whether due to lack of response or other reasons, has substantial clinical and economic implications in patients with psoriasis. Further analyses with larger sample sizes are needed to better characterize significant differences between anti-TNF responders and insufficient responders. However, findings from this study may help make clinicians aware of imbalances in baseline characteristics of patients who respond or have an insufficient response and identify those patients with moderate to severe psoriasis who may benefit from a different approach to care and/or a biologic therapy with a different mechanism of action.

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A.S. Van Voorhees has served on an advisory board for Dermira, Novartis, Allergan, DermTech, and Valeant and has served as a consultant for Dermira, Novartis, and AbbVie; M.A. Mason and N. Guo are employees of Corrona, LLC; L.R. Harrold has received a grant from Pfizer, has served as a consultant for AbbVie, BMS, and Roche, and is an employee and stockholder of Corrona, LLC; A. Guana was an employee of Novartis at the time of this study; H. Tian is an employee of Novartis; V. Herrera is an employee and stockholder of Novartis; B.E. Strober has served as a consultant for Corrona, LLC.

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