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Persistence of tumor necrosis factor inhibitor or conventional synthetic disease-modifying antirheumatic drug monotherapy or combination therapy in psoriatic arthritis in a real-world setting

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Abstract

This study described treatment patterns in a psoriatic arthritis (PsA) patient registry for new or ongoing tumor necrosis factor inhibitor (TNFi) monotherapy, conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapy, or TNFi/csDMARD combination therapy. This retrospective analysis included adults with PsA who enrolled in the Corrona PsA/spondyloarthritis registry between March 21, 2013 (registry initiation), and January 31, 2017, and received an approved TNFi and/or csDMARD as "existing use" starting before registry entry or "initiated use" starting on/after registry entry. Therapy persistence was defined as index therapy use for ≥ 12 months without a treatment gap of ≥ 30 days. Among the evaluable patients with existing TNFi monotherapy ($n = 251$), csDMARD monotherapy ($n = 225$), and combination therapy ($n = 214$), 93, 87, and 87% were persistent for ≥ 12 months, and another 6, 5, and 5%, respectively, had no change with < 12 months of follow-up after first use. Among evaluable patients who initiated use of TNFi monotherapy ($n = 26$), csDMARD monotherapy ($n = 35$), and combination therapy ($n = 15$), 50, 43, and 53% were persistent for ≥ 12 months, and another 27, 20, and 20%, respectively, had no change with < 12 months of follow-up after first use. After initiation of index therapy, most changes (19–27% of patients) were discontinuation; 4–13% switched biologic therapy during follow-up. The results of this analysis of real-world treatment patterns in a PsA patient registry suggest that nonpersistence for TNFi monotherapy, csDMARD monotherapy, or TNFi/csDMARD combination therapy occurs more commonly after initiation of therapy than in patients with existing therapy. Trial registration: NCT02530268.

Keywords Psoriatic arthritis · Biological therapy · Tumor necrosis factor-alpha · Methotrexate · Antirheumatic agents

Introduction

Psoriatic arthritis (PsA)—a chronic, immune-mediated, inflammatory disease characterized by joint pain, swelling, and stiffness—is usually associated with psoriatic skin lesions [1]. Several treatment guidelines are available for PsA, including 2015 guidelines from the European League Against Rheumatism [2], 2015–2016 guidelines from the Group for Research and Assessment of Psoriasis and

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Psoriatic Arthritis [3], and 2017–2018 guidelines being developed by the National Psoriasis Foundation and American College of Rheumatology. Each recommends treatment options for PsA based on the severity of disease and its presentation. Mild PsA may respond to nonsteroidal anti-inflammatory drugs or intra-articular corticosteroid injections. PsA that is moderate or severe, that does not respond to these therapies, or that involves domains such as dactylitis or peripheral arthritis may be treated with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate, sulfasalazine, and leflunomide, but there are few clinical trials to support these therapies [2, 3]. Alternatively, patients with dactylitis, peripheral arthritis, axial disease, or enthesitis may receive biologic treatment, usually with a tumor necrosis factor inhibitor (TNFi).

Several controlled clinical trials have shown the efficacy and tolerability of TNFi therapy in patients with moderate-to-severe PsA, either as TNFi monotherapy or TNFi plus csDMARD in combination [4–9]. If TNFi treatment fails or is not appropriate, then newer therapies such as interleukin (IL)-12/IL-23 inhibitors, IL-17 inhibitors, abatacept, and tofacitinib may also be considered as alternatives [2, 3]. Published guidelines for PsA do not provide clear guidance on treatment pathways pertaining to restarting therapy after a treatment gap or switching between therapies.

The use of a disease registry to examine real-world treatment patterns can provide insight into whether initiation of treatment for PsA is consistent with the current guidelines and available clinical research. Understanding real-world treatment patterns may also inform future PsA treatment guidelines. Thus, the objective of this study was to describe treatment patterns for new or ongoing TNFi/csDMARD therapy in PsA patients participating in a nationwide registry.

Materials and methods

Data source

This was a retrospective analysis of data from a cohort of PsA patients. The source population consisted of individuals who enrolled in the Corrona PsA/spondyloarthritis (SpA) registry. This independent, prospective, observational, disease-based registry includes adults (18 years or older) diagnosed by a rheumatologist to have PsA, axial or peripheral SpA, or ankylosing spondylitis. As of December 2017, the registry database included information on 2526 patients recruited at 35 private and academic practice sites in 22 states across the United States, with data from 10 767 patient visits and 5928 patient-years of follow-up (median, 3.3 years). Overall objectives of the registry are to understand the epidemiology and natural history of these conditions, including comorbidities, prescribing practices, and comparative effectiveness of treatments, in a real-world setting.

The Corrona PsA/SpA registry was established in accordance with the Declaration of Helsinki. All participating investigators were required to obtain full Institutional Review Board approval for conducting noninterventional research involving human subjects with a limited dataset. Sponsor approval and continuing review were obtained through a central Institutional Review Board (IRB) (New England Independent Review Board, NEIRB No. 120160070). Sponsor approval was first obtained on February 27, 2013. For academic investigative sites that did not receive a waiver to use the central IRB, full board approval was obtained from the respective governing IRBs and documentation of approval was submitted to Corrona prior to initiating any study procedures. Informed consent was obtained from all individual participants included in the study. The study is registered with http://www.clinicaltrials.gov (NCT02530268).

Study eligibility criteria

This analysis included patients with a diagnosis of PsA who enrolled in the registry between March 21, 2013 (registry initiation), and January 31, 2017, and who received TNFi monotherapy, csDMARD monotherapy, or TNFi/csDMARD combination therapy during this period. The csDMARD category comprised methotrexate, hydroxychloroquine, leflunomide, and sulfasalazine. The TNFi category comprised therapies that were approved for the treatment of PsA before registry initiation (etanercept, adalimumab, infliximab, and golimumab). After the index date (first recorded use) for TNFi and/or csDMARD therapy, patients were required to have at least 6 months of follow-up. Thus, the entire study period was from March 21, 2013, to July 31, 2017. Of 1608 patients in the registry during the study period, 1266 had the necessary follow-up and were included in the analysis.

The Corrona PsA/SpA registry excludes patients with a diagnosis of rheumatoid arthritis, systemic lupus erythematosus, or any other form of autoimmune inflammatory arthritis as well as patients who are participating in or planning to participate in a clinical trial with a nonmarketed or marketed investigational drug (i.e., phase I–IV drug trial). This analysis did not have patient exclusion criteria beyond those of the Corrona PsA/SpA registry.

Data collection

The Corrona PsA/SpA registry collects data from patients and their treating rheumatologists, including information on disease duration, prognosis, disease severity and activity, medical comorbidities, use of medications (biologics,

csDMARDs, and prednisone), and adverse events. Follow-up assessments, which are completed during routine clinical encounters, are requested at least as often as every 6 months. Validated tools are used to measure the disease severity and activity. Enthesitis severity is measured with the Spondyloarthritis Research Consortium of Canada (SPARCC) scale for tenderness from 0 to 16 [10]. Dactylitis severity is measured as the number of digits with dactylitis present from 0 to 20. The percentage of body surface area affected is recorded. Nail psoriasis severity is measured on a visual analog scale from 0 to 100. Physicians measure and record tender joint count from 0 to 68, swollen joint count from 0 to 66 (excluding hips), and Disease Activity Score from 28 joints with C-reactive protein (DAS28-CRP) [11, 12]. Patients complete the Health Assessment Questionnaire modified for Spondyloarthropathies (HAQ-S) with scores from 0 (no difficulty) to 3 (unable to do) [13], global skin assessment and global joint assessment from 0 (no disease activity) to 100 (most disease activity), and a pain visual analog scale from 0 (no pain) to 100 (worst pain). Patient and physician global disease assessments are combined with 28 swollen and tender joint counts to calculate the Clinical Disease Activity Index (CDAI) from 0 to 76, where <2.9 is remission, 2.9–10.0 low disease activity, 10.1–22.0 moderate disease activity, and >22.0 high disease activity [14]. Disease Activity in Psoriatic Arthritis (DAPSA) scores are calculated from joint counts (68 tender/66 swollen), CRP, and patient assessments of disease activity and pain, yielding scores consistent with remission (0–4) or mild (5–14), moderate (15–28), or high (>28) disease activity [15]. Patients use the Work Productivity and Activity Impairment questionnaire to report the effect of PsA/SpA on work (percentage of hours missed, impairment while at work, and work hours affected) and daily activities [16–18].

Statistical analysis

For this descriptive analysis, no hypothesis was generated a priori for statistical comparisons between or across the treatment cohorts. Demographics, clinical characteristics, and disease activity at the index date were summarized by index therapy for all PsA patients in the registry who received a TNFi or csDMARD at least once during the study period and had at least 1 follow-up visit at least 6 months after the index date. Treatment patterns were summarized by index therapy for the subset of patients who completed the 12-month study visit between 9 and 15 months postindex (12 ± 3 months). Each analysis was conducted separately for two categories of treatment—"existing use" starting before registry entry or "initiated use" starting on/after registry entry.

Treatment patterns of interest based on medication use reported in the registry included treatment persistence, discontinuation, switch, and restart (Table 1). Persistence was defined as recorded use of the index therapy for at least 12 months after the index date without any treatment gap of at least 30 days. Discontinuation was defined as any treatment gap of at least 30 days without a subsequent prescription for the index therapy during follow-up. Restarting therapy was defined as a stoppage of index therapy for at least 30 days and restarting the index therapy after the treatment gap, without starting another therapy. Switching was defined as discontinuation of the index therapy and initiation of another therapy during follow-up. Patients with at least 6 months of follow-up postindex but less than 12 months of follow-up after the first use of the index therapy could not be defined as achieving treatment persistence; if they did not discontinue, switch, or restart therapy during this follow-up, they were categorized as having "no change (<12 months)."

The following treatment patterns were also examined (Table 1): stopping therapy was defined as stopping all PsA-related drugs and not receiving any other drug therapy after a gap in therapy of at least 30 days; therapy

Table 1 Treatment pattern definitions

Treatment pattern	Definition
Persistence	Continuous use for at least 12 months without a treatment gap of at least 30 days
No change for <12 months	Continuous use without a treatment gap of at least 30 days, with less than 12 months of follow-up after first use
Discontinuation	A treatment gap of at least 30 days, with no subsequent use of the index medication
Restart	A treatment gap of at least 30 days, then restarted the same therapy after the gap (without discontinuation or therapy switch/add-on)
Stop	A treatment gap of at least 30 days, with no subsequent use of any PsA medication during follow-up
Switch	Discontinuation of index medication, then initiation of another medication
Add-on	Continuation of index medication with initiation of another medication
Reduction	Discontinuation of either TNFi or csDMARD, with continuation of the other index medication (i.e., switch from combination to monotherapy)

csDMARD conventional synthetic disease-modifying antirheumatic drug, *PsA* psoriatic arthritis, *TNFi* tumor necrosis factor inhibitor

add-on (in the TNFi monotherapy or csDMARD monotherapy cohorts) was defined as the initiation of additional medication(s) along with continuation of index medication; reduction in therapy (in the combination therapy cohort) was defined as the discontinuation of a biologic or nonbiologic and continuing TNFi monotherapy or csDMARD monotherapy; and dose stretching included patients who received a Food and Drug Administration (FDA)–approved dose of a TNFi at the index date, and less than the FDA-approved dose of that TNFi during follow-up.

Results

Existing therapy: patient characteristics at the index date

At registry entry, 1144 patients with existing therapy received treatment as TNFi monotherapy ($n=421$), csDMARD monotherapy ($n=347$), or combination therapy ($n=376$), of whom 690 were evaluable at 12 months. In the analysis of demographics and clinical characteristics by existing index therapy, the mean age at the index date was 57.7 years for csDMARD monotherapy and 51.9–53.9 years in the other groups (Table 2). Women comprised 59% of patients receiving existing TNFi monotherapy and 46–50% of patients in the other groups. Prior csDMARD use was reported for 46% of patients in the existing TNFi monotherapy group and 98–100% of patients in the other groups.

In the analysis of PsA disease activity and severity at the index date by existing index therapy, the mean scores for disability, work impairment, enthesitis, dactylitis, body surface area, and nail psoriasis were generally consistent with low disease activity, and those for CDAI and DAPSA were consistent with low or moderate disease activity (Table 2). At the index date, peripheral involvement was reported for 77–87% of patients and axial involvement for 7–14%. The mean score for DAS28-CRP was 2.8 in the TNFi monotherapy group and 3.1 in each of the other groups. The mean CDAI scores for TNFi monotherapy, csDMARD monotherapy, and combination therapy were 9.7, 11.6, and 11.7, respectively, and the mean DAPSA scores were 13.9, 17.2, and 16.5, respectively. The mean scores for disability and work impairment were low among existing therapy patients, with the mean HAQ-S scores ranging from 0.2 to 0.3 and percentage of work hours affected overall ranging from 15 to 18%. The mean duration of PsA was 10.5 years in the csDMARD monotherapy group and 13.0 years each in the TNFi monotherapy and combination therapy groups.

Existing therapy: treatment patterns postindex

Of 1144 patients with existing therapy, 690 (60%) patients were evaluable for treatment patterns because they had a 12-month follow-up visit between 9 and 15 months postindex for existing TNFi monotherapy ($n=251$), csDMARD monotherapy ($n=225$), or combination therapy ($n=214$). Most patients with existing TNFi monotherapy, csDMARD monotherapy, or combination therapy achieved either treatment persistence for at least 12 months (93, 87, and 87%, respectively) or no change in therapy with less than 12 months of follow-up after first use (6, 5, and 5%, respectively; Table 3). The postindex treatment patterns of discontinuation of index therapy, switching to another biologic, and restarting therapy after an interruption each occurred in less than 5% of patients in each group, apart from discontinuation of combination therapy in 8% of patients. TNFi dose stretching was reported for 10 (4%) patients in the TNFi monotherapy group and 3 (1%) patients in the combination therapy group.

Initiated therapy: patient characteristics at the index date

Initiation of therapy starting on or after registry enrollment was reported for 122 patients who initiated TNFi monotherapy ($n=43$), csDMARD monotherapy ($n=56$), or combination therapy ($n=23$), of whom 76 were evaluable at 12 months. In the analysis of demographics and clinical characteristics by initiated index therapy (Table 4), the mean age at the index date was 55.8 years for csDMARD monotherapy and 50.7–52.3 years in the other groups. Women comprised 43–48% of patients receiving initiated therapy. History of csDMARD use was reported for 30% of patients in the initiated TNFi monotherapy group, 0% in the initiated csDMARD monotherapy group, and 57% in the combination therapy group.

In the analysis of PsA disease activity and severity at the index date by initiated index therapy, the mean scores for CDAI, DAPSA, disability, work impairment, enthesitis, dactylitis, body surface area, and nail psoriasis were consistent with low or moderate disease activity (Table 4). At the index date, peripheral involvement was reported for 78–91% of patients and axial involvement for 5–13%. The mean DAS28-CRP scores for TNFi monotherapy, csDMARD monotherapy, and combination therapy were 3.4, 3.8, and 2.9, respectively. The mean CDAI scores for TNFi monotherapy, csDMARD monotherapy, and combination therapy were 12.7, 16.2, and 12.2, respectively, and the mean DAPSA scores were 19.2, 24.7, and 19.1, respectively. The mean HAQ-S scores ranged from 0.3 to 0.4, and the percentage of work hours affected overall ranged from 19 to 29%.

Table 2 Existing therapy: patient characteristics at the index date

Patient characteristic	TNFi ($n=421$)	csDMARD ($n=347$)	Combination ($n=376$)
Age, years	51.9 ± 12.3	57.7 ± 13.3	53.9 ± 11.3
Sex, female	244 (59)	158 (46)	185 (50)
Race, White	386 (92)	326 (94)	327 (87)
Currently employed	275 (65)	188 (54)	222 (59)
Body mass index			
Normal/underweight	53 (13)	62 (18)	65 (17)
Overweight	144 (34)	92 (27)	96 (26)
Obese	202 (48)	182 (52)	204 (54)
Concurrent psoriasis	366 (87)	300 (86)	312 (83)
Axial involvement	59 (14)	26 (7)	33 (9)
Peripheral involvement	324 (77)	302 (87)	312 (83)
History of comorbidities			
Cardiovascular	217 (52)	189 (54)	190 (51)
Malignancy	33 (8)	30 (9)	26 (7)
Diabetes	58 (14)	56 (16)	55 (15)
Serious infection	16 (4)	22 (6)	20 (5)
History of nonTNFi biologic use[a]	4 (1)	0 (0)	3 (1)
History of csDMARD use	192 (46)	347 (100)	369 (98)
Methotrexate	175 (42)	313 (90)	349 (93)
Other csDMARD[b]	53 (13)	73 (21)	72 (19)
Current prednisone use	13 (3)	30 (9)	20 (5)
Duration of PsA, years	13.0 ± 9.9	10.5 ± 10.2	13.0 ± 10.1
Enthesitis	74 (18)	52 (15)	75 (20)
SPARCC enthesitis (1[c]–16)	4.3 ± 3.5	4.4 ± 3.2	4.1 ± 2.8
Dactylitis	27 (6)	25 (7)	12 (3)
Dactylitis count (1[c]–20)	1.7 ± 1.4	1.9 ± 1.2	2.1 ± 1.4
Body surface area, %	4.9 ± 8.7	4.8 ± 9.3	5.0 ± 11.9
Body surface area > 3%	121 (30)	100 (31)	94 (26)
Nail psoriasis (0–100)	5.6 ± 12.4	8.1 ± 22.6	7.2 ± 14.3
DAS28-CRP (2–10)	2.8 ± 1.0	3.1 ± 1.0	3.1 ± 1.0
Tender joint count (0–68)	3.3 ± 7.4	4.0 ± 8.4	4.5 ± 9.4
Swollen joint count, excluding hips (0–66)	1.3 ± 2.9	2.2 ± 4.7	1.7 ± 3.3
Physician global assessment (0–100)	12.0 ± 15.5	15.5 ± 17.4	15.3 ± 17.4
Patient global joint assessment (0–100)	41.7 ± 32.3	42.7 ± 30.8	43.3 ± 31.2
Patient global skin assessment (0–100)	40.6 ± 32.0	40.9 ± 30.2	42.2 ± 31.0
Patient-reported pain (0–100)	31.6 ± 28.5	36.2 ± 29.1	34.8 ± 27.8
Clinical disease activity index (0–76)	9.7 ± 6.6	11.6 ± 9.2	11.7 ± 8.4
DAPSA (0–164)	13.9 ± 12.8	17.2 ± 16.7	16.5 ± 15.4
HAQ-S (0–3)	0.2 ± 0.4	0.3 ± 0.4	0.3 ± 0.4
Work productivity and activity impairment			
Work hours missed, %[d]	3.5 ± 13.4	1.3 ± 8.6	2.7 ± 10.5
Impairment while working, %[d]	13.8 ± 20.3	14.6 ± 18.9	15.4 ± 19.8
Work hours affected overall, %[d]	15.2 ± 21.7	14.9 ± 18.6	17.5 ± 22.4
Daily activities impaired, %[d]	16.3 ± 22.3	17.8 ± 21.9	19.3 ± 22.8

Results are shown as mean ± standard deviation or number of patients (%)

csDMARD conventional synthetic disease-modifying antirheumatic drug, *DAPSA* Disease Activity in Psoriatic Arthritis, *DAS28-CRP* Disease Activity Score from 28 joints with C-reactive protein, *HAQ-S* Health Assessment Questionnaire modified for spondyloarthropathies, *PsA* psoriatic arthritis, *SPARCC* Spondyloarthritis Research Consortium of Canada, *TNFi* tumor necrosis factor inhibitor

[a]Abatacept, tocilizumab, anakinra, rituximab, secukinumab, tofacitinib, or ustekinumab

[b]Hydroxychloroquine, leflunomide, or sulfasalazine

[c]Patients with no enthesitis/dactylitis (values of 0) were not included in calculations of mean counts

[d]Patients rated percentage of impairment specifically related to PsA or spondyloarthritis

Table 3 Existing therapy: postindex treatment patterns

Treatment pattern	TNFi ($n=251$)	csDMARD ($n=225$)	Combination ($n=214$)
Persistence ≥ 12 months	233 (92.8)	196 (87.1)	186 (86.9)
Total time on drug, months	68.6 ± 46.4	82.5 ± 78.1	49.8 ± 37.7
Time after index, months	11.9 ± 2.0	11.8 ± 2.2	11.7 ± 2.4
Dose stretching	10 (4.0)	0 (0.0)	3 (1.4)
No change for < 12 months	14 (5.6)	11 (4.9)	11 (5.1)
Change in therapy	4 (1.6)	18 (8.0)	17 (7.9)
Discontinuation	3 (1.2)	8 (3.6)	17 (7.9)
Time on drug, months	8.9 ± 1.8	8.3 ± 1.9	8.5 ± 2.3
Switch			
To another biologic	2 (0.8)	2 (0.9)	4 (1.9)
To methotrexate	0 (0.0)	1 (0.4)	–
Add-on			
Added another biologic	0 (0.0)	7 (3.1)	–
Added methotrexate	2 (0.8)	1 (0.4)	–
Reduction			
Dropped biologic	–	–	3 (1.4)
Dropped methotrexate	–	–	8 (3.7)
Stopped	0 (0.0)	1 (0.4)	5 (2.3)
Restarted	0 (0.0)	3 (1.3)	1 (0.5)
Time to restart, months	–	7.5 ± 0.2	0.0 ± 0.0

Results are shown as mean ± standard deviation or number of patients (%)

csDMARD conventional synthetic disease-modifying antirheumatic drug, *TNFi* tumor necrosis factor inhibitor

The mean duration of PsA was 5.7 years in the csDMARD monotherapy group and 10.1–10.2 years in the other groups.

Initiated therapy: treatment patterns postindex

Of the 122 patients who initiated therapy, 76 (62%) were evaluable for treatment patterns because they had a 12-month follow-up visit between 9 and 15 months postindex for initiated TNFi monotherapy ($n=26$), csDMARD monotherapy ($n=35$), or combination therapy ($n=15$). Among the patients with initiated TNFi monotherapy, csDMARD monotherapy, or combination therapy, approximately half achieved treatment persistence for at least 12 months (50, 43, and 53%, respectively), and 20% or more had no change in the index therapy during less than 12 months of follow-up after first use (27, 20, and 20%, respectively; Table 5). In the initiated TNFi monotherapy, csDMARD monotherapy, and combination therapy groups, the discontinuation of index therapy was reported for 19, 26, and 27% of patients, respectively, and switching to another biologic (or from a csDMARD to a biologic) for 4, 11, and 13% of patients, respectively; restarting therapy after an interruption of at least 30 days was not reported for any patient (Table 5). TNFi dose stretching was not reported for any patient with initiated therapy.

Discussion

In this real-world study of PsA patients, most of the reported use of TNFi monotherapy, csDMARD monotherapy, or TNFi/csDMARD combination therapy was existing when the patient enrolled in the Corrona PsA/SpA registry. Although the retrospective analysis was neither designed nor powered for comparisons across groups, a few apparent differences were noted. Compared to patients with existing TNFi monotherapy, patients with existing csDMARD monotherapy at registry enrollment were 6 years older, were less likely to be female, and had a PsA duration that was 2.5 years shorter. Other demographics, clinical characteristics, and disease activity were similar across the groups for existing therapy at the index date. Across the treatment groups, patients with existing therapy had DAS28-CRP scores that were mostly consistent with remission or low disease activity as well as low scores at the index date (i.e., registry entry for existing therapy) for several measures of disease activity, disability, or work impairment. The mean scores for DAPSA, a composite measure that includes each of the key components of PsA [15], were near the cutoff between mild and moderate disease activity. These results suggest that PsA was stable among patients who were already being treated with TNFi or csDMARD therapy when they entered the registry. However, the registry was

Table 4 Initiated therapy: patient characteristics at the index date

Patient characteristic	TNFi ($n=43$)	csDMARD ($n=56$)	Combination ($n=23$)
Age, years	50.7 ± 14.0	55.8 ± 14.1	52.3 ± 13.5
Sex, female	19 (44)	24 (43)	11 (48)
Race, White	40 (91)	51 (91)	23 (100)
Currently employed	29 (66)	28 (50)	14 (61)
Body mass index			
Normal/underweight	9 (21)	4 (7)	1 (4)
Overweight	14 (33)	12 (21)	8 (35)
Obese	18 (40)	37 (66)	8 (35)
Concurrent psoriasis	38 (88)	49 (88)	15 (65)
Axial involvement	4 (9)	3 (5)	3 (13)
Peripheral involvement	39 (91)	50 (89)	18 (78)
History of comorbidities			
Cardiovascular	13 (30)	28 (50)	9 (39)
Malignancy	5 (11)	2 (4)	2 (9)
Diabetes	7 (16)	6 (11)	1 (4)
Serious infection	2 (5)	3 (5)	1 (4)
History of nonTNFi biologic use[a]	2 (5)	0 (0)	0 (0)
History of csDMARD use	13 (30)	0 (0)	13 (57)
Methotrexate	10 (23)	0 (0)	11 (48)
Other csDMARD[b]	4 (9)	0 (0)	3 (13)
Current prednisone use	1 (2)	4 (7)	2 (9)
Duration of PsA, years	10.2 ± 10.5	5.7 ± 6.7	10.1 ± 7.8
Enthesitis	14 (32)	8 (14)	3 (13)
SPARCC enthesitis (1[c]–16)	3.1 ± 3.0	4.0 ± 3.5	1.7 ± 0.6
Dactylitis	7 (16)	14 (25)	4 (17)
Dactylitis count (1[c]–20)	1.1 ± 0.4	2.1 ± 0.8	2.8 ± 2.2
Body surface area, %	6.2 ± 8.8	5.4 ± 8.9	1.3 ± 2.1
Body surface area > 3%	18 (41)	20 (38)	4 (18)
Nail psoriasis (0–100)	11.9 ± 18.8	5.9 ± 15.2	10.3 ± 23.3
DAS28-CRP (2–10)	3.4 ± 0.7	3.8 ± 0.8	2.9 ± 1.0
Tender joint count (0–68)	3.5 ± 5.0	5.3 ± 6.6	4.6 ± 6.9
Swollen joint count, excluding hips (0–66)	2.1 ± 2.8	4.2 ± 5.1	2.9 ± 4.8
Physician global assessment (0–100)	26.1 ± 22.2	24.3 ± 19.1	24.4 ± 23.3
Patient global joint assessment (0–100)	37.0 ± 30.0	39.0 ± 24.4	50.0 ± 32.9
Patient global skin assessment (0–100)	39.2 ± 29.2	42.4 ± 24.2	48.6 ± 30.5
Patient-reported pain (0–100)	38.9 ± 30.0	49.1 ± 27.2	37.0 ± 31.3
Clinical disease activity index (0–76)	12.7 ± 7.4	16.2 ± 8.5	12.2 ± 9.1
DAPSA (0–164)	19.2 ± 13.3	24.7 ± 17.1	19.1 ± 28.4
HAQ-S (0–3)	0.3 ± 0.4	0.3 ± 0.3	0.4 ± 0.6
Work productivity and activity impairment			
Work hours missed, %[d]	3.0 ± 7.6	10.2 ± 28.7	1.7 ± 5.8
Impairment while working, %[d]	16.7 ± 21.2	23.9 ± 17.1	17.7 ± 19.8
Work hours affected overall, %[d]	20.1 ± 24.1	28.5 ± 24.5	19.2 ± 20.6
Daily activities impaired, %[d]	25.7 ± 27.2	30.4 ± 25.6	26.4 ± 25.6

Results are shown as mean ± standard deviation or number of patients (%)

csDMARD conventional synthetic disease-modifying antirheumatic drug, *DAPSA* Disease Activity in Psoriatic Arthritis, *DAS28-CRP* Disease Activity Score from 28 joints with C-reactive protein, *HAQ-S* Health Assessment Questionnaire modified for spondyloarthropathies, *PsA* psoriatic arthritis, *SPARCC* Spondyloarthritis Research Consortium of Canada, *TNFi* tumor necrosis factor inhibitor

[a]Abatacept, tocilizumab, anakinra, rituximab, secukinumab, tofacitinib, or ustekinumab

[b]Hydroxychloroquine, leflunomide, or sulfasalazine

[c]Patients with no enthesitis/dactylitis (values of 0) were not included in calculations of mean counts

[d]Patients rated percentage of impairment specifically related to PsA or spondyloarthritis

Table 5 Initiated therapy: postindex treatment patterns

Treatment pattern	TNFi ($n=26$)	csDMARD ($n=35$)	Combination ($n=15$)
Persistence ≥ 12 months	13 (50.0)	15 (42.9)	8 (53.3)
Total time on drug, months	15.9 ± 5.4	16.9 ± 8.7	16.0 ± 5.0
Time after index, months	13.3 ± 1.2	13.3 ± 1.5	13.3 ± 0.9
Dose stretching	0 (0.0)	0 (0.0)	0 (0.0)
No change for < 12 months	7 (26.9)	7 (20.0)	3 (20.0)
Change in therapy	6 (23.1)	13 (37.1)	4 (26.7)
Discontinuation	5 (19.2)	9 (25.7)	4 (26.7)
Time on drug, months	9.2 ± 2.4	8.0 ± 2.1	7.5 ± 0.7
Switch			
To another biologic	1 (3.8)	4 (11.4)	2 (13.3)
To methotrexate	0 (0.0)	0 (0.0)	–
Add-on			
Added another biologic	0 (0.0)	4 (11.4)	–
Added methotrexate	1 (3.8)	0 (0.0)	–
Reduction			
Dropped biologic	–	–	0 (0.0)
Dropped methotrexate	–	–	3 (20.0)
Stopped	2 (7.7)	5 (14.3)	0 (0.0)
Restarted	0 (0.0)	0 (0.0)	0 (0.0)
Time to restart, months	–	–	–

Results are shown as mean ± standard deviation or number of patients (%)

csDMARD conventional synthetic disease-modifying antirheumatic drug, *TNFi* tumor necrosis factor inhibitor

not designed to determine how many patients required dose escalation to achieve stable disease control before registry entry or how long those dose adjustments were required.

In the examination of postindex treatment patterns among patients with existing therapy who completed a 12-month follow-up visit between 9 and 15 months postindex (12 ± 3 months), almost all were persistent on that therapy. Most patients (87–93% in each existing therapy group) satisfied the study definition of treatment persistence for at least 12 months. Another 5–6% of patients in each group had no change in index therapy but less than 12 months of follow-up after first use. Only 2% of patients with existing TNFi monotherapy and 8% with existing csDMARD monotherapy or combination therapy had any change in therapy postindex. Treatment patterns were generally similar between patients with existing monotherapy or existing combination therapy, suggesting that the concomitant use of a csDMARD and TNFi did not influence treatment persistence for either existing therapy.

Patient characteristics and treatment patterns were analyzed separately for patients who initiated therapy with a TNFi or csDMARD after enrolling in the registry. Despite comprising less than 10% of the study population, this cohort had several notable characteristics. Prior csDMARD use was reported for 30–57% of patients who initiated therapy (compared with 46–100% of patients with existing therapy). Compared with patients with existing therapy, those who initiated therapy appeared to have higher disease activity, more dactylitis, and more work impairment at the index date. Each of these findings is consistent with stable disease management in the patients with existing therapy versus the patients who needed to start new therapy. Patients who initiated therapy also had a shorter duration of PsA than the patients with existing therapy. For both initiated and existing therapy, csDMARD monotherapy was started 3.5–4.5 years sooner than either TNFi monotherapy or TNFi/csDMARD combination therapy in the treatment course for PsA. Earlier use of csDMARDs than TNFi was supported by older treatment guidelines for PsA [19], whereas more recent treatment guidelines for PsA support the use of TNFi therapy early in the treatment pathway [2, 3]. In this analysis of real-world treatment of PsA patients between 2013 and 2017, more than half of the initiated therapy was either TNFi monotherapy or TNFi/csDMARD combination therapy, and few of these patients had prior treatment for PsA, suggesting that many PsA patients now start treatment with a regimen that includes a TNFi.

In the examination of postindex treatment patterns for initiated therapy, approximately 30% of patients changed index therapy by the 12-month follow-up visit. These patients typically discontinued the index therapy without restarting it. Persistence results for initiated therapy in this analysis

are consistent with numerous previous analyses reporting that PsA patients often discontinue therapy in the first 12–24 months [20–43]. Our results extend those findings by showing that once PsA patients were on established TNFi/csDMARD therapy (existing use) and in a state of remission/low disease activity, they were highly likely to continue on that therapy without changes. Thus, the observed discrepancies in treatment persistence between initiated and existing use suggest that patients required a change in initiated therapy because they did not respond to it or did not tolerate it well. Confounding by indication was possible; disease severity was generally mild in all cohorts and was within the same range across existing and initiated therapy, but some differences were seen for prior csDMARD use. Previous registry studies provided similar results but were conducted either outside the United States [25–39] or they used a subset of PsA patients from a registry in the United States that was designed primarily for patients with rheumatoid arthritis [40–43]. Our study used data from a registry in the United States that was specifically designed to collect information about patients with PsA. A systematic review of the previous registries was beyond the scope of this work, but results from previous registries (see APPENDIX) may provide insight into areas for future research as the data collected from the Corrona PsA/SpA registry mature. Those analyses could include explorations of longer term treatment patterns, predictors for treatment persistence, and clinical outcomes after treatment persistence or treatment discontinuation in PsA patients.

The TNFi category for this analysis included etanercept, adalimumab, infliximab, and golimumab, but it did not include biologics that were approved for the treatment of PsA after the study period began, including the TNFi certolizumab and the nonTNFi biologics ustekinumab, secukinumab, ixekizumab, and abatacept. It also excluded biologics that were approved for use in other conditions but not in PsA at the start of the study period. Additional analyses would be needed to determine whether other biologics have treatment patterns and persistence rates that are similar to those for established TNFi therapies. The study examined decreased usage through either therapy discontinuation or restarting after a treatment gap but did not examine increased usage through dose escalation, which previous studies reported for more than half of the PsA patients who received TNFi therapy [31, 44–48]. Another potential limitation of this analysis was the small number of patients with initiated use, who comprised less than 10% of the study population. As a result, a few patients with changes in therapy during follow-up had a substantial effect on treatment persistence rates for initiated use. This analysis included data from centers across the United States, but it is unknown whether the results are generalizable to other countries. This analysis did not examine treatment outcomes.

The results of this analysis of real-world treatment patterns in a PsA patient registry suggest that nonpersistence for TNFi monotherapy, csDMARD monotherapy, or TNFi/csDMARD combination therapy occurs more commonly for newly initiated therapy than for existing therapy. After stabilization of TNFi or csDMARD therapy in PsA patients, treatment persistence for 12 months or more is common. In this analysis of patients with PsA in a nationwide registry study, TNFi monotherapy or TNFi/csDMARD combination therapy was initiated several years later than csDMARD monotherapy. New treatment guidelines for PsA support the use of TNFi monotherapy or combination therapy early in the treatment course. Additional research is needed to examine whether PsA patients receive TNFi earlier as new treatment guidelines are disseminated and implemented in clinical practice.

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Compliance with ethical standards

Conflict of interest PJM has received research grants from AbbVie, Amgen Inc., Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Sun Pharmaceutical Industries Ltd., and UCB; has been a consultant for AbbVie, Amgen Inc., Bristol-Myers Squibb, Celgene, Galapagos, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries Ltd., UCB, and Zynerba; and has been a speaker for AbbVie, Amgen Inc., Bristol-Myers Squibb, Celgene, Genentech, Janssen, Novartis, Pfizer, and UCB. NAA and DHC are employees and stockholders of Amgen Inc. SR, CJE, RWH, and JDG are employees of Corrona, LLC. CJE is a stockholder of Corrona, LLC, and a mem-

ber of an advisory board for Merck. JDG is a stockholder of Corrona, LLC, and has been a consultant to Genentech, Janssen, Pfizer, Eli Lilly, and Novartis. GAA and MMFG were stockholders of Amgen Inc. and employees of Amgen Inc. when the work was conducted. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen Inc., Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo, Eli Lilly and Company, Genentech, Gilead, GlaxoSmithKline, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Ortho Dermatologics (Bausch Health), Pfizer Inc., Regeneron, Roche, Sun, and UCB.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Data sharing The Corrona dataset is based on a large US multicenter study adhering to a number of institutional review boards, with complex logistics. Patients did not provide consent to raw data sharing during the data collection for this purpose, and the Corrona data sharing policies do not permit raw data sharing for this purpose. An aggregated limited dataset from the current analyses is available to qualified investigators with an approved protocol. Data requests may be sent to Corrona, represented by Dr. Jeffrey D. Greenberg MD MPH, NYU School of Medicine, New York, NY, e-mail jgreenberg@corrona.org.

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