Changes in Treatment Patterns in Patients with Psoriatic Arthritis Initiating Biologic and Nonbiologic Therapy in a Clinical Registry

Philip J. Mease, Tamara Lesperance, Mei Liu, David H. Collier, Marc Mason, Sabrina Deveikis, and Neil A. Accortt

ABSTRACT. ***Objective.*** Treatment options for psoriatic arthritis (PsA) have increased and improved in the past decade; treatment patterns in PsA remain poorly understood. Understanding current practices would aid in treatment management of patients with PsA.

Methods. This observational study was based on data from the Corrona registry of adult patients with PsA in North America collected between January 1, 2004, and December 31, 2012. Patients were divided among 3 therapy cohorts: tumor necrosis factor inhibitor (TNFi) monotherapy, methotrexate (MTX) monotherapy, and TNFi and MTX combination therapy. Patients were further divided among 3 study periods to understand changes over time: 2004–2006, 2007–2009, and 2010–2012. Data were collected on persistence, discontinuation, restarting, switching, adding/dropping therapy, and dose stretching.

Results. This study included 520 patients: 190 TNFi monotherapy, 217 MTX monotherapy, and 113 combination therapy; 110 from 2004 to 2006, 192 from 2007 to 2009, and 218 from 2010 to 2012. Over time, the proportion of patients initiating TNFi monotherapy decreased, while the proportion initiating combination therapy remained constant. The percentage of patients who were persistent decreased over time across all therapy cohorts, but remained higher in TNFi monotherapy than in other cohorts. Duration of persistence decreased over time. Patients initiating MTX monotherapy were more likely than their TNFi counterparts to add therapy.

Conclusion. Treatment patterns in patients with PsA have changed from 2004 to 2012. Physicians are not more likely to initiate TNFi monotherapy, although clinical evidence supporting its effectiveness has increased over this study period, and patients remain more persistent with it. (J Rheumatol First Release January 15 2017; doi:10.3899/jrheum.160343)

Key Indexing Terms:
PSORIATIC ARTHRITIS TUMOR NECROSIS FACTOR INHIBITOR PERSISTENCE

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Psoriatic arthritis (PsA) is a chronic, inflammatory disease characterized by inflammation of the joints, the surrounding ligaments and tendons, and skin[1,2]. Symptoms associated with PsA can range from mild to very severe; common therapies for moderate or severe PsA include disease-modifying antirheumatic drugs (DMARD)[2]. DMARD encompass nonbiologic [such as methotrexate (MTX)] and biologic types [especially the class of tumor necrosis factor inhibitors (TNFi)] and can be taken as monotherapy or combination therapy. Previous studies have shown that the efficacy of TNFi therapy alone and in combination with MTX is similar[3,4,5,6,7,8,9,10], although some studies reveal improvements in drug survival in patients receiving concurrent TNFi and MTX[4,5].

Treatment goals for PsA include inhibition of structural damage and improvement of quality of life[11,12,13], while treatment decisions for PsA depend on the severity of different symptoms in different body areas[14]. Treatment patterns and treatment management for PsA are currently poorly understood. Because diverse treatment options are

available and clinical features are highly heterogeneous, understanding patterns of treatment — including which therapy options are accompanied by longer persistence — would help inform treatment decisions to maximize their benefits. As knowledge and awareness of PsA and its treatments have grown in recent years, it is also important to identify any changes in treatment patterns over time. The primary objective of our study was to provide a description of real-world treatment patterns among patients with PsA following initiation of TNFi and/or MTX therapy over the course of 3 study periods. The secondary objective was to evaluate factors or reasons for initiation and discontinuation of therapy among all patients, and add-on therapy among patients initiating monotherapy and the dropping of therapy by patients initiating combination therapy during study followup.

MATERIALS AND METHODS

Study design. This observational study analyzed data from a North American clinical registry of patients with PsA.

Study population. Patients with PsA who were enrolled as a subpopulation in the Corrona Rheumatoid Arthritis registry and newly initiated TNFi and/or MTX therapy between January 1, 2004, and December 31, 2012, were selected for our study. Patients were divided into cohorts by their index therapy: (1) TNFi monotherapy, (2) MTX monotherapy, and (3) TNFi and MTX combination therapy (hereafter referred to as combination therapy). Index therapy was defined by the first use of TNFi and/or MTX. Cohorts were further evaluated in 3-year study periods defined by enrollment date to evaluate and compare trends over time in each of the cohorts: (1) 2004–2006, (2) 2007–2009, and (3) 2010–2012.

Patients were included in the study if they had a diagnosis of PsA; were at least 18 years of age; had newly initiated treatment with adalimumab (ADA), etanercept (ETN), golimumab (GOL), infliximab, MTX, or a combination of a TNFi with MTX during the study period; and had ≥ 6 months of followup after index therapy initiation. A history of medication use was obtained for all patients upon enrollment; these were reported by the physician on the enrollment form and could include medical reports and patient recall. There were no exclusion criteria.

Ethics. This study used de-identified patient-level data and did not require institutional review board review.

Data source. The Corrona registry collects data from patients with PsA. As of March 2014, patients have been recruited from 166 private and academic practice sites across 40 states in the United States, with 651 participating rheumatologists. The registry includes more than 6000 patients, covering 26,908 visits and about 13,520 patient-years.

Definition of treatment patterns of interest. Persistence was defined as continuous use of index therapy without a treatment gap of ≥ 30 days measured over a 12-month followup period; a subset of patients was measured for persistence over an 18-month followup period. Of the patients who were persistent for 12 months (or 18 months), length of persistence was measured throughout the entire study, regardless of the patient's study period. Additionally, all other treatment patterns described below were observed throughout the entire study, not just within the patient's study period. Discontinuation was defined as a treatment gap of ≥ 30 days without another prescription for the index therapy throughout the study. Restarting was defined as a gap in index therapy ≥ 30 days and restarting the index therapy after the discontinuation. Switching was defined as initiation of a non-index therapy (biologic or nonbiologic) after discontinuation of the index therapy. Adding was defined as initiation of additional therapy (i.e., adding MTX to TNFi monotherapy or adding a TNFi to MTX monotherapy); dropping was defined as discontinuing either TNFi or MTX for patients who initiated combination therapy. Stopping was defined as stopping all systemic PsA-related therapies and not receiving any other therapy after a treatment gap of ≥ 30 days. Patients could have multiple therapy-switching and therapy-adding events.

Dose stretching was defined as any reduction in dose from a standard dose of therapy. This was only considered in patients who were persistent and receiving TNFi; for patients taking combination therapy, dose stretching was not considered for MTX. These are the specific definitions of dose reduction for the TNFi of interest: ADA < 40 mg every other week or < 80 mg every month; ETN < 50 mg every week or < 200 mg every month; GOL < 50 mg (subcutaneous injection) every month, < 50 mg every month if started at 100 mg every month, and 25 mg every month or 50 mg every 8 weeks if started at 50 mg every month.

Reasons for change in therapy. Reasons for change in therapy included side effects, social reasons, lack of effect, and doing well. Side effects included both serious and minor ones, and fear of side effects. Social reasons included cost, preference, and frequency of administration. Lack of effect included inadequate response and failure to maintain initial response. Doing well included remission and a physician's perception of the patient's disease activity (e.g., low disease activity and not active disease). Patients could have up to 3 reasons in order of importance for changing therapy. Data regarding reasons for change in therapy were completed by patients' physicians at their discretion and were not required in this study.

Patient clinical characteristics were recorded at the time of therapy change. Clinical Disease Activity Index (CDAI) is a composite score of swollen joint count, tender joint count, patient global disease activity, and evaluator global disease activity[15]. CDAI severity categories include remission (≤ 2.8), low (2.8 to ≤ 10), moderate (10 to ≤ 22), and high (> 22). The modified Health Assessment Questionnaire is a shortened version, with 8 questions (vs 20) from the 8 categories assessed[16]. The physician's global assessment skin assessment is an evaluation of the skin on a scale of 0–100 (clear to very severe) provided by the physician.

Statistical analysis. Primary and secondary outcomes were analyzed descriptively for patients with ≥ 6 months of followup data after therapy initiation. Patients were categorized by their therapy cohort (TNFi monotherapy, MTX monotherapy, and combination therapy) and study period (2004–2006, 2007–2009, and 2010–2012, inclusive). Baseline demographic and clinical characteristics were recorded at therapy initiation. Duration of persistence and time to discontinuation and restarting were also summarized. No safety data were analyzed.

RESULTS

Baseline characteristics. Demographic and clinical characteristics at therapy initiation are shown in Table 1; the flow of patients from enrollment in the Corrona registry to study initiation is shown in Supplementary Figure 1, available with the online version of this article. In the study (N = 520), there were 51.9% women; mean (SD) age was 49.6 (12.5) years, and duration of PsA was 5.3 (7.7) years. The percentage of patients initiating TNFi monotherapy decreased over time, while the percentage initiating combination therapy remained constant. In more recent study periods, the time between PsA diagnosis and therapy initiation shortened; however, time to initiation of TNFi monotherapy tended to be longer than time to initiation of MTX monotherapy or combination therapy, while time to initiation of MTX monotherapy was shortest across all study periods (Table 1). While CDAI at therapy initiation was consistently highest in patients receiving combination therapy at all study periods, CDAI remained above 12 in all cohorts in all study periods. A greater percent-

Table 1. Demographic and clinical characteristics at drug initiation in each study period.

Characteristics	2004–2006			2007–2009			2010–2012		
	TNFi Mono, n = 51	MTX Mono, n = 36	Combo, n = 23	TNFi Mono, n = 69	MTX Mono, n = 83	Combo, n = 40	TNFi Mono, n = 70	MTX Mono, n = 98	Combo, n = 50
Sex, female, n (%)	20 (39)	21 (58)	17 (74)	26 (38)	43 (52)	19 (48)	41 (59)	50 (51)	33 (66)
Age, yrs, mean (SD)	49.9 (10.1)	52.6 (14.5)	51.5 (10.3)	48.2 (13.3)	51.4 (12.4)	47.2 (14.2)	47.6 (12.2)	51.4 (12.6)	47.0 (11.5)
Race, white, n (%)	49 (96)	35 (97)	23 (100)	66 (96)	78 (94)	37 (93)	69 (99)	92 (94)	49 (98)
Duration of PsA, yrs, mean (SD)	8.4 (8.4)	2.8 (5.0)	7.6 (7.5)	6.7 (8.7)	4.3 (6.5)	7.2 (8.1)	6.6 (8.9)	2.7 (6.7)	4.2 (6.3)
History of RA, n (%)	2 (4)	2 (6)	3 (13)	2 (3)	4 (5)	1 (3)	1 (1)	3 (3)	1 (2)
History of PsO[a], n (%)	n/a	n/a	n/a	30 (43)	30 (36)	15 (38)	34 (49)	46 (47)	21 (42)
History of comorbidities, n (%)									
Cardiovascular	2 (4)	4 (11)	1 (4)	3 (4)	3 (4)	4 (10)	4 (6)	11 (11)	2 (4)
Malignancy	2 (4)	1 (3)	2 (9)	5 (7)	5 (6)	2 (5)	9 (13)	2 (2)	4 (8)
Diabetes	5 (10)	4 (11)	4 (17)	7 (10)	1 (1)	7 (18)	6 (9)	9 (9)	2 (4)
Serious infection[b]	n/a	n/a	n/a	0 (0)	0 (0)	0 (0)	4 (6)	3 (3)	4 (8)
mHAQ, mean (SD)	0.24 (0.30)	0.36 (0.40)	0.47 (0.41)	0.38 (0.44)	0.34 (0.35)	0.50 (0.59)	0.39 (0.43)	0.38 (0.40)	0.39 (0.35)
CDAI, mean (SD)	12.8 (10.9)	16.8 (13.3)	17.7 (10.8)	12.6 (12.5)	14.4 (10.4)	17.7 (12.1)	14.4 (11.2)	14.9 (11.5)	17.9 (12.2)
CDAI categories[c], n (%)									
Remission	12 (26)	3 (9)	1 (4)	12 (20)	11 (14)	1 (3)	7 (10)	6 (6)	5 (10)
Low	8 (17)	10 (29)	5 (22)	25 (38)	19 (24)	11 (28)	23 (33)	34 (35)	11 (22)
Moderate	18 (38)	11 (32)	12 (52)	17 (26)	33 (41)	15 (38)	28 (40)	40 (41)	18 (36)
High	9 (19)	10 (29)	5 (22)	11 (17)	17 (21)	13 (33)	12 (17)	18 (18)	16 (32)
PGA, mean (SD)	24.8 (20.3)	31.3 (22.4)	34.8 (21.5)	24.9 (23.0)	26.0 (17.8)	32.9 (24.9)	32.3 (22.1)	31.0 (18.6)	32.8 (22.0)
PGA skin assessment[b], mean (SD)	n/a	n/a	n/a	30.9 (32.1)	42.8 (30.7)	38.3 (28.8)	26.1 (22.8)	20.3 (17.8)	17.9 (18.7)

[a] PsO measure was not routinely collected in the CORRONA RA questionnaire before 2007. [b] Serious infection and PGA skin assessment measures were not included in the CORRONA RA questionnaire before 2008. [c] CDAI categories: remission: ≤ 2.8; low: 2.8 to ≤ 10, moderate: 10 to ≤ 22; high > 22. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate; PsA: psoriatic arthritis; RA: rheumatoid arthritis; PsO: psoriasis; n/a: not applicable; mHAQ: modified Health Assessment Questionnaire; CDAI: Clinical Disease Activity Index; PGA: physician's global assessment.

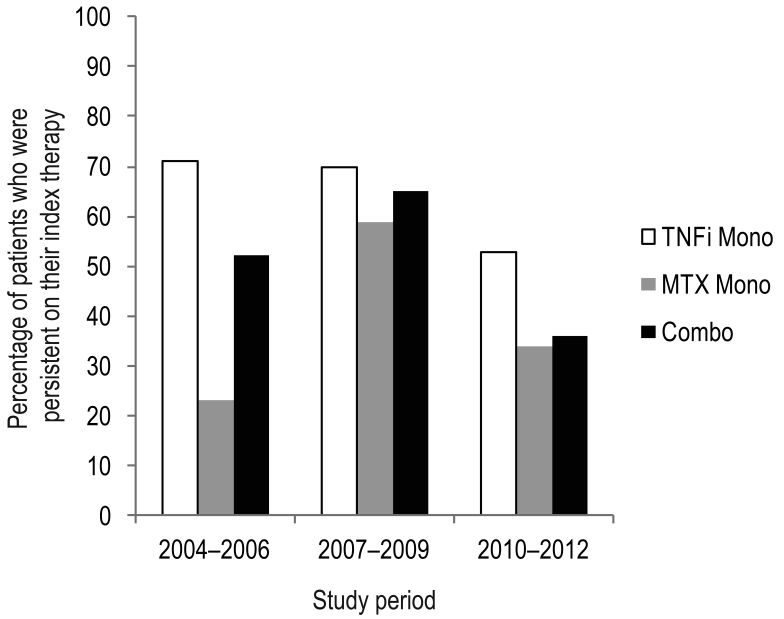

Figure 1. Percentage of patients in each study period who were persistent on their index therapy for at least 12 months. Patients who were persistent had no treatment gap of ≥ 30 days. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate; Combo: combination.

age of women initiated combination therapy during the earliest study period compared with later study periods.

Persistence with initial therapy. Across the 3 therapy cohorts, the percentage of patients who were persistent at 12 months on their index therapy decreased over the course of the study (Figure 1). During each study period, the percentage of patients who were persistent was higher among those who initiated TNFi monotherapy than among those who initiated MTX monotherapy or combination therapy (Figure 1).

Discontinuation, restart, and switch of initial therapy. The percentage of patients who discontinued their index therapy in each therapy cohort generally decreased over time among all therapy cohorts (Figure 2A). The percentage of patients who restarted their index therapy after a gap of ≥ 30 days also decreased (Figure 2B). The percentage of patients who switched their monotherapy (from their index TNFi to another TNFi, TNFi to MTX, or MTX to TNFi) remained relatively steady over the 3 study periods (Figure 2C). Similarly, the percentage of patients initiating combination therapy who switched to another TNFi remained steady from the earliest to most recent study period (9% in 2004–2006 to 8% in 2010–2012), with a spike to 40% in the interim (2007–2009; Figure 2D). The duration between therapy initiation and both discontinuation and restart decreased over time (Table 2).

Add-on to or reduction in initial therapy. Among patients who initiated monotherapy, those receiving MTX were more likely than those receiving TNFi to add a therapy, especially during the most recent study period (28% vs 11%; Figure 3A). In all study periods, patients initiating combination therapy were more likely to drop MTX than TNFi: 57% vs 13% (2004 to 2006), 38% vs 20% (2007 to 2009), and 28% vs 6% (2010 to 2012; Figure 3B).

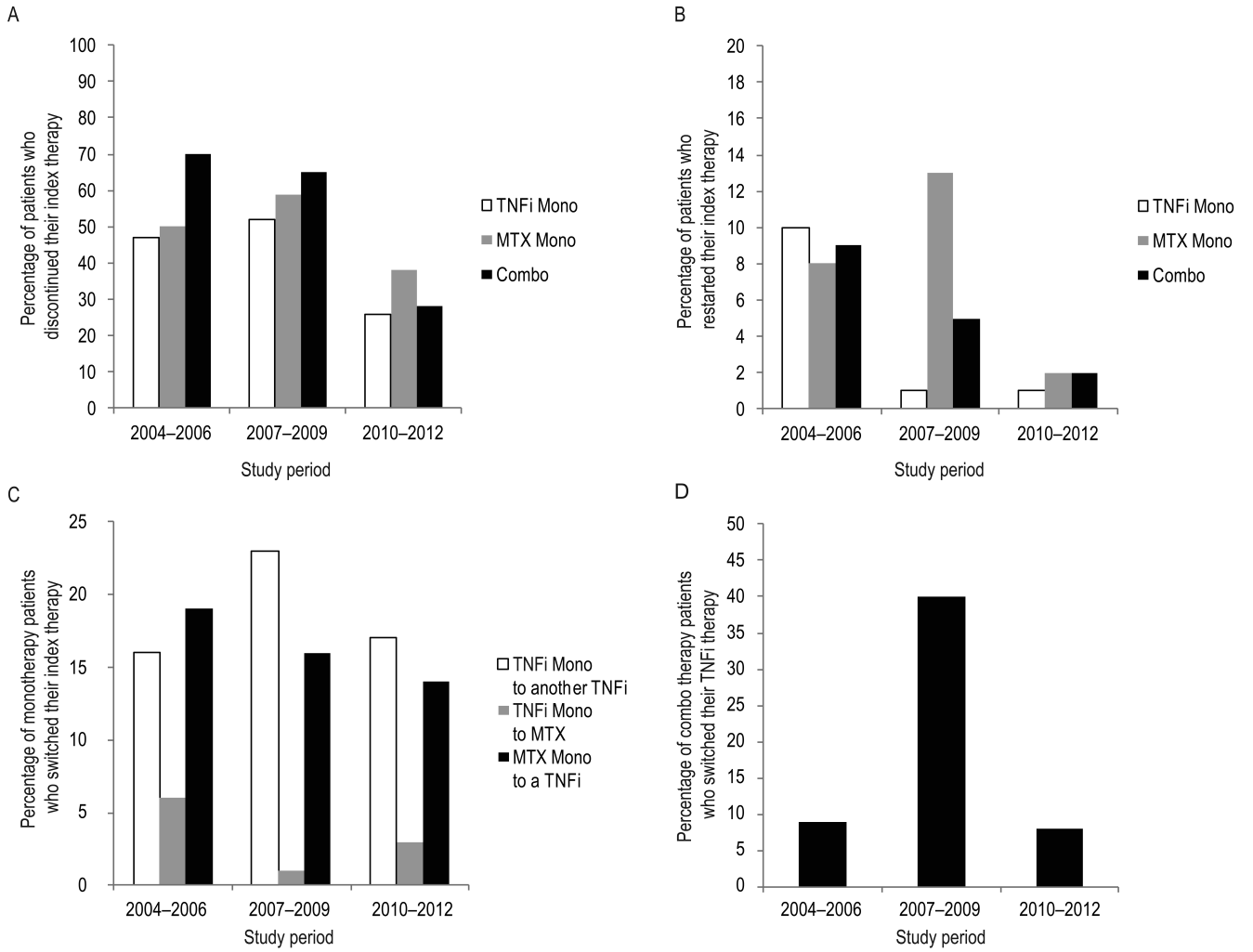

Figure 2. The percentage of patients in each study period who (A) discontinued their index therapy (experienced a treatment gap of ≥ 30 days), (B) restarted their index therapy after a treatment gap of ≥ 30 days, (C) switched from their index monotherapy to another monotherapy (TNFi to another TNFi or MTX, or MTX to TNFi), or (D) switched to another TNFi in their combination therapy after a treatment gap of ≥ 30 days. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate; Combo: combination.

Table 2. Length of time to change in index therapy in each study period.

Treatment Pattern	2004–2006			2007–2009			2010–2012		
	TNFi Mono, n = 51	MTX Mono, n = 36	Combo, n = 23	TNFi Mono, n = 69	MTX Mono, n = 83	Combo, n = 40	TNFi Mono, n = 70	MTX Mono, n = 98	Combo, n = 50
Persistence*									
n (%)	36 (71)	23 (64)	12 (52)	48 (70)	49 (59)	26 (65)	37 (53)	33 (34)	18 (36)
Length, mos, mean (SD)	46.0 (21.8)	38.3 (27.2)	46.0 (27.9)	31.8 (15.7)	30.2 (13.8)	31.2 (13.4)	19.6 (6.6)	17.5 (5.1)	21.3 (6.5)
Discontinuation†									
n (%)	24 (47)	18 (50)	16 (70)	36 (52)	49 (59)	26 (65)	18 (26)	37 (38)	14 (28)
Time to, mos, mean (SD)	24.1 (19.3)	27.6 (28.2)	20.1 (19.9)	16.6 (11.2)	14.2 (19.7)	19.7 (14.1)	9.6 (4.9)	7.3 (3.3)	10.3 (7.0)
Restart†									
n (%)	5 (10)	3 (8)	2 (9)	1 (1)	11 (13)	2 (5)	1 (1)	2 (2)	1 (2)
Time to, mos, mean (SD)	9.8 (3.0)	19.5 (22.3)	17.6 (16.2)	6.5 (n/a)	7.6 (4.9)	4.0 (1.9)	2.8 (n/a)	3.8 (3.3)	4.3 (n/a)

* Persistence was measured at 12 months. † Length of persistence, discontinuation, and restart were measured throughout the duration of the entire study. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate; Combo: combination therapy; n/a: not applicable.

Stopping initial therapy. In the earliest study period, patients initiating TNFi monotherapy were numerically more likely than their MTX counterparts to stop therapy (20% vs 8%; Figure 4). In the most recent study period, this trend reversed, with patients initiating MTX monotherapy more likely than their TNFi counterparts to stop therapy (13% vs 10%; Figure 4). In all the study periods, patients initiating combination therapy were less likely than both monotherapy cohorts to stop therapy (Figure 4).

Time to change in therapy. Duration of persistence decreased over the course of the 3 study periods (Table 2). Length of persistence in patients initiating TNFi monotherapy, MTX monotherapy, and combination therapy fell from 46, 38, and 46 months, respectively, in 2004–2006 to 20, 18, and 21 months in 2010–2012. Likewise, the time to discontinuation and restart decreased over the course of the study periods. Time to discontinuation in patients initiating TNFi monotherapy, MTX monotherapy, and combination therapy fell from 24, 28, and 20 months, respectively, in 2004–2006 to 10, 7, and 10 months in 2010–2012. Time to restart in patients initiating TNFi monotherapy, MTX monotherapy, and combination therapy fell from 10, 20, and 18 months, respectively, in 2004–2006 to 3, 4, and 4 months in 2010–2012.

Dose stretching of TNFi. Dose stretching was assessed in patients who were persistent ≥ 12 months and receiving TNFi. The percentage of patients in the monotherapy and combination therapy cohorts who reduced their TNFi dose decreased numerically over the course of the study from 18% and 17% (2004–2006), respectively, to 12% and 10% (2007–2009), and 1% and 6% (2010–2012; Supplementary Figure 2, available with the online version of this article). Dose stretching was relatively uncommon among patients in the TNFi monotherapy cohort in the most recent study period.

Reasons for change in therapy. The majority of patients who stopped, switched, added to their monotherapy, or dropped a therapy from their combination therapy did so because of (in order of frequency) lack of effect, social reasons, and/or side effects (data not shown). Data on reasons for change in therapy were available for about half of the patients in this study: TNFi monotherapy N = 97 (stopped n = 26, switched n = 42, and added n = 29), MTX monotherapy N = 121 (stopped n = 26, switched n = 34, and added n = 61), and combination therapy N = 83 (stopped n = 5, switched n = 22, and dropped n = 56). Patients who switched therapy primarily did so because of lack of effect: 59% from TNFi monotherapy, 41% from MTX monotherapy, and 64% from combination therapy. Patients who added to their monotherapy also primarily did so because of lack of effect: 56% to TNFi and 55% to MTX. Patients who reduced their combination therapy primarily did so because of social reasons (44%). "Doing well" was infrequently cited as a reason patients changed therapy.

Mean CDAI at therapy change was above 12 in patients initiating monotherapy with both TNFi (12.3) and MTX (14.2) who added therapy, while mean CDAI was lower in patients initiating combination therapy who dropped a therapy (10.1). Across all therapy cohorts, among those who stopped, switched, added to, or reduced their therapy, patients primarily belonged to the low CDAI category ($2.8 < \text{CDAI} \leq 10$) at the time of therapy change: 43% of patients from the TNFi monotherapy cohort, 60% from MTX monotherapy, and 60% from combination therapy with low CDAI stopped; 69% from TNFi monotherapy, 67% from MTX monotherapy, and 50% from combination therapy switched; 59% from TNFi monotherapy and 52% from MTX monotherapy added to their initial therapy, and 64% from combination therapy reduced their initial therapy.

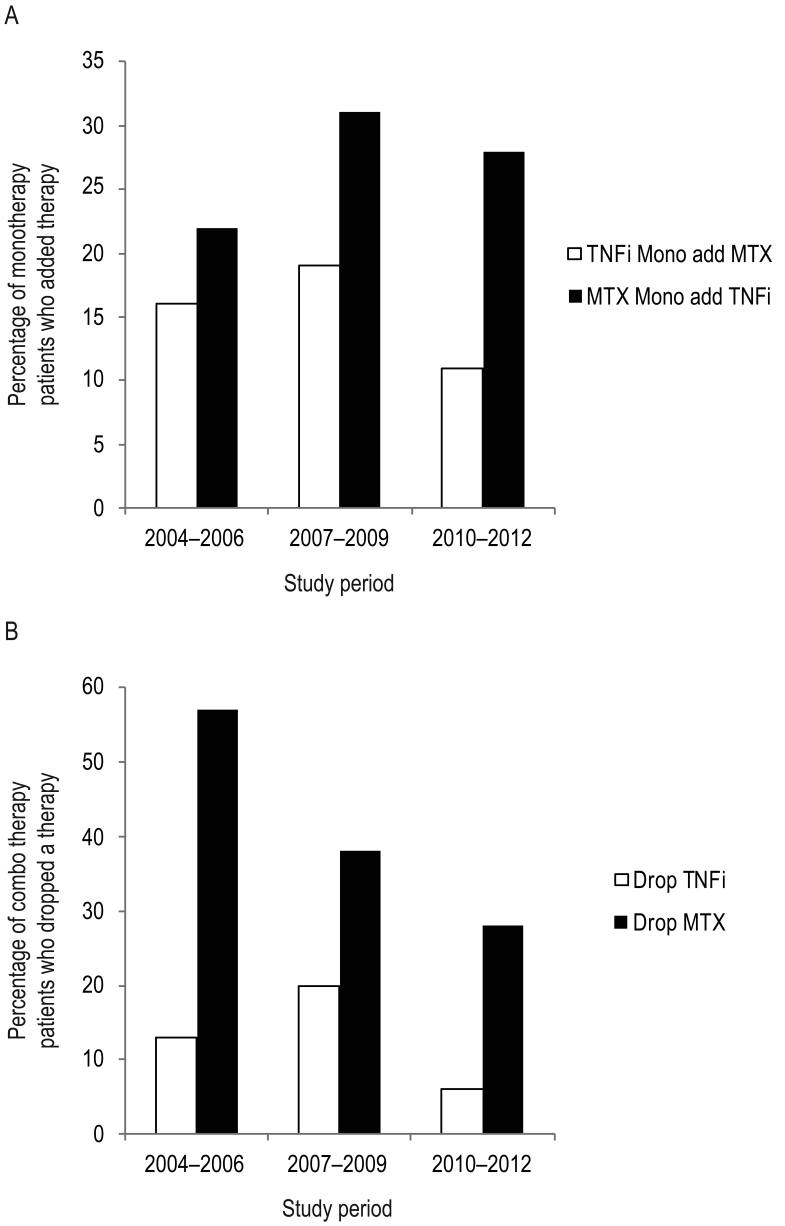

Figure 3. A. Percentage of patients in each study period who added a therapy to their monotherapy [MTX to TNFi monotherapy (white bars) or TNFi to MTX monotherapy (black bars)]. Patients could have multiple add-on events. B. The percentage of patients in each study period who dropped either TNFi (white bars) or MTX (black bars) from their combination therapy and continued with MTX or TNFi monotherapy, respectively. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate.

DISCUSSION

Using data from the Corrona registry of patients in North America with PsA, treatment patterns were evaluated between 2004 and 2012. Patients were stratified according to their initial therapy (TNFi monotherapy, MTX monotherapy, and combination therapy) and study period (2004–2006, 2007–2009, and 2010–2012, inclusive). Persistence with initial therapy decreased over time, although patients initiating TNFi monotherapy tended to be more persistent than other patients. Throughout the study, patients initiating MTX monotherapy were more likely to transition to combination therapy than their TNFi counterparts, while patients initiating combination therapy were more likely to drop MTX than TNFi. Patients initiating combination therapy were less likely to stop therapy than those initiating monotherapy.

This study enables an overview of how PsA treatment patterns have changed over time. By evaluating patients in 3 study periods, we have observed that, among patients who

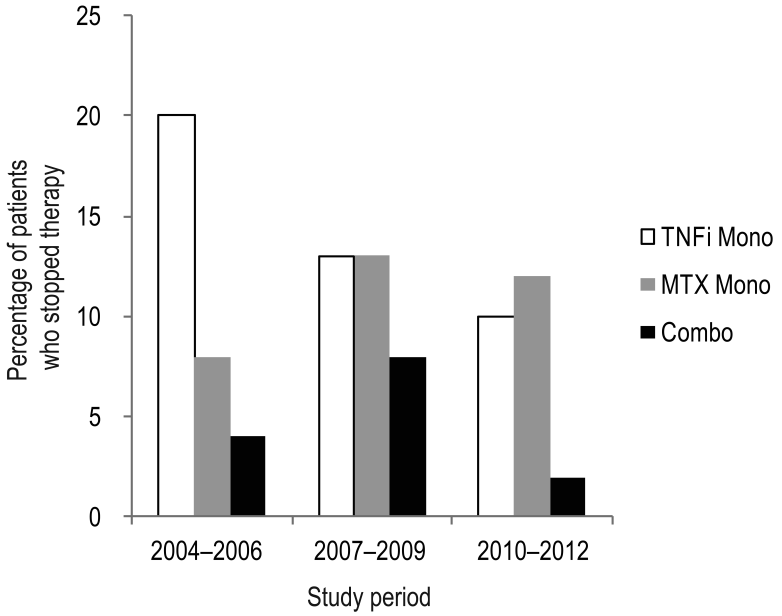

Figure 4. Percentage of patients in each study period who stopped therapy. Patients who stopped all therapy did not receive additional therapy after a treatment gap of ≥ 30 days. TNFi: tumor necrosis factor inhibitor; Mono: monotherapy; MTX: methotrexate; Combo: combination.

initiated TNFi monotherapy, those who switched have consistently been more likely to switch to another TNFi than MTX. In recent years, patients who initiated MTX monotherapy have become less likely to switch to a TNFi. During the earliest and most recent study periods, patients who initiated combination therapy had similar rates of switching to another TNFi; during the interim period, these patients experienced a spike in switching to another TNFi. Dose stretching among patients receiving TNFi decreased over time. The percentage of patients who were persistent on their index therapy decreased in all therapy cohorts. The percentages of patients who discontinued, restarted, switched, or dropped therapy did not show a concomitant increase. Length of persistence and time to discontinuation and restart decreased over time. In particular, persistence while taking TNFi monotherapy steadily decreased, despite the clinical effectiveness of TNFi monotherapy in the treatment of PsA demonstrated in a variety of clinical trials[3,8,17,18,19].

Patients change their therapy for a variety of reasons. Lack of effect was the primary reason given, while doing well was not common. Patients who experienced lack of effect may have had an inadequate response or failure to maintain initial response. Among patients who stopped, switched, added, or reduced therapy, patients were primarily classified as having low CDAI (2.8 to ≤ 10) at the time of therapy change. While lack of effect is well documented as a major reason to change therapy[20,21,22], it is notable that 60% of patients with change-of-therapy data in our study stopped, switched, added, or reduced therapy while in low disease activity (LDA). Patients may have stopped therapy to determine whether they could continue doing well off therapy. They may have added a therapy if they were trying to attain remission (CDAI ≤ 2.8), or reduced therapy to determine whether they could maintain LDA on 1 medication.

Persistence rates in our study were comparable to or higher than those reported in other studies of patients with PsA followed for 1 year[23,24,25,26,27,28]. Across the 3 therapy cohorts and study periods, persistence rates ranged from 52% to 71%, except the 34% in the MTX monotherapy cohort and 36% in the combination therapy cohort from 2010 to 2012. Persistence rates have generally hovered around 50%–60% in analyses of healthcare databases: 50% for monotherapy with biologic DMARD and 53% for combination biologic and nonbiologic DMARD; 54% for biologic DMARD and 35% for MTX; 50% in patients receiving TNFi; and ranging from 48% to 76% in patients receiving either ADA or ETN[23,24,25,26,27,28]. Rates of adding MTX therapy to TNFi monotherapy in our study (16% in 2004–2006, 19% in 2007–2009, and 11% in 2010–2012) are comparable to the 15% observed in one study[28] and higher than the 3% observed in another[27]. In the latter study, the rate of adding biologic therapy to MTX monotherapy was higher than the rates observed in our study (17% vs 22% in 2004–2006, 31% in 2007–2009, and 28% in 2010–2012).

The 30-day gap we used to indicate discontinuation was shorter than the 45-, 60-, and 90-day gaps used in other studies. Sensitivity analyses were conducted to evaluate the effects of (1) changing the definition of discontinuation to a 60-day gap and (2) modifying the definition of persistence to 18 months of followup (Supplementary Table 1, available

with the online version of this article). The 18-month persistence data followed a pattern similar to the 12-month definition. Lengthening the treatment gap resulted in the inclusion of 2 additional patients compared with the 30-day definition.

Understanding reasons for discontinuation may help physicians to guide patients with subsequent therapy decisions. Patients who discontinue treatment because of lack of efficacy may benefit from switching therapy. In a study of patients who initiated therapy with a TNFi, responses to the second, or even third, TNFi were lower than responses to the initial, but 40%–50% of patients still achieved the American College of Rheumatology criteria for 20% improvement[29,30,31]. Persistence on the second TNFi tends to be lower than that for the initial TNFi[26].

Limitations of our study are typical of those associated with observational studies. Because the patients were not randomly placed in therapy groups, there is the risk of selection bias and channeling bias. Confounding may have been introduced, because therapy groups may not have been entirely balanced on baseline characteristics. Confounding by indication may also have been a source of bias, based on variables that have influenced patient treatment courses and outcomes, including disease activity, with greater activity increasing the possibility of more aggressive treatment and the choice of combination therapy. CDAI has not been validated as a disease activity measure in PsA. Because the registry is not based on an inception cohort and patients could enter at any time during disease duration, there is the risk of misclassification as a result of recall bias. Patients may also have been lost to followup. The data source for our study was a North American clinical registry, so the results may not be generalizable to regions outside the United States. Within each therapy cohort and study period, sample sizes were small. These small sample sizes, combined with the descriptive nature of our study, did not allow for meaningful statistical testing nor analyses to identify independent predictors of different therapy changes. Treatment pattern outcomes were not mutually exclusive, i.e., a patient could have qualified for more than 1 variable. Whereas persistence was defined at 12 (or 18) months, all other treatment patterns were measured throughout the entire study. As a result, followup time was shorter for more recent study periods, so fewer patients in the most recent study period had the opportunity to discontinue, restart, switch, etc.

Any differences in treatment patterns between groups should be interpreted with caution. Reasons for a change in therapy were collected by physicians at their discretion and were not a requirement, which may have led to missing information. Future efforts are needed to better identify patients who do not remain persistent or switch/stop therapy for reasons other than lack of efficacy or safety concerns. Larger studies are needed to better understand the reasons patients in LDA alter their current therapies.

Treatment patterns in patients with PsA have changed from 2004 to 2012, including earlier TNFi initiation and more cycling. This may be due to the increasing number of treatment options available and the increased focus on achievement of an LDA state. However, physicians do not appear to be more likely to initiate TNFi monotherapy, even though the clinical evidence supporting its effectiveness increased over the same study period and patients remain more persistent with it.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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