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Treatment Patterns and Costs for Anti-TNFα Therapy in Patients with Ankylosing Spondylitis

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Abstract

Objective: Limited information exists on real-world use of anti-tumor necrosis factor-α (TNFα) biologic agents in ankylosing spondylitis (AS). This study evaluated the treatment patterns and costs of anti-TNFα biologic therapy and disease-modifying antirheumatic drugs (DMARDs) in patients with AS.

Methods: MarketScan claim databases were used to identify anti-TNFα biologic treatment-naïve AS patients (aged ≥ 18 years that had not undergone anti-TNFα biologic therapy in the previous 6 months) who initiated anti-TNFα biologic treatment between October 1, 2009 and September 30, 2010. Frequency of anti-TNFα biologic switching, duration, treatment modification, and medical and pharmacy drug costs for each line of anti-TNFα biologic therapy was analyzed during the 3-year follow-up.

Results: We identified 337 eligible patients with AS. First-line anti-TNFα biologics were: etanercept (n=115), adalimumab (n=129), infliximab (n=38), and golimumab (n=15). Patients who did not switch were persistent with their first-line agent for a longer duration (505 days) than those who switched to a second-line (336 days) or third-line (325 days) anti-TNFα biologic agent. Time to first treatment modification was shorter for those who switched to second-line (88 days) and third-line (6 days) therapy versus those who remained on first-line therapy (160 days). Monthly per member medical costs were greatest for nonswitchers ($354) than for patients who received second-line ($225) or third-line ($112) anti-TNFα biologic treatment. Overall pharmacy drug costs were similar for patients with first-line ($1899), second-line ($1955) or third-line and further ($1890) therapy.

Conclusion: Patients with AS who switched anti-TNFα biologic therapy had more modifications to their treatment during the follow-up period. Those who switched to second- or third-line anti-TNFα biologic therapy had lower medical costs compared with those who remained with first-line treatment; however, pharmacy costs were similar among all.

Keywords: Anti-TNFα biologic treatment; DMARDs; Treatment patterns; Costs; Persistence; Switch; Treatment modification

Introduction

Ankylosing spondylitis (AS) is a chronic, inflammatory, rheumatic disease that primarily affects the spine, and in some cases, the peripheral joints and certain articular sites [1,2]. In the United States (US), the prevalence of AS is estimated to be between 0.2% and 0.5% [3,4] and is associated with several comorbidities, including ischemic heart disease, hypertension, hyperlipidemia, and type 2 diabetes, which further contributes to disease burden [5].

Biologics are a class of drugs with disease-modifying properties that mitigate the signs and symptoms of AS and include the tumor necrosis factor-α (TNFα) inhibitors etanercept, adalimumab, infliximab, certolizumab pegol, and golimumab [6-11]. These biologic drugs are approved for use in treating AS and are the most commonly used disease-modifying biologic treatments in the US [12-17].

Treatment goals for AS are to maximize long-term health-related quality-of-life and social participation by controlling the signs and symptoms of the disease [18-20]. Specifically, the aims are to mitigate joint pain and stiffness, disease progression, and systematic sequelae with the ultimate goal of disease remission-defined as absence of discernible disease activity [19-22]. The Assessment of Spondyloarthritis International Society (ASAS) and European League against Rheumatism (EULAR) recommend the use of conventional Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) as first-line therapy, and the use of anti-TNFα biologics for patients who are nonresponsive and have persistently high-disease activity despite conventional treatments [20]. Although, to date, no direct comparisons of the various anti-TNFα biologics in patients with AS have been reported, they appear to have comparable efficacy, with a clinical response rate ranging from 50% to 60% [20,23].

One US study found that, during their first year after starting anti-TNFα therapy, about two-thirds of patients with AS were either were persistent (no switch in medication or ≥ 45 days on therapy) with treatment or discontinued and subsequently restarted treatment with the same anti-TNFα biologic [24]. The remaining patients either switched to another TNFα inhibitor or withdrew from treatment [24]. Adjuvant therapy, such as NSAIDs or disease-modifying anti-rheumatic drugs (DMARDs), is sometimes added to enhance the effectiveness of an anti-TNFα biologic. The reasons for switching or modifying a specific anti-TNFα treatment may include adverse events (AEs), lack of efficacy, or patient disease characteristics [25-27]. Several studies have indicated that patients who switch anti-TNFα biologics may respond successfully to the new anti-TNFα agent, irrespective of the reason for switching [23,28-34]. This, in part, may be due to anti-TNFα biologics differing in chemical structure, mechanism of action, and safety profiles [23]. The guidelines recommend that switching to a second TNFα inhibitor might be beneficial especially in patients with loss of response [20]; although they do not provide clear guidance on switching beyond second-line anti-TNFα therapy [20]. In addition, the guidelines give no strong recommendations for the use of adjuvant therapy in treating AS, [20] and the current trend regarding the choice of adjunctive therapy in patients with AS is unclear [35].

Prior studies have assessed the treatment patterns of AS patients initiating anti-TNFα biologic treatment [23,24,28,36-39]. However, little is known with regard to the costs associated with each line of anti-TNFα treatment or with the addition of adjunctive therapy in treating AS. Multiple factors can affect the medical and drug costs including disease severity, functional disability, treatment response, dosing schedules, patient adherence, and switching anti-TNFα therapy [2,40]. None of these studies investigated the use of biologics in AS patients and how the healthcare or drug costs in this patient population change during each line of therapy. This study sought to fill this gap in the literature and to provide managed care payers and healthcare providers with an understanding of AS treatment patterns in real-world clinical practice and the economic impact of treatment changes in AS patients. The purpose of this study was to evaluate the treatment patterns and costs of anti-TNFα biologic therapy and DMARDs in patients with AS in the US.

Materials and Methods

Data source

This retrospective observational study used data from January 1, 2005 to September 30, 2013, from two Truven Health MarketScan® Research Databases: the Commercial Claims and Encounters Database (Commercial) and the Medicare Supplemental and Co-ordination of Benefits Database (Medicare). The Commercial Database is a medical and drug insurance claims database of unique de-identified patients that include active employees, early retirees, Consolidated Omnibus Budget Reconciliation Act (COBRA) continuers covered under employer-sponsored plans including exclusive provider organization, fee-for-service (FFS), preferred provider organizations (PPOs), point-of-service (POS), indemnity plans, and health maintenance organizations (HMOs) [41,42]. The Medicare database contains the healthcare information of retirees with Medicare supplemental insurance paid for by the employer, and includes the Medicare-covered and the employer-paid portion of the payment, and any out-of-pocket patient expenses [41]. Medical claims are linked to outpatient prescription drug claims and person-level enrollment data through the use of unique enrollee identifiers. Both databases furnish detailed cost, use, and outcomes data in both inpatient and outpatient settings. The databases contain patient information including demographics, healthcare utilization, comprehensive prescription drug information, and payment costs. All study data were accessed using techniques compliant with the Health Insurance Portability and Accountability Act of 1996, and no identifiable or protected health information was extracted during the course of the study [43]; therefore, the study did not require informed consent or institutional review board approval.

Sample selection and patient population

Patients were identified based on claims for an anti-TNFα biologic treatment of interest during the treatment identification period of October 1, 2009 through September 30, 2010. The index (initiation) date was defined as the first observed claim for an anti-TNFα biologic without any anti-TNFα biologic use in the previous 6 months (baseline). The follow-up period was identified as the 3 years that followed the index date. The biologics included were those that had an indication for AS during the study period such as etanercept, [12] adalimumab, [13] infliximab, [14] and golimumab [16]. DMARDs of interest were azathioprine, [44] hydroxychloroquine sulfate, [45] leflunomide, [46] sulfasalazine, [47] cyclosporine, [48] methotrexate, [49] and the phosphodiesterase 4 inhibitor, apremilast [50].

To be eligible for inclusion in this analysis, patients had to be age ≥18 years with at least one or more non–rule-out International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) claim for AS (ICD-9-CM code 720.0) during the index date and after January 1, 2005. Patients were excluded if they had an ICD-9-CM code for rheumatoid arthritis (RA) (714.x) or psoriatic arthritis (PsA) (696.0) recorded in claims during the 6-month baseline period and the 3-year follow-up period. Patients who were not continuously enrolled in medical and pharmacy benefits for 6 months before the index date and through the 3-year follow-up period were excluded.

Demographic and baseline patient characteristic variables

Demographic categorical variables of interest included age, gender, geographic region (Northeast, North central, South, West, Unknown), and insurance type (HMO and POS capitation, FFS, Unknown). Clinical categorical variables included first-line anti-TNFα therapy and comorbidities. Comorbidities of interest included type 2 diabetes (ICD-9-CM: 249.0, 250.0, 357.2, 362.0, 366.41), hypertension (ICD-9-CM: 362.11, 401.0-405.0, 437.2), hyperlipidemia (ICD-9-CM: 272.0-272.4), and ischemic heart disease (ICD-9-CM: 410.0-414.0, 414.12, 414.2, 414.3, 414.8, and 414.9).

Outcome measures

The study outcome measures were the number of patients on first-, second-, or third-line or further anti-TNFα biologic therapy. A patient was regarded on the nth-line of anti-TNFα treatment (i.e., first, second, third, or beyond) if they initiated the nth kind of anti-TNFα treatment. Other outcome measures included persistent use of an anti-TNF biologic (defined as time from initiation of the treatment line to discontinuation [e.g., a gap in treatment of > 60 days]) or as time to switch to the next treatment line, or whichever came first. Time to first treatment modification was defined as the time from initiation of a

line of anti-TNFα treatment to first modification of that line of treatment. Treatment modifications included biologic dose increase or decrease, DMARD dose increase, decrease, add-on, removal, and medication drug change. All-cause healthcare resource costs (per member per month [PMPM]) at each line of therapy, including medical (hospitalizations, office visits, emergency room [ER] visits) and pharmacy drug costs (anti-TNFα therapy and DMARDs) were also collected.

Statistical analysis

All data were analyzed descriptively. Patient-level analysis included demographics, number of patients on one or more lines of anti-TNFα therapy, number of patients initiating each anti-TNFα agent of interest, and number of patients who switched treatments (any switch or one or more switches).

Subgroup analysis reported the mean (standard deviation [SD]) timeframe (in days) patients remained on treatment for each line of treatment, timeframe for patients to switch to the next line of treatment, and timeframe from the initiation of treatment to the first treatment modification.

Medical and pharmacy drug costs were calculated by line of treatment. Medical costs included hospitalizations, office, and ER visits. Pharmacy drug costs included anti-TNFα biologic plus DMARD medication costs. For each of the outcomes, the PMPM value was calculated as total costs incurred from initiation of anti-TNFα treatment to discontinuation of treatment, or end of the 3-year follow-up period (whichever happened first), the number of months from initiation to treatment discontinuation or end of the follow-up period (whichever happened first).

Results

Demographics and baseline characteristics

A total of 337 patients with AS met the sample selection criteria and started anti-TNFα treatment between October 1, 2009 and September 30, 2010 (Figure 1). The majority of patients (88.1%) were persistent on their first-line anti-TNFα biologic (Table 1). At the index date, the mean age was similar across lines of treatment and a higher percentage of males than females were observed in each group across all lines of treatment. About one-third of patients with AS who received first- and second-line treatment resided in the Southern portion of the United States. The majority of patients (82.5%) had FFS healthcare insurance. The most common first-line anti-TNFα biologics were adalimumab (43.4%) and etanercept (38.7%). The most common first-line therapy for patients who received two or more lines of therapy was etanercept (≥ 60%). During the 3-year follow-up, 54.3% of patients had comorbidities of which the most common were hypertension (38.3%) and hyperlipidemia (27.6%) (Table 1).

	Patients With Only First-line Biologic Therapy (n=297)*	Patients With Second-line Biologic Therapy (n=30)†	Patients With Third-line or Greater Biologic Therapy (n=10)*†	Overall (N=337)
Age (y), mean (SD)	44.6 (12.3)	44.6 (10.7)	51.2 (9.2)	44.8 (12.1)
Female, n (%)	86 (29.0)	14 (46.7)	4 (40.0)	104 (30.9)
US region, n (%)				
Northeast	39 (13.1)	6 (20.0)	1 (10.0)	46 (13.6)
North central	73 (24.6)	4 (13.3)	3 (30.0)	80 (23.7)
South	101 (34.0)	11 (36.7)	1 (10.0)	113 (33.5)
West	84 (28.3)	9 (30.0)	5 (50.0)	98 (29.1)
Unknown	0	0	0	0
Health insurance, n (%)				
FFS	246 (82.8)	25 (83.3)	7 (70.0)	278 (82.5)
HMO and POS capitation	45 (15.2)	5 (16.7)	2 (20.0)	52 (15.4)
Missing/unknown	6 (2.0)	0	1 (10.0)	7 (2.1)
Index biologic therapies, n (%)				
Etanercept	115 (38.7)	19 (63.3)	6 (60.0)	140 (41.5)
Adalimumab	129 (43.4)	7 (23.3)	2 (20.0)	138 (40)
Infliximab	38 (12.8)	1 (3.3)	2 (20.0)	41 (12.2)
Golimumab	15 (5.1)	3 (10.0)	0 (0)	18 (5.3)

Comorbidities, n (%)‡				
Type 2 diabetes	54 (18.2)	3 (10.0)	4 (40.0)	61 (18.1)
Hypertension	114 (38.4)	9 (30.0)	6 (60.0)	129 (38.3)
Hyperlipidemia	84 (28.3)	6 (20.0)	3 (30.0)	93 (27.6)
Ischemic heart disease	24 (8.1)	1 (3.3)	1 (10.0)	26 (7.7)
Any of the above	161 (54.2)	14 (46.7)	8 (80.0)	183 (54.3)

*Biologic therapy refers to the following anti-TNFα agents: etanercept, adalimumab, infliximab, and golimumab. †Among this group of patients, 6 (1.7% of AS groups) switched to a fourth-line of biologic treatment. ‡Identification was based on non–rule-out diagnoses. AS: Ankylosing Spondylitis; FFS: Fee-For-Service; HMO: Health Maintenance Organization; POS: Point-Of-Service; SD: Standard Deviation; TNFα: Tumor Necrosis Factor-A.

Table 1: Summary of demographics and baseline characteristics.

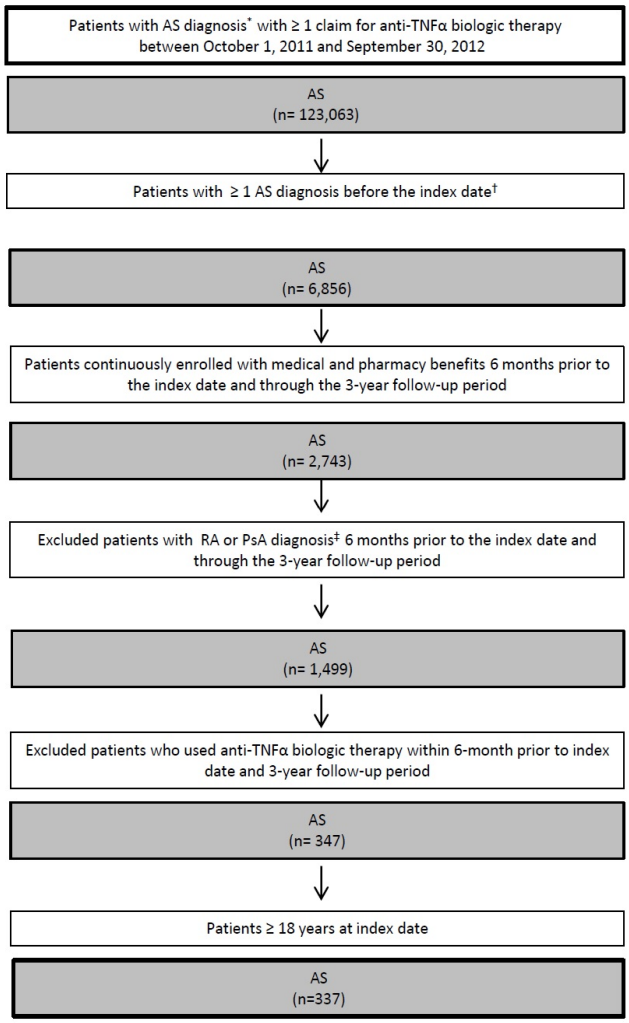

Figure 1: Patient selection flowchart. *The index date is the date of the use of the first anti-TNFα biologic. †A diagnosis of AS was established according to the ICD-9-CM code 720.0. ‡The ICD-9-CM codes for RA (ICD-9-CM code: 714.x) or PsA (ICD-9-CM code: 696.0) were used for diagnosis. AS: Ankylosing Spondylitis; ICD-9-CM: International Classification Of Diseases, Ninth Revision, Clinical Modification; PsA: Psoriatic Arthritis; RA: Rheumatoid Arthritis; TNFα: Tumor Necrosis Factor-A.

Persistent use, time to switch, and time to treatment change of anti-TNFα therapy

Patients with AS who received only first-line anti-TNFα therapy were persistent on treatment for a longer timeframe (505.1 days or about 17 months) than those who received second-line (335.9 days or about 11 months) or at least third-line (325.2 days or about 9 months) treatment (Table 2). Patients who did not switch from first-line therapy were slower (160 days or about 5 months) to modify their anti-TNFα treatment compared with patients who received two or at least three lines of therapy (≤ 87.7 days or about < 3 months).

The percentage of patients in each group that modified their DMARD medication during first-line treatment was small (range, 10% to 30%) and was similar to the modification of the second- and third-line or further treatment patterns. Patients who received second-line therapy switched from first-line therapy after modification more rapidly than patients who received third-line or greater of anti-TNFα biologic treatments (157 days or approximately 5 months vs 243.7 days or approximately 8 months) (Table 2).

In general, treatment modification for first-line, second-line, third-line, or additional therapy involved add-on of a DMARD (6.7%, 3.3%, and 10.0%, respectively), removal of a DMARD (5.7%, 3.3%, and 10%), or change to another DMARD (2.0%, 0%, and 10.0%) during the study. No patients increased or decreased their DMARD dose. Only 2 patients modified the dose of their anti-TNFα biologic agent; 1 patient in the first-line treatment group increased their dose, and another patient in the second-line treatment group decreased the dose.

Medical and drug costs

Medical costs PMPM were greater for patients in the first-line only treatment group ($354) than for those in the second- ($225) or third-line and additional therapy groups ($112) (Table 3). The medical costs PMPM for first-line anti-TNFα biologic was highest in patients that received only one anti-TNFα agent, followed by patients who received two and at least three anti-TNFα biologic agents.

For patients with at least three lines of anti-TNFα therapy, each additional line of treatment was associated with progressively lower medical costs compared with the first-treatment line. Overall pharmaceutical costs were about $1900 PMPM across all patient groups. Patients who received only first-line treatment had higher first-line pharmaceutical costs than the other two groups. The addition of each line of anti-TNFα biologic treatment was associated with an increase in pharmacy costs for both patients with second- and third-line or additional therapy.

	Patients With Only First-line Biologic Therapy (n=297)*	Patients With Second-line Biologic Therapy (n=30)*	Patients with Third-line or Greater Biologic Therapy (n=10)*
Persistent use of anti-TNFα biologic therapy (days), mean (SD)†			
First-line	505.1 (418.6)	335.9 (295.1)	325.2 (221.1)
Second-line	N/A	443.4 (335.7)	196.1 (220.2)
Third-line and more	N/A	N/A	156.5 (165.2)
Time to switch anti-TNFα biologic therapy(days), mean (SD)‡			
First-line	N/A	336.9 (295.1)	326.2 (221.1)
Second-line	N/A	N/A	197.1 (220.2)
Third-line and more	N/A	N/A	59.5 (41.1)
Time to first modification of anti-TNFα biologic therapy (days), mean (SD)§,¶			
First-line	160.0 (262.5)	87.7 (106.4)	6.0 (6.0)
Second-line	N/A	187.8 (238.4)	53.7 (93.0)
Third-line and more	N/A	N/A	29.7 (25.8)
Time from first modification of anti-TNFα biologic therapy to switch (days), mean (SD)‖			
First-line	N/A	157 (76.0)	243.7 (197.3)
Second-line	N/A	N/A	255.0 (370.9)
Third-line and more	N/A	N/A	13.0 (0.0)

*Anti-TNFα biologic therapy refers to the following anti-TNFα agents: etanercept, adalimumab, infliximab, and golimumab.

†Persistence use was defined as time from initiation of the line of treatment to discontinuation (a gap in treatment of > 60 days) of the line of treatment or switch to the next line of treatment (whichever came first).

‡Time to switch is defined as time from initiation of the line of anti-TNFα biologic treatment to switch to the next line of anti-TNFα treatment.

§Time to first modification of anti-TNFα biologic therapy was defined as time from initiation of the line of anti-TNFα biologic treatment to first modification on that line of treatment.

¶Modification of anti-TNFα biologic therapy included: biologic dose increase or dose decrease, DMARD added, changed, removed, or DMARD dose increase/ decrease; Benchmark DMARD to identify first-line DMARD change: most recent DMARD in 60-day prior to index biologics; Benchmark DMARD to identify second-/third-line DMARD change: most recent DMARD in the previous line.

‖Time from first modification of anti-TNFα biologic therapy to switch was defined as time from first modification on the line of anti-TNFα biologic treatment to switch to the next line of treatment.

AS: Ankylosing Spondylitis; N/A: Not Available; SD: Standard Deviation; TNFα: Tumor Necrosis Factor-A.

Table 2: Summary of treatment patterns for anti-TNFα biologic therapy in patients with AS for the 3-year follow-up period.

	Patients With Only First-line Biologic Therapy (n=297)‡	Patients With Second-line Biologic Therapy (n=30)‡	Patients With Third-line or Greater Biologic Therapy (n=10)‡
Medical Cost PMPM, Mean (SD)§,¶			
First-line	$354 ($2688)	$220 ($350)	$125 ($100)
Second-line	N/A	$242 ($341)	$111 ($103)
Third-line and more	N/A	N/A	$99 ($67.0)
Overall	$354 ($2688)	$225 ($243)	$112 ($60.0)
Pharmacy Cost PMPM Mean (SD)¶,‖			
First-line	$1899 ($1048)	$1779 ($595)	$1779 ($420)
Second-line	N/A	$2232 ($968)	$1928 ($1280)
Third-line and more	N/A	N/A	$2141 ($1150)
Overall	$1899 ($1048)	$1955 ($442)	$1890 ($393)

*Cost PMPM is defined as the cost incurred from initiation of treatment to discontinuation or end of follow-up period (whichever comes first)/the number of months from initiation of treatment to discontinuation or end of follow-up period (whichever comes first).

†Costs of capitation patients were replaced with fee-for-service proxy; all costs were adjusted by consumer price index.

‡Biologic therapy refers to the following anti-TNFα agents: etanercept, adalimumab, infliximab, and golimumab.

§Medical cost=hospitalization cost+ER cost+office visit cost.

Number of months is defined as the rounding of number of days on treatment divided by 30. If number of months equals to 0, then it is assigned as 1.

‖Pharmacy cost=Biologic treatment cost+DMARD treatment cost.

DMARD: Disease-Modifying Antirheumatic Drug; ER: Emergency Room; PMPM: Per Member Per Month; SD: Standard Deviation; TNFα: Tumor Necrosis Factor-A.

Table 3: Mean medical and pharmacy cost PMPM of AS patients receiving anti-TNFα therapy for the 3-year follow-up period*†.

Discussion

In this descriptive claims-based study, treatment patterns of patients with AS who remained on their first-line anti-TNFα biologic differed from that of patients who switched treatment. Treatment patterns were similar between patients with second- and third-line anti-TNFα therapies. Of the 337 patients who started treatment with an anti-TNFα biologic, the majority of patients were persistent on their first-line therapy during the 3-year follow-up. Adalimumab and etanercept were the most commonly used first-line biologics with etanercept being the most frequently used first-line biologic for switchers (both for the second-line and third-line and additional treatment groups); and adalimumab being most commonly used agent for nonswitchers. Hypertension and hyperlipidemia were the most frequent comorbidities across all treatment groups.

Persistence on first-line biologic for patients who switched anti-TNFα treatment was shorter than that for patients who did not switch. The time to switch treatment became progressively shorter for those patients who received at least three lines of therapy. The frequency of treatment modification was low (≤ 30% across patient groups), and mostly involved add-on, removal, or change in DMARD treatment. The time to first modification was shortest for the first-line treatment in patients who switched. Overall medical costs were greatest for patients who received only one line of biologic treatment ($354) than for patients who had two lines ($225) or at least three lines ($112) of treatment. Generally, pharmacy drug costs were similar across patient groups (range, $1890 to $1955).

Our findings are consistent with prior studies which found that most patients did not switch biologic treatment during the predefined observation period [18,24,28,39,51-53]. Two US studies investigated the frequency of switching anti-TNFα biologics after initiating treatment with etanercept, adalimumab, infliximab, [24,52] or golimumab [52] in patients with AS. Similar to our study, the most common first-line agents were etanercept (51% and 44.4%) and adalimumab (35% and 51.1%) [24,52]. Our study and that of Howe et al [52] found that adalimumab was the most frequently used first-line treatment while Bonafede et al noted the most common starting treatment was etanercept [24]. In the prior studies, the frequency of persistent use (no gap in biologic treatment ≥ 45 days and without switch to another anti-TNFα biologic) ranged from about 42% to 64%, and about 4% to 13% of patients switched to a new biologic [24,52,53]. The remaining patients either discontinued treatment or restarted the first-line biologic following a gap in therapy of ≥ 45 days.

Our findings suggest that a subgroup of patients who eventually switch biologic therapy change their anti-TNFα biologic treatment more rapidly than nonswitchers. In addition, patients with at least three lines of treatment are more apt to switch or modify their treatment than the other two groups. The reasons for the different treatment patterns across groups are not clear, but may indicate differences in response to anti-TNFs, AEs, comorbidities, change of physicians or health insurance, or patient preference.

Our study did not evaluate the potential reasons for switching or modifying treatment. Two prior studies found that, in patients with AS, about 30% to 36% discontinued or switched their anti-TNFα biologic treatment due to AEs [24,51] or lack of treatment effect [28]. Other predictors of biologic treatment discontinuation included being female, absence of peripheral arthritis, as well as lower erythrocyte sedimentation rate and C-reactive protein levels [51]. Higher disease activity was another predictor of discontinuation [51] or switching [28]. It is possible that switchers may be more refractory to treatment, possibly due to chronic disability or comorbidities [28].

Little is known about the cost of switching from one anti-TNFα biologic to another in patients with AS. We found that the medical costs were lower in patients who switched to a second- or at least a third-line anti-TNFα agent compared with patients who were persistent on their starting agent. We saw little difference in the overall pharmacy drug costs between patients who were persistent on their first-line biologic and those that were not; although nonswitchers had higher first-line drug costs than switchers. Even though the sample size was small, we did see an increase in medication costs as a patient moved from first- to third-line therapy. This may suggest that patients who switched biologic therapy require additional medications possibly due to disease progression or the presence of comorbidities. We did not separate out the cost for the specific anti-TNFα biologic or DMARD for each line of treatment from the total drug cost, and consequently cannot properly address how each of these variables influenced overall pharmacy drug costs.

Although two prior studies evaluated the cost of treating patients with AS, [18,40] our study is the first to assess costs associated with switching to multiple lines of anti-TNFα treatment. Consistent with our findings, medication costs made up a significant amount of the total cost and higher cost was associated with the index (first-line) anti-TNFα treatment than nonindex treatment [18]. In addition, and similar to our study, most patients remained on their index anti-TNFα agent [18].

A major limitation of our study is that we only evaluated continuous users. We did not capture patients who stopped using an anti-TNFα therapy and subsequently restarted with that same therapy. In addition, we excluded all patients who discontinue treatment for >60 days. Another limitation of our analysis was that it used claims data which do not capture the reason for switching. We also did not evaluate treatment response and its possible association with switching; therefore, it is not clear how factors such as physician beliefs, tolerability, efficacy, treatment modification, or treatment discontinuation affected switching. Our study was retrospective and descriptive in design. The retrospective nature limits the analysis to only patients that were clinically diagnosed with AS during this time period. The study was also limited to patients with commercial health coverage or private Medicare supplemental coverage. Consequently, findings cannot be generalizable to people with Medicaid, other insurance, or no insurance. In addition, diagnoses on claims may be coded incorrectly or not coded at all, thereby potentially introducing measurement error with respect to ICD-9-CM-based variables. This study did not take into consideration the possible effect on costs of discounts, rebates, or other price concessions. Our study did not evaluate stopping and restarting of therapy or whether the frequency of switching or restarting of treatment differed across the anti-TNFα agents studied. Interpretation of the data regarding patients who received three or more lines of ant-TNFα biologic treatment is limited by the small (n=10) sample size.

Conclusion

We found that treatment patterns differed between patients who switched than those who did not switch their first-line anti-TNFα biologic therapy. Treatment patterns were similar between patients with second- and third-line therapies. Patients who switched therapies were quicker to switch from and modify the initial anti-TNFα biologic

therapy than those patients who did not switch. Increasing the number of anti-TNFα treatment switches was associated with lower medical costs but not pharmaceutical costs, indicating the importance of the cost contribution of switching anti-TNFα treatment to total costs. The findings also highlight a subgroup of patients with multiple lines of therapy that may not be responding adequately to treatment. Our findings give managed care payers and healthcare providers an understanding of AS treatment patterns in real-world clinical practice and the economic impact of treatment changes in these patients.

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