


Treatment Persistence and Healthcare Costs Among Patients with Rheumatoid Arthritis Changing Biologics in the USA

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ABSTRACT

Introduction: After a patient with rheumatoid arthritis (RA) fails tumor necrosis factor inhibitor (TNFi) treatment, clinical guidelines support either cycling to another TNFi or switching to a different mechanism of action (MOA), but payers often require TNFi cycling before they reimburse switching MOA. This study examined treatment persistence, cost, and cost per persistent patient among MOA switchers versus TNFi cyclers.

Methods: This study of Commercial and Medicare Advantage claims data from the Optum Research Database included patients with RA and

at least one claim for a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) between January 2012 and September 2015 who changed to another TNFi or a different MOA therapy (abatacept, tocilizumab, or tofacitinib) within 1 year. The index date was the date of the change in therapy. Treatment persistence was defined as no subsequent switch or 60-day gap in therapy for 1 year post-index. RA-related costs included plan-paid and patient-paid amounts for inpatient, outpatient, and pharmacy claims. Medication costs included index and post-index costs of TNFi and different MOA therapies.

Results: There were 581 (38.3%) MOA switchers and 935 (61.7%) TNFi cyclers. The treatment persistence rate was significantly higher for MOA switchers versus TNFi cyclers (47.7% versus 40.2%, $P = 0.004$). Mean 1-year healthcare costs were significantly lower among MOA switchers versus TNFi cyclers for total RA-related costs (\$37,804 versus \$42,116; $P < 0.001$) and medication costs (\$29,001 versus \$34,917; $P < 0.001$). When costs were divided by treatment persistence, costs per persistent patient were lower among MOA switchers versus TNFi cyclers: \$25,436 lower total RA-related cost and \$25,999 lower medication costs.

Conclusion: MOA switching is associated with higher treatment persistence and lower healthcare costs than TNFi cycling. Reimbursement policies that require patients to cycle TNFi before switching MOA may result in suboptimal outcomes for both patients and payers.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that is characterized by synovitis (i.e., joint swelling) in at least one joint without an alternative etiology [1]. Treatment guidelines for RA recommend initiating treatment with a conventional synthetic disease-modifying antirheumatic drug (DMARD) such as methotrexate [2–4]. Previously, if disease activity remained moderate or high despite DMARD monotherapy, the recommendation was to switch to combination DMARD therapy or treatment with a tumor necrosis factor inhibitor (TNFi). If the initial TNFi was ineffective or poorly tolerated, patients could either switch to a different mechanism of action (MOA) or cycle to another TNFi. Recent updates to RA treatment guidelines recommend the use of different MOA therapies earlier in the treatment paradigm [5, 6]. Other MOA therapies now are recommended either as an alternative option to a TNFi for first-line biological therapy [5] or as an option for second-line therapy after a TNFi instead of cycling to another TNFi [6].

The changes to the treatment guidelines are supported by emerging evidence of better treatment persistence, clinical outcomes, and lower costs with a different MOA compared with a TNFi. Recent analyses have reported that treatment persistence is better after switching to a different MOA compared with TNFi cycling [7–10]. Emerging data from clinical studies show that outcomes also favor MOA switching over TNFi cycling. A randomized, open-label study of 300 patients with RA and an insufficient response to a TNFi reported that MOA switchers had approximately twice the odds of TNFi cyclers to achieve a good or moderate European League Against Rheumatism (EULAR) response

24 weeks after the change in therapy (odds ratio 2.06; 95% confidence interval [CI] 1.27–3.37; $P = 0.004$) [11]. A different MOA therapy also may be a more cost-effective choice, being both more effective and less expensive than a TNFi in the treatment of RA [12].

Despite the evidence to support switching to a different MOA, TNFi cycling is more common than MOA switching in clinical practice [7–10, 13–20]. A likely contributor to the greater frequency of TNFi cycling across populations and across studies is that as a result of contracting and manufacturer rebates, many payers require a patient to cycle TNFi before the patient can access a different MOA [21]. Another possible contributor was the availability of TNFi before different MOA therapies, leading to greater physician familiarity and comfort with TNFi therapy.

In clinical practice, poor treatment persistence (i.e., discontinuation of therapy) and poor treatment adherence (i.e., using a therapy less often than as prescribed) may undermine the intended effects of therapies for RA, thereby contributing to ineffective treatment [22]. Poor treatment persistence after dispensing a medication for RA also may lead to costly medication expenditures for unused medications. The objective of this study was to examine cost per persistent patient with RA after switching from a TNFi to a different MOA versus cycling to another TNFi.

METHODS

Study Design

This retrospective study used both Commercial claims data and Medicare Advantage claims data from the Optum Research Database. All records were de-identified and no identifiable protected health information was extracted or accessed during the study, pursuant to the US Health Insurance Portability and Accountability Act. Because the study did not involve the collection, use, or transmittal of individually identifiable data, and data were collected in the setting for the usual care of the patient, institutional review board approval to conduct this study was not necessary.

Patients

The study included patients who were continuously enrolled in either a commercial health plan or a Medicare Advantage health plan with both a medical and pharmacy benefit. All patients had at least one claim for a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) between January 1, 2012, and September 30, 2015. The analysis was designed to examine a change in therapy regardless of how long the prior TNFi was used. Thus, the patient's first lifetime use of the TNFi could occur before the first TNFi claim in this period. Analyzed patients were continuously enrolled for at least 6 months before and at least 12 months after the first TNFi claim, were at least 18 years of age as of the first TNFi claim, and had a diagnosis of RA (ICD-9: 714.0x) in the primary or secondary position in the 6 months before or 30 days after the first TNFi claim.

During the 1-year period after the first TNFi claim, patients changed therapy to a different targeted DMARD, either by cycling to another TNFi or by switching to a different MOA therapy (abatacept, tocilizumab, or tofacitinib). The date of the switch to a different targeted DMARD during this period was considered the index date for TNFi cycling or MOA switching. After the change in therapy on the index date, patients were required to be continuously enrolled in a Commercial or Medicare Advantage health plan with medical and pharmacy benefit for at least 12 months to allow for examination of outcomes and costs for 1 year post-index. Patients were allowed to have a variable length follow-up of at least 1 year, ending with the earlier of disenrollment from the health plan or September 30, 2015.

Patients were excluded from the study if they were diagnosed with another autoimmune condition (Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriasis, psoriatic arthritis, or juvenile idiopathic arthritis). Study variables were evaluated for two cohorts of biologic switchers: TNFi cyclers, who received a TNFi pre-index and a different TNFi at index; and MOA switchers, who received a TNFi pre-index and a different MOA therapy at index.

Outcomes

Duration of treatment persistence was examined over the variable length follow-up up to 2 years and during the first 12 months of follow-up. Treatment patterns were determined during the first 12 months post-index for each patient. Persistence with the index treatment was measured as days to therapy discontinuation or switching. Discontinuation of the index treatment was defined as an observed gap in therapy of at least 60 days following the runout date of a fill/infusion.

Total RA-related costs of diagnosis and treatment in the 1-year post-index period were based on paid amounts of adjudicated claims (inpatient, outpatient, and pharmacy), using the sum of plan-paid and patient-paid amounts. Costs were attributed to RA for a non-diagnostic medical claim with a RA diagnosis in any position or a hospitalization with a diagnosis of RA in any position at any time during the stay. RA-related medications included both targeted DMARDs (TNFi or different MOA) and conventional DMARDs (hydroxychloroquine, leflunomide, methotrexate, or sulfasalazine). Separate analyses were conducted for cost of claims paid for all targeted DMARDs in the 1-year post-index period. The cost of targeted DMARDs was adjusted to account for inflation using a biologic-specific inflation factor. The cost of all other services was adjusted for inflation using the medical component of the Consumer Price Index. To derive the cost per persistent patient over 1 year, costs in the 1-year post-index period were divided by the total number of patients who were persistent for 1 year after TNFi cycling or MOA switching.

Statistical Analysis

For each analysis, results were stratified by study cohort (TNFi cyclers or MOA switchers) and *P* values were calculated to compare the cohorts. Chi square tests were performed for categorical measures and ANOVA was utilized for continuous measures. Kaplan–Meier analyses were conducted for persistence during the variable length follow-up with estimates provided at

Table 1 Patient demographics

	Total (N = 1516)	MOA switchers (N = 581)	TNFi cyclers (N = 935)	P value: MOA switchers versus TNFi cyclers
Age, years, mean (SD)	52.5 (11.3)	53.6 (11.2)	51.9 (11.3)	0.005
Gender, <i>n</i> (%)				
Male	297 (19.6)	100 (17.2)	197 (21.1)	0.066
Female	1219 (80.4)	481 (82.8)	738 (78.9)	0.066
Insurance, <i>n</i> (%)				
Commercial	1273 (84.0)	475 (81.2)	798 (85.4)	0.064
Medicare	243 (16.0)	106 (18.2)	137 (14.7)	0.064
Number of targeted DMARDs received ^a				
<i>n</i>	1516	581	935	
Mean (SD)	0.87 (0.84)	1.07 (1.0)	0.75 (0.70)	<0.001
0	520 (34.3)	169 (29.1)	351 (37.5)	<0.001
1	755 (49.8)	267 (46.0)	488 (52.2)	0.018
2+	241 (15.9)	145 (25.0)	96 (10.3)	<0.001
Days from earliest biologic to index, <i>n</i> (%) ^a				
<i>n</i>	996	412	584	
Mean (SD)	681.44 (694.2)	727.55 (711.9)	648.91 (680.2)	0.078
< 180 days	310 (20.5)	115 (19.8)	195 (20.9)	0.618
180 to < 360 days	209 (13.8)	83 (14.3)	126 (13.5)	0.657
360 to < 540 days	68 (4.5)	37 (6.4)	31 (3.3)	0.005
540 to < 720 days	63 (4.2)	27 (4.7)	36 (3.9)	0.450
> 720 days	346 (22.8)	150 (25.8)	196 (21.0)	0.029
Days from earliest RA claim (diagnosis or treatment), <i>n</i> (%) ^a				
<i>n</i>	1515	581	934	
Mean (SD)	750.9 (719.7)	815.2 (733.2)	710.8 (708.6)	0.006
< 180 days	296 (19.5)	100 (17.2)	196 (21.0)	0.073
180 to < 360 days	414 (27.3)	148 (25.5)	266 (28.5)	0.206
360 to < 540 days	137 (9.0)	49 (8.4)	88 (9.4)	0.518
540 to < 720 days	100 (6.6)	43 (7.4)	57 (6.1)	0.320
720 + days	568 (37.5)	241 (41.5)	327 (35.0)	0.011

DMARD disease-modifying antirheumatic drug, MOA mechanism of action, RA rheumatoid arthritis, SD standard deviation, TNFi tumor necrosis factor inhibitor

^a Based on a variable pre-index period with all available data; missing data were not included in the count

discrete intervals through the first 2 years of follow-up. Median persistence with 95% CI was determined from the Kaplan–Meier analysis. The number and percentage of patients who were persistent with the index therapy at 1 year was identified and used in the calculation of cost per persistent patient. Total RA-related costs and targeted DMARD costs in the 1-year post-index period were analyzed descriptively. To control for baseline differences between the TNFi cyclers and MOA switchers, multivariable analyses were conducted to examine 1-year persistence (logistic), follow-up RA-related healthcare cost (generalized linear model [GLM]), and follow-up cost of targeted DMARDs (GLM). Covariates for each model included cohort (TNFi cycling versus MOA switching), age group (18–44 or 45–64, versus 65+), gender, commercial insurance versus Medicare Advantage, index year, region, an aggregate score for comorbid conditions (Charlson comorbidity index [23, 24]), use of DMARDs during baseline, count of RA medications in a variable length baseline, total baseline cost, total baseline RA-related cost, and count of baseline office visits.

RESULTS

Study Population

The study population of 1516 patients included 581 (38.3%) MOA switchers and 935 (61.7%) TNFi cyclers (Table 1). Mean age at the index date (the date of MOA switching or TNFi cycling) was 52.5 years, most patients (80.4%) were female. Most patients (84.0%) were commercially insured; the other 16.0% were insured by Medicare Advantage. Differences were observed between the cohorts for demographics and prior therapy, including the mean number of targeted DMARDs received any time pre-index (1.07 for MOA switchers and 0.75 for TNFi cyclers; $P < 0.001$) or the mean time from the first TNFi claim to the index date (727.6 versus 648.9 days, respectively; $P = 0.078$).

Treatment Persistence

From the Kaplan–Meier analysis, median treatment persistence over the variable length follow-up after the change in therapy on the index

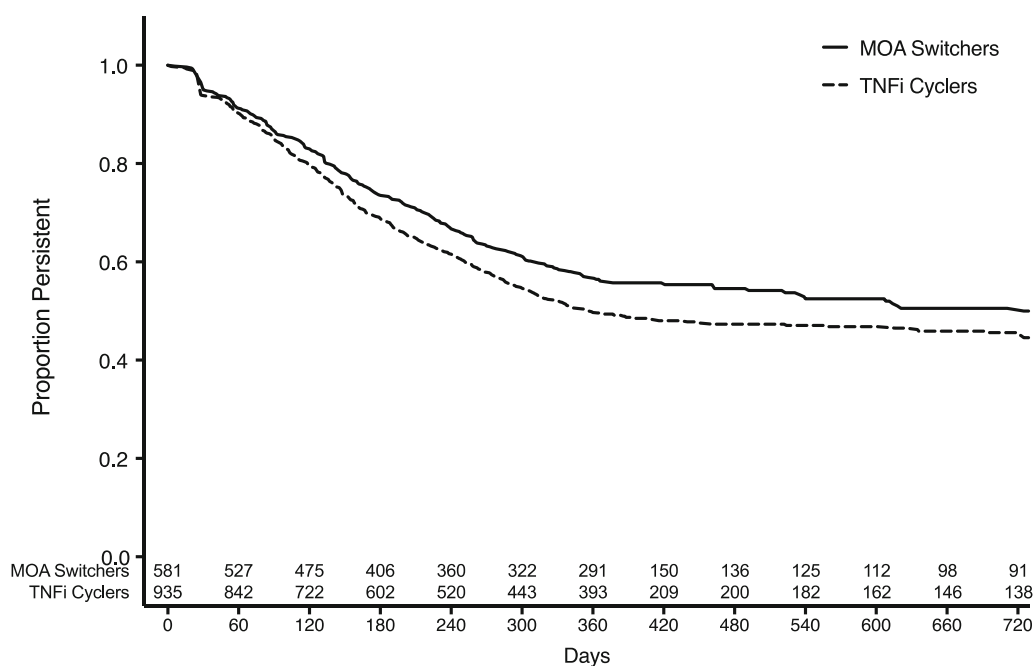


Fig. 1 Kaplan–Meier plot for treatment persistence after cycling to another tumor necrosis factor inhibitor (TNFi cycling) or switching from a TNFi to a different mechanism of action (MOA)

date was 366 days (95% CI 311–618) for MOA switchers and 279 days (95% CI 257–306) for TNFi cyclers (Fig. 1). The 1-year treatment persistence rate was 47.7% for MOA switchers and 40.2% for TNFi cyclers ($P = 0.004$) (Fig. 2). Significant differences between MOA switchers and TNFi cyclers also were observed for switching (29.6% versus 39.6%; $P < 0.001$) and restarting after a 60-day treatment gap (10.2% versus 6.8%; $P = 0.022$). A similar proportion of patients—approximately 13% in each cohort—discontinued targeted DMARD therapy (i.e., had a treatment gap of at least 60 days without a subsequent restart).

In the multivariable analysis that included treatment cohort and baseline patient characteristics as covariates (Table 2), TNFi cyclers had significantly lower odds of treatment persistence at 1 year than MOA switchers (OR = 0.72; 95% CI 0.58–0.89; $P = 0.003$). Other statistically significant predictors of 1-year persistence post-index in the multivariable analysis were geographic region (Midwest versus South), comorbidity index score, total expenditure pre-index, and RA-related total expenditure pre-index.

Cost

The mean costs for 1-year post-index were significantly lower among MOA switchers versus TNFi cyclers, including \$4311 lower total RA-related costs (\$37,804 versus \$42,116; $P < 0.001$) and \$5916 lower targeted DMARD costs (\$29,001 versus \$34,917; $P < 0.001$) (Fig. 3a). In each cohort, the health plan paid 93–95% of the costs and the patient paid 5–7% of the costs. In the multivariable analyses that included treatment cohort and baseline patient characteristics as covariates, MOA switchers had significantly lower costs than TNFi cyclers at 1 year for RA-related costs (cost ratio = 0.89; 95% CI 0.84–0.94; $P < 0.001$) (Table 3) and targeted DMARD costs (cost ratio = 0.84; 95% CI 0.79–0.88; $P < 0.001$) (Table 4). Other statistically significant predictors of 1-year post-index costs in the multivariable analyses included age 45–64 years (compared with age 65+ years), total pre-index expenditures, and office visit count pre-index.

When costs were divided by the treatment persistence rates, the estimated costs per

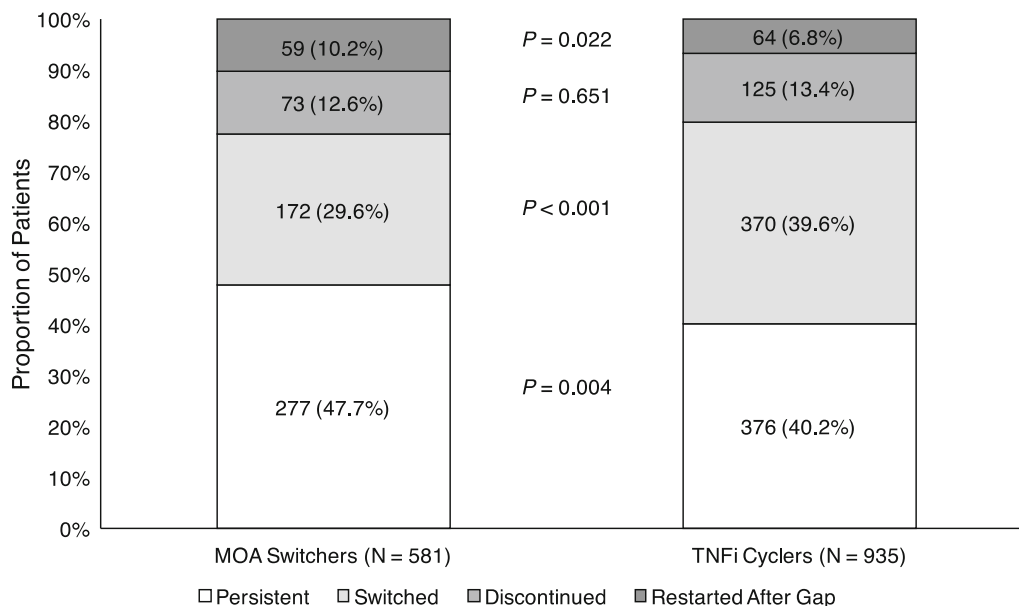


Fig. 2 Treatment patterns during the 1-year post-index period. MOA mechanism of action, TNFi tumor necrosis factor inhibitor

Table 2 Multivariable analysis of predictors for 1-year persistence

	Odds ratio	Lower 95% CI	Upper 95% CI	P value
Patient cohort (ref = MOA switchers)				
TNFi cyclers	0.717	0.576	0.894	0.003
Age group (ref = 65+)				
18–44	0.660	0.435	1.001	0.050
45–64	0.812	0.565	1.167	0.260
Male (ref = female)	1.134	0.871	1.477	0.350
Insurance plan type (ref = commercial)				
Medicare	1.278	0.912	1.790	0.154
Index year (ref = 2012)				
2013	0.891	0.684	1.161	0.394
2014	0.773	0.510	1.173	0.226
Region (ref = South)				
Northeast	1.310	0.876	1.960	0.189
Midwest	1.371	1.067	1.762	0.014
West	1.116	0.825	1.510	0.477
Charlson comorbidity index	0.854	0.741	0.984	0.029
Hydroxychloroquine pre-index	1.014	0.775	1.325	0.922
Leflunomide pre-index	0.918	0.663	1.269	0.603
Methotrexate pre-index	1.137	0.914	1.414	0.250
Sulfasalazine pre-index	1.171	0.785	1.745	0.439
Count of unique RA medications pre-index	0.971	0.839	1.125	0.698
Total expenditure pre-index/\$1000	0.981	0.964	0.998	0.027
RA-related total expenditure pre-index/\$1000	1.027	1.010	1.045	0.002
Office visit count pre-index	0.997	0.980	1.014	0.703
Patient paid amount for index claim	1.000	1.000	1.000	0.684

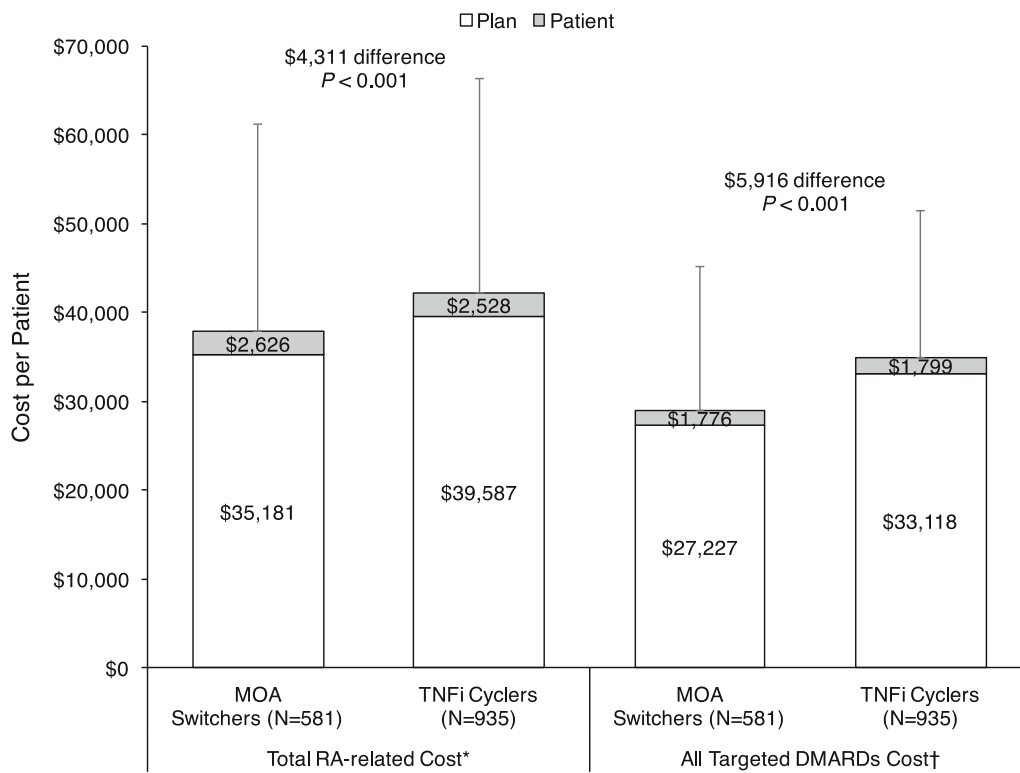
MOA mechanism of action, RA rheumatoid arthritis, ref reference, TNFi tumor necrosis factor inhibitor

persistent patient over the 1-year follow-up period were lower among MOA switchers versus TNFi cyclers, including \$25,436 lower total RA-related cost per persistent patient and \$25,999 lower targeted DMARD costs per persistent patient (Fig. 3b).

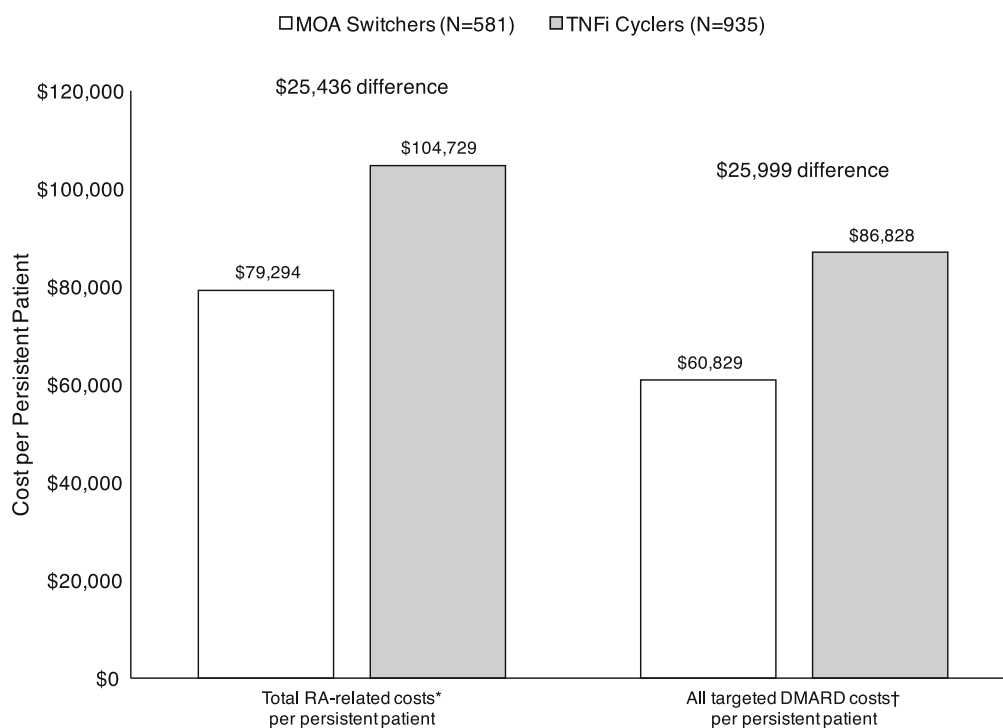
DISCUSSION

In this real-world study of more than 1500 patients with RA who received a TNFi and then required a switch in therapy, MOA switchers had a longer treatment duration than TNFi

(A) Mean (SD) costs per patient in 1-year follow-up period



(B) Estimated cost per persistent patient over 1-year follow-up period



◀ **Fig. 3** One-year cost per patient and per persistent patient. Asterisk total RA-related cost includes amount paid for diagnosis and treatment related to RA. Dagger all targeted DMARDs cost includes cost for both the index therapy and any other targeted DMARD in the first year post-index. *DMARD* disease-modifying antirheumatic drug, *MOA* mechanism of action, *RA* rheumatoid arthritis, *SD* standard deviation, *TNFi* tumor necrosis factor inhibitor. **a** Mean (SD) costs per patient in 1-year follow-up period. **b** Estimated cost per persistent patient over 1-year follow-up period

cyclers and were more likely to be persistent on treatment at 1 year. Other analyses reported similar findings, with better treatment persistence rates among MOA switchers compared with TNFi cyclers [7–10], but those studies did not examine the cost per persistent patient. Consistent findings for treatment persistence across different patient populations may have clinical implications for the management of RA, because greater treatment persistence and adherence have been reported to improve clinical outcomes in RA [22]. This analysis was not designed to examine treatment effectiveness, but several previous retrospective analyses, registry studies, and prospective clinical studies have reported greater treatment effectiveness after MOA switching compared with TNFi cycling [8, 9, 11, 16, 20, 25–28].

Based in part on the emerging evidence, recent updates to RA treatment guidelines placed increased emphasis on the use of different MOA therapies [5, 6]. Because these guidelines were updated after the study period for our analysis, additional research is needed to determine whether the recent changes to the treatment guidelines will influence clinical practice and lead to increased use of different MOA therapies compared with TNFi.

This analysis also examined the healthcare costs paid by the plan and the patient after switching to a different MOA or cycling to another TNFi. The mean cost was significantly lower among the MOA switchers than the TNFi cyclers, both for the total cost of care for RA, as well as for the total cost of the targeted DMARDs in the first year after the change in therapy. In multivariable analyses that included

baseline patient characteristics, the costs continued to be significantly lower among the MOA switchers. Previous research has reported that persistent patients have higher costs for TNFi therapy compared with non-persistent patients, but lower non-drug costs [29]. The results of our study indicate that switching to a different MOA may lower not only the non-drug healthcare costs but also the drug costs compared with TNFi cycling because the observed difference in mean RA-related costs was driven largely by lower targeted DMARD costs among MOA switchers versus TNFi cyclers. Thus, MOA switchers were persistent on therapy for longer, yet they had lower targeted DMARD costs. In this analysis, targeted DMARD costs included not only those for the index targeted DMARD but also those for other targeted DMARDs when patients changed therapy again post-index. TNFi cyclers were significantly more likely than MOA switchers to change therapy again post-index. After these subsequent changes in therapy, the need for more costly loading doses for the new therapy may have contributed to the observed difference in the total cost of targeted DMARDs.

The final step in this analysis was to examine the cost per persistent patient in each cohort. When the costs and treatment persistence rates were combined, MOA switchers had lower cost per persistent patient than TNFi cyclers. These findings, combined with previous evidence that MOA switching simultaneously lowers costs and improves clinical outcomes compared with TNFi cycling [9], suggest that MOA switching is associated with economic and clinical advantages for RA patients and their health plans when a change in therapy is required.

Because this was a retrospective analysis of claims data, the patient populations were not stratified or balanced before the change in therapy, so multivariable analyses were used to adjust for differences at baseline. Other statistically significant predictors of non-persistence in the multivariable analysis included comorbidity index score and total healthcare expenditure before the change in therapy, which suggests that patients with more severe disease were less likely to persist on therapy after cycling TNFi or switching to a different MOA. Greater pre-index

Table 3 Multivariable analysis of predictors for 1-year RA-related costs

	Cost ratio	Lower 95% CI	Upper 95% CI	P value	Predicted value
Patient cohort (ref = TNFi cyclers)					
MOA switchers	0.888	0.838	0.941	< 0.001	\$37,557
TNFi cyclers	Ref.	–	–	–	\$42,280
Age group (ref = 65+)					
18–44	1.020	0.911	1.141	0.732	–
45–64	1.120	1.015	1.236	0.024	–
Male (ref = female)	1.062	0.990	1.140	0.094	–
Insurance plan type (ref = commercial)					
Medicare	0.935	0.854	1.025	0.151	–
Index year (ref = 2012)					
2013	1.026	0.957	1.100	0.473	–
2014	0.976	0.876	1.087	0.657	–
Region (ref = South)					
Northeast	1.082	0.973	1.204	0.147	–
Midwest	1.048	0.980	1.120	0.169	–
West	1.089	1.005	1.179	0.038	–
Charlson comorbidity index	0.997	0.962	1.033	0.863	–
Hydroxychloroquine pre-index	0.974	0.907	1.045	0.465	–
Leflunomide pre-index	0.971	0.892	1.057	0.497	–
Methotrexate pre-index	1.036	0.978	1.097	0.225	–
Sulfasalazine pre-index	1.028	0.925	1.143	0.609	–
Count of unique RA medications pre-index	0.997	0.959	1.037	0.897	–
Total expenditure pre-index/\$1000	1.004	1.001	1.007	0.015	–
RA-related total expenditure pre-index/\$1000	1.003	0.999	1.006	0.144	–
Office visit count pre-index	1.008	1.004	1.012	< 0.001	–

MOA mechanism of action, RA rheumatoid arthritis, ref reference, TNFi tumor necrosis factor inhibitor

expenditures and greater pre-index office visits also predicted higher costs after a change in therapy.

Several potential limitations of the analysis are noted. A claims data study does not provide the reasons for discontinuation of therapy, which could be as a result of adverse events, lack of efficacy, cost burden, or even clinical

remission. In future research, it would be useful to combine the findings from this study with additional context around why patients discontinue both the prior TNFi and the new therapy after TNFi cycling or MOA switching, including possible patient-specific psychological determinants of persistence. Another area for future research is to examine treatment

Table 4 Multivariable analysis of predictors for 1-year targeted DMARD costs

	Cost ratio	Lower 95% CI	Upper 95% CI	P value	Predicted value
Patient cohort (ref = TNFi cyclers)					
MOA switchers	0.837	0.793	0.883	< 0.001	\$29,146
TNFi cyclers	Ref.	–	–	–	\$34,831
Age group (ref = 65+)					
18–44	1.092	0.985	1.211	0.095	–
45–64	1.143	1.044	1.252	0.004	–
Male (ref = female)	1.012	0.948	1.081	0.723	–
Insurance plan type (ref = commercial)					
Medicare	0.944	0.868	1.028	0.185	–
Index year (ref = 2012)					
2013	1.041	0.976	1.111	0.225	–
2014	1.040	0.940	1.150	0.450	–
Region (ref = South)					
Northeast	1.026	0.929	1.133	0.617	–
Midwest	0.951	0.894	1.012	0.112	–
West	1.015	0.942	1.093	0.702	–
Charlson comorbidity index	0.994	0.961	1.027	0.702	–
Hydroxychloroquine pre-index	0.993	0.930	1.060	0.827	–
Leflunomide pre-index	1.007	0.930	1.090	0.858	–
Methotrexate pre-index	1.053	0.998	1.111	0.058	–
Sulfasalazine pre-index	1.005	0.910	1.110	0.926	–
Count of unique RA medications pre-index	0.957	0.922	0.992	0.018	–
Total expenditure pre-index/\$1000	0.993	0.990	0.996	< 0.001	–
RA-related total expenditure pre-index/\$1000	1.011	1.008	1.015	< 0.001	–
Office visit count pre-index	1.002	0.998	1.006	0.290	–

DMARD disease-modifying antirheumatic drug, MOA mechanism of action, RA rheumatoid arthritis, ref reference, TNFi tumor necrosis factor inhibitor

persistence for intravenous versus subcutaneous therapies. Claims data are collected for payment and not for research, and they do not include clinical outcomes such as disease severity. We could not control for RA disease activity at the time of biologic initiation and patients were not randomized to treatment with a TNFi or

different MOA DMARD, so causality cannot be inferred from the results. Drug costs in claims do not include the effect of confidential discounts or rebates. Because the first TNFi claim in the study period was not necessarily the patient's first lifetime use of a TNFi, it was possible that patients had an unobserved history of

other targeted DMARD therapy before the study period. Other MOA DMARDs that were not available during the study period, such as sarilumab [30, 31], sirukumab [32], or baricitinib [33], may change which biologics are used in the management of RA.

This study did not examine outcomes separately for individual medications within each class. Previous analyses of TNFi cycling or switching to a different MOA after TNFi failure compared either switching to a single non-TNFi versus TNFi cycling [16, 20, 25–28] or broadly compared switching to any non-TNFi versus TNFi cycling [8, 9, 11]. This approach is supported by studies in the frontline treatment setting, which have shown that response rates generally are similar among TNFi and other MOA [34]. However, randomized studies have shown that response to monotherapy with an antibody to IL-6 such as tocilizumab or sarilumab is greater than the response to monotherapy with a TNFi when methotrexate treatment fails [31, 35]. The relevance of these results to second-line therapy after TNFi failure remains to be determined.

CONCLUSIONS

After changing TNFi therapy, RA patients who switched to a different MOA had higher treatment persistence and lower healthcare costs than TNFi cyclers, resulting in lower healthcare costs per persistent patient among the MOA switchers. The health plan was responsible for most of the cost of care for these patients. Reimbursement policies that require patients to cycle TNFi before they switch to a different MOA may result in suboptimal outcomes for both patients and payers.

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Compliance with Ethics Guidelines. All records were de-identified and no identifiable protected health information was extracted or accessed during the study, pursuant to the US Health Insurance Portability and Accountability Act. Because the study did not involve the collection, use, or transmittal of individually identifiable data, and data were collected in the setting for the usual care of the patient, institutional review board approval to conduct this study was not necessary.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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