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Comparative Treatment Patterns Among Psoriasis Patients Using Adalimumab, Etanercept, or Ustekinumab

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Psoriasis is a chronic, immune-mediated, inflammatory skin disease affecting as many as 7.4 million Americans, or 3.2%of the United States population 20 years and older.[1] Plaque psoriasis is the most common form and manifests as elevated red lesions covered by scaling silvery plaques. Psoriasis affects health-related quality of life, treatments can be costly and time-consuming, and patients with more severe psoriasis experience a greater negative impact on their quality of life.[2-4]

Three subcutaneously administered biologic drugs, adalimumab (ADA),[5,6] etanercept (ETA),[7,8] and ustekinumab (UST),[9-12] are effective for use in the treatment of moderate to severe plaque psoriasis and improve health-related quality of life.[13-15] ADA and ETA block the cytokine tumor necrosis factor-alpha (TNF-alpha) that is associated with inflammation.[16] ADA is recommended for administration as an initial 80-mg dose (induction dose) followed by 40 mg every other week starting 1 week after the initial dose (maintenance period).[7] ETA is recommended for administration as a 50-mg dose twice per week for 3 months (induction period) followed by a step down to a 50-mg dose once per week (maintenance period).[5] UST, the most recently approved of the 3 biologics (approved September 25, 2009), selectively targets the cytokines interleukin 12 and 23 that are associated with psoriasis inflammation.[10,17] UST is recommended to be administered at weeks 0 and 4, and then every 12 weeks thereafter. It is dosed by weight: 45 mg for patients ≤100 kg and 90 mg for patients >100 kg.[9]

All 3 products can be administered by healthcare professionals or self-administered by patients. Adjustments to the dosing and administration schedules of ADA and ETA are necessary for those responding suboptimally to the standard dosing regimen.[18,19] Currently, few studies have been published comparing UST with the other subcutaneous biologic medications used to treat psoriasis in real-world clinical practice.[20] The objectives of this study were to examine the dosing and timing of UST and to compare patient characteristics, dose escalation, discontinuation, restarts, and switching with the subcutaneous TNF-alpha inhibitors, ADA and ETA.

ABSTRACT

Objective: This retrospective study compared the treatment patterns of ustekinumab (UST), with recommended maintenance administration every 12 weeks, with adalimumab (ADA) and etanercept (ETA), administered weekly or every other week, for the treatment of plaque psoriasis.

Methods: Persons with psoriasis ≥18 years and having ≥1 medical or pharmacy claim for UST or ≥1 pharmacy claim for ADA or ETA, from February 8, 2010, to January 31, 2011, were selected from the MarketScan databases and assigned to mutually exclusive cohorts. Patient characteristics and dose escalation were described during the 12-month pre-index period and 12-month follow-up period, respectively. Differences in baseline characteristics were adjusted using inverse probability of treatment weights. Pairwise comparisons of rates of discontinuations, restarts, and switches were made between ADA and UST and between ETA and UST.

Results: A total of 2933 ADA, 4011 ETA, and 583 UST patients were selected. Patients in the UST cohort had higher baseline comorbidity scores and greater exposure to multiple psoriasis drugs at baseline. Dose escalation was observed in 7.8% of ADA patients, 30.9% of ETA patients, and 18.2% of UST patients. Discontinuations were seen in 38.6% of UST patients, 53.3% of ADA patients, and 56.2% of ETA patients. Restarts were seen in 8.9% of UST patients, 17.5% of ADA patients, and 23.1% of ETA patients. Switching to a nonindex medication occurred in 14.8% of UST patients compared with 22.0% of ETA patients and in 14.4% of UST patients compared with 20.8% of ADA patients.

Conclusions: Discontinuations, restarts, and switches were common for all 3 biologics, but were significantly lower among patients with psoriasis receiving UST compared with those receiving ADA or ETA.

Am J Pharm Benefits. 2016;8(5):191-198

PRACTICAL IMPLICATIONS

Patients with moderate to severe psoriasis treated with subcutaneous biologics frequently experience medication changes, interruptions, and discontinuations. These disruptions were more common among adalimumab- and etanercept-treated patients than patients initiating ustekinumab treatment.

- Psoriasis patients initiating ustekinumab had a higher baseline comorbid burden and treatment intensity compared with patients receiving adalimumab or etanercept.
- Discontinuation, restarts, and switches were common among all psoriasis patients receiving subcutaneous biologics.
- Medication changes were less frequent among psoriasis patients initiating ustekinumab compared with those receiving etanercept or adalimumab.

METHODS

Data Source

This retrospective analysis used the Truven Health MarketScan Commercial Claims and Encounters and Medicare Supplemental Databases, which contain administrative healthcare claims for inpatient and outpatient medical and outpatient pharmacy services. Individuals in the databases are insured through a variety of private health plans, including preferred provider organizations, indemnity plans, and health maintenance organizations. The Medicare database contains claims for individuals insured through Medicare supplemental commercial insurance. Both Medicare-covered and insurer-covered services are included due to coordination of benefits. These databases include enrollment data from approximately 150 large employers and health plans across the United States, which provide private healthcare coverage and contain more than 60 million covered lives per year. Data are de-identified and are fully compliant with the Health Insurance Portability and Accountability Act of 1996. As this study did not involve the collection, use, or transmittal of individually identifiable data, it did not require Institutional Review Board review or approval.

Patient Identification

Persons who were included in the analyses were ≥18 years; had ≥1 pharmacy claim for ADA, ETA, or UST, or had ≥1 medical claim for UST, between February 8, 2010, and January 31, 2011 (index date); had at least 12 months of pre- and postindex continuous enrollment in medical and pharmacy benefits; and had at least 1 nondiagnostic claim with a diagnosis of psoriasis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] 696.1) on the index date or during the 12-month pre-index period. Patients with a diagnosis of any of the following conditions on the index date, or during the 12-month pre-index period, were excluded: rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, ankylosing spondylitis. Patients were selected into 3 mutually exclusive cohorts (ADA, ETA, UST) based the index drug.

Measures Assessed During the 12-month Pre-index Period

The Charlson Comorbidity Index (CCI)[21] and individual comorbidities were assessed using the *ICD-9-CM* codes on nondiagnostic medical claims during the baseline period. Psoriasis treatments were also assessed during the baseline period. Per-patient healthcare expenditures were measured using paid amounts for adjudicated claims. Psoriasis-related expenditures were measured using medical claims with a diagnosis of psoriasis and pharmacy claims for any psoriasis treatment.

Dose Escalation

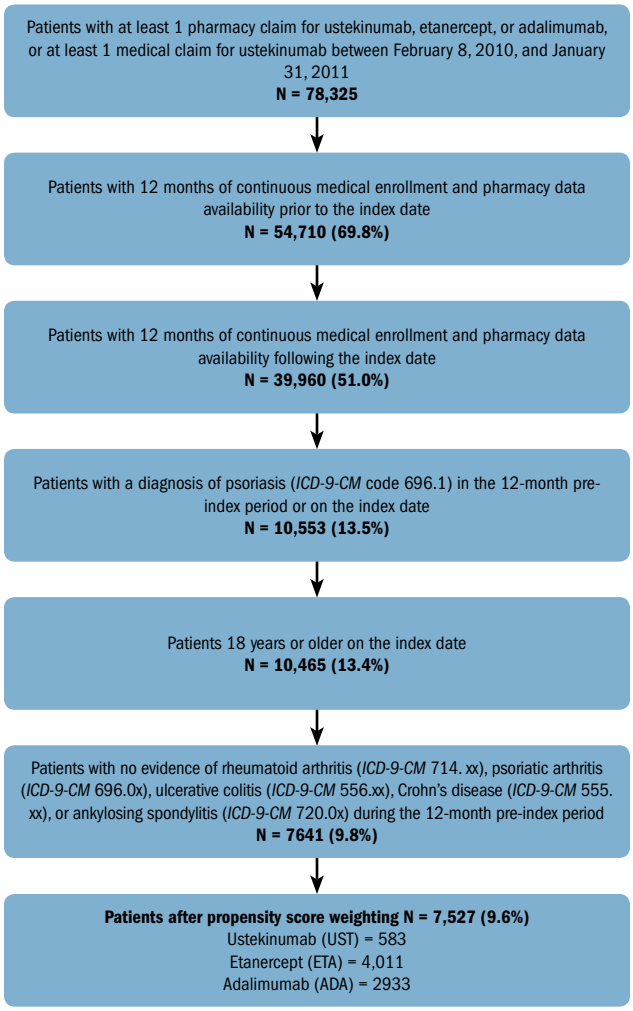
For UST medical claims, the dose was imputed using the amount paid on the claim and data for the wholesale acquisition cost at the time of the claim. This imputation was applied in <5% of the UST cohort. The dose for pharmacy claims was computed by multiplying drug strength (specified by the National Drug Code) by the quantity.

Dose escalation for UST was defined as the presence of any claim with a dose higher than the patient's initial dose. For ADA and ETA, maintenance dose escalation was defined as an average weekly dose ([total dispensed dose]/[days' supply/7]) in the maintenance period >15% higher than the maintenance dose recommended on the product label. The ADA maintenance period was defined as starting with the second ADA claim, and the ETA maintenance period was defined as the period starting 91 days after the index date.

Discontinuation, Restart, and Switching

Discontinuation was defined as a treatment gap ≥90 days after the end of the days' supply on a pharmacy claim for ADA and ETA, which allowed for refill of a 90-day mail order pharmacy claim before a patient discontinued. For UST, discontinuation was defined as a treatment gap ≥168 days after the end of the days' supply for pharmacy claims or the effective days' supply for medical claims (28 days for the first claim and 84 days for subsequent claims). A treatment gap of twice the dosing interval for UST (168 days) was selected after a review of the literature.[20] Treatment restart was defined as the presence of a prescription or medical claim for the index medication following discontinuation of the index medication. Treatment switch was defined by the presence of a prescription claim for a nonindex biologic medication following discontinuation of the index medication.

Figure 1. Patient Attrition



Statistical Analyses

Pairwise descriptive comparisons of demographics, comorbidities, healthcare expenditures, and psoriasis treatments in the pre-index period were made between ADA and UST and between ETA and UST. Chi-squared tests were conducted for differences in dichotomous or categorical variables, and *t* tests were conducted for comparisons of continuous variables. To address potential selection bias, a propensity-score–based inverse probability of treatment weighting (IPTW) was used. IPTW was used to reduce the observed differences in the outcomes due to the drug assignment rather than other underlying differences, such as age and comorbidities.[22,23]

Two logistic regression models were estimated: 1 to compute the propensity score for the choice of ADA versus UST and 1 for ETA versus UST. The variables used in the models included demographics, pre-period comorbidities and expenditures, and the counts of pre-period psoriasis treatments. The results of these models were used to assign a weight (inverse of the propensity score) to each patient. The comparisons of the proportions of patients who discontinued, restarted, or switched were conducted using the weighted data. To further control for remaining imbalance in baseline characteristics, Cox proportional hazards models were used to estimate the hazard ratios for discontinuation comparing ADA versus UST and ETA versus UST.

RESULTS

There were 2933 ADA, 4011 ETA, and 583 UST patients who received a psoriasis diagnosis who met the selection criteria (Figure 1).

Pre-period Demographic and Clinical Characteristics

Patients in the UST cohort were slightly older, and there was a higher proportion of UST (10.5%) patients ≥65 years compared with ADA (7.8%; $P = .033$). UST patients had a higher average CCI (0.46) compared with ADA (0.35; $P = .004$) and ETA (0.37; $P = .02$). The UST cohort had a higher proportion of patients with dyslipidemia (23.3%) compared with ADA (18.9%; $P = .015$) and ETA (20.2%; $P = .083$), and a higher proportion of patients who had been given an obesity diagnosis (6.3%) compared with ADA (3.8%; $P = .004$) and ETA (3.5%; $P < .001$). Patients in the UST cohort had significantly higher pre-period total and psoriasis-related healthcare expenditures than the ADA cohort, but expenditures were not significantly different than those of the ETA cohort (Table 1).

Most UST patients (93.1%), 78.4% of ADA patients, and 72% of ETA patients had a previous topical, systemic, or biologic treatment ($P < .001$ in all comparisons). Receipt of the index treatment as third-line or higher (2+ prior biologic therapies other than the index drug) was observed in 29.2% of UST patients compared with 8.5% of ADA ($P < .001$) and 2.4% of ETA ($P < .001$) patients. The UST patients were all taking UST for the first time, whereas 70.0% of the ADA patients ($P < .001$) and 82.3% of the ETA patients ($P < .001$) had taken their respective drugs during the pre-period (Table 2).

UST Dose Timing

The median number of days between UST doses 1 and 2 was 28, as recommended in the drug's label (Figure 2). The mean and median number of days between subsequent doses were slightly higher than the 84 days in the prescribing guidelines.

Dose Escalation

Overall, dose escalation was 18.2% among UST patients (Figure 3). At the second dose, only 1.3% of patients

Table 1. Unadjusted Comparison of Baseline Patient Characteristics

	Ustekinumab (UST) N = 583		Etanercept (ETA) N = 4011		Adalimumab (ADA) N = 2933		ETA vs UST *P*	ADA vs UST *P*
Age, years (mean, SD)	49.9	13.1	49.8	12.8	48.9	12.3	.778	.058
Aged 65 years and older (n, %)	61	10.5%	380	9.5%	229	7.8%	.449	.033
Male (n, %)	321	55.1%	2353	58.7%	1708	58.2%	.099	.157
Presence of capitated claims (n, %)	18	3.1%	225	5.6%	137	4.7%	.011	.089
Medicare is primary payer (n, %)	61	10.5%	367	9.1%	218	7.4%	.308	.013
Health plan type (n, %)								
Comprehensive	53	9.1%	351	8.8%	228	7.8%	.787	.284
Exclusive provider organization	9	1.5%	89	2.2%	59	2.0%	.292	.454
Health maintenance organization	60	10.3%	568	14.2%	400	13.6%	.011	.029
Point of service	67	11.5%	356	8.9%	298	10.2%	.041	.336
Preferred provider organization	340	58.3%	2259	56.3%	1686	57.5%	.363	.709
Point of service with capitation	2	0.3%	14	0.3%	12	0.4%	.982	.817
Consumer-driven health plan	25	4.3%	222	5.5%	149	5.1%	.212	.421
High-deductible health plan	12	2.1%	56	1.4%	35	1.2%	.216	.097
Other	15	2.6%	96	2.4%	66	2.3%	.792	.635
Charlson Comorbidity Index score (mean, SD)	0.46	1.01	0.37	0.85	0.35	0.81	.02	.004
Number of unique 3-digit *ICD-9-CM* diagnosis codes (mean, SD)	10.49	7.58	9.43	6.59	9.47	6.58	<.001	<.001
Number of unique medications (mean, SD)	12.05	8.67	10.09	7.53	10.84	7.93	<.001	<.001
Pre-period total healthcare expenditures (mean, SD)	$22,462	$17,679	$21,519	$16,587	$18,562	$14,399	.204	<.001
Pre-period psoriasis-related expenditures (mean, SD)	$15,832	$13,983	$16,450	$11,212	$13,595	$9590	.229	<.001
Comorbid conditions (N, %)								
Anxiety	33	5.7%	176	4.4%	138	4.7%	.168	.327
Cardiovascular disease	217	37.2%	1421	35.4%	1043	35.6%	.398	.445
Depression	40	6.9%	292	7.3%	225	7.7%	.715	.498
Diabetes	91	15.6%	511	12.7%	389	13.3%	.055	.132
Dyslipidemia	136	23.3%	811	20.2%	555	18.9%	.083	.015
Hypertension	173	29.7%	1122	28.0%	816	27.8%	.394	.363
Obesity	37	6.3%	140	3.5%	110	3.8%	<.001	.004
Prior topical therapy[a,b] (n, %)								
Betamethasone and combinations	140	24.0%	864	21.5%	640	21.8%	.177	.244
Calcipotriene	35	6.0%	285	7.1%	182	6.2%	.329	.853
Clobetasol propionate	272	46.7%	1402	35.0%	1137	38.8%	<.001	<.001
Fluocinonide	44	7.5%	277	6.9%	205	7.0%	.57	.632
Prior phototherapy	55	9.4%	182	4.5%	178	6.1%	<.001	.003

(continued)

had escalated from 45 mg to 90 mg. At dose 3, 12.2% of patients who had initiated at 45 mg were taking the 90-mg dose. The proportion of escalators at doses 4, 5, and 6 were 15.5%, 16.9%, and 18.5%, respectively. Maintenance dose escalation was 7.8% among ADA patients and 30.9% among ETA patients.

IPTW Comparisons of Baseline Characteristics

The propensity models of UST versus ADA and UST versus ETA resulted in weighted cohorts that were well balanced in terms of demographics, CCI, comorbidities, and pre-period healthcare expenditures. The major differences that remained after weighting were the proportions with various types of pre-period treatments. The weighted UST cohorts had higher proportions of patients with any pre-period biologic, systemic, or topical therapy other than the index drug (90.5% of UST vs 80.3% of ADA; $P<.001$; 91.6% of UST vs 74.2% of ETA; $P<.001$) and higher proportions of patients with prior phototherapy (9.4% of UST vs 6.4% of ADA; $P=.008$; 11.3% of UST vs 5.0% of ETA; $P<.001$).

Table 1. Unadjusted Comparison of Baseline Patient Characteristics

	Ustekinumab (UST) N = 583		Etanercept (ETA) N = 4011		Adalimumab (ADA) N = 2933		ETA vs UST *P*	ADA vs UST *P*
Prior systemic therapy[a,b] (n, %)								
Acitretin	46	7.9%	106	2.6%	144	4.9%	<.001	.004
Cyclosporine	53	9.1%	51	1.3%	72	2.5%	<.001	<.001
Methotrexate	106	18.2%	279	7.0%	383	13.1%	<.001	.001
Dexamethasone oral	24	4.1%	146	3.6%	160	5.5%	.569	.185
Methylprednisolone oral	76	13.0%	475	11.8%	407	13.9%	.407	.59
Prednisone oral	60	10.3%	310	7.7%	286	9.8%	.034	.689
Triamcinolone oral	161	27.6%	742	18.5%	675	23.0%	<.001	.017
Prior biologic therapy (n, %)								
Adalimumab	136	23.3%	114	2.8%	2052	70.0%	<.001	<.001
Alefacept	12	2.1%	3	0.1%	7	0.2%	<.001	<.001
Etanercept	120	20.6%	3300	82.3%	347	11.8%	<.001	<.001
Golimumab	4	0.7%	1	0.0%	1	0.0%	<.001	<.001
Infliximab	35	6.0%	6	0.1%	15	0.5%	<.001	<.001
Prior biologic therapies other than index drug (n, %)								
0	219	37.6%	680	17.0%	752	25.6%	<.001	<.001
1	194	33.3%	3233	80.6%	1933	65.9%	<.001	<.001
2	170	29.2%	98	2.4%	248	8.5%	<.001	<.001
Prior systemic therapies other than index drug (n, %)								
0	250	42.9%	2451	61.1%	1492	50.9%	<.001	<.001
1	193	33.1%	1120	27.9%	908	31.0%	.01	.307
2	91	15.6%	332	8.3%	392	13.4%	<.001	.151
3	49	8.4%	108	2.7%	141	4.8%	<.001	<.001
Prior biologic, systemic, and topical therapies other than index drug (n, %)								
No topical, systemic or biologic	40	6.9%	1125	28%	633	21.6%	<.001	<.001
Any topical, systemic, biologic	543	93.1%	2886	72%	2300	78.4%	<.001	<.001
Topical only	82	14.1%	1265	32%	631	21.5%	<.001	<.001
Systemic only	53	9.1%	619	15%	482	16.4%	<.001	<.001
Biologic only	47	8.1%	27	1%	87	3.0%	<.001	<.001
Topical and systemic	121	20.8%	874	22%	813	27.7%	.571	<.001
Topical and biologic	81	13.9%	34	1%	141	4.8%	<.001	<.001
Systemic and biologic	60	10.3%	21	1%	50	1.7%	<.001	<.001
Topical, systemic, and biologic	99	17.0%	46	1%	96	3.3%	<.001	<.001

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification.*

[a]No patients had pre-period claims for the following treatments: topical triamcinolone, oral cortisone, oral hydrocortisone, abatacept, anakinra, certolizumab pegol, rituximab, tocilizumab, ustekinumab.

[b]Less than 5% of patients had pre-period claims for the following treatments: anthralin, diflorasone diacetate, pimecrolimus cream, tacrolimus ointment, tazarotene, hydroxyurea, isotretinoin, leflunomide, mycophenolate mofetil, sulfasalazine, prednisolone (oral).

IPTW Comparisons of Discontinuations, Restarts, and Switches

Smaller proportions of the UST cohort discontinued, restarted, or switched than in the other cohorts (P <.001 for all comparisons). Specifically, 38.6% of UST discontinued versus 53.3% of ADA, 8.9% of UST restarted versus 17.5% of ADA, and 14.4% of UST switched versus 20.8% of ADA. Also, 38.6% of UST discontinued versus 56.2% of ETA, 8.9% of UST restarted versus 23.1% of ETA, and 14.8% of UST switched versus 22.0% ETA (Table 2).The results of the multivariate proportional hazard models indicated a lower hazard of discontinuing for UST compared with either drug. The hazard ratio of discontinuing and 95% CI for UST versus ADA was 0.626 (95% CI, 0.580-0.676) and for UST versus ETA, 0.586 (95% CI, 0.545-0.629).

Table 2. Unadjusted Comparison of Baseline Patient Characteristics

	Ustekinumab (UST) N = 583		Etanercept (ETA) N = 4011		UST vs ETA	Ustekinumab (UST) N = 583		Adalimumab (ADA) N = 2933		UST vs ADA
	N	%	N	%	P	N	%	N	%	P
Patients discontinuing	225	38.6%	2253	56.2%	<.001	225	38.6%	1564	53.3%	<.001
Restart of index medication	52	8.9%	927	23.1%	<.001	52	8.9%	513	17.5%	<.001
Switch to a nonindex medication	86	14.8%	881	22.0%	<.001	84	14.4%	610	20.8%	<.001
	Mean	SD	Mean	SD	P	Mean	SD	Mean	SD	P
Days to discontinuation[a]	229	444	237	182	.354	228	392	231	182	.815
Days to restart[b]	248	243	187	115	<.001	250	220	192	117	<.001
Days to switch[c]	340	567	336	218	.756	334	501	307	217	.036

[a]Days from index date to discontinuation date (end of days' supply).
[b]Days from discontinuation date to restart of index drug.
[c]Days from index date to prescription for non-index study medication.

DISCUSSION

This study found that prior to starting UST treatment, patients with psoriasis initiating UST treatment had higher comorbidity rates and higher baseline healthcare costs compared with patients who were initiating or continuing ADA or ETA. Also, a higher proportion of UST patients were on a third-line biologic therapy. After using the IPTW technique to balance the baseline characteristics of the 3 cohorts, the UST cohort had the lowest rates of discontinuation, restarts, or switches during 1 year of follow-up. Cox proportional hazards models adjusted for any remaining imbalances and showed that UST patients had a significantly lower hazard of discontinuation compared with ADA or ETA patients.

Clinical studies have shown that dose escalation may improve effectiveness for those with severe disease who are inadequately or only partially responding to the standard dosing regimens of all 3 of the drugs.[18,19] The dosing intervals of UST were consistent with the prescribing guidelines, and dose escalation occurred in 18.2% of UST patients. Maintenance dose escalation occurred in 7.8% of ADA patients and 30.9% of ETA patients. This study did not examine whether shortening or lengthening the interval between doses contributed to dose escalation, nor did we have clinical information to understand the reason(s) for dose escalation.

One study used a physician survey to evaluate the baseline characteristics of patients with psoriasis treated with ADA, ETA, or UST and found that UST had a higher proportion of patients with prior biologic use: 62.5% of UST 90 mg, 55.4% of UST 45 mg, 14.4% of ADA, and 25.0% of ETA.[24] The highest average number of baseline comorbidities was found in the UST 90-mg group (1.6), while the UST 45-mg group (1.1) was similar to ADA (1.2) and ETA (1.1).

Several studies have examined therapy discontinuation among patients with psoriasis treated with all 3 of our study drugs, each showing that discontinuation of psoriasis treatments was common, but that discontinuation rates were lowest among UST patients.[20,25,26] Feldman and colleagues used administrative claims data to evaluate medication utilization patterns of first-line ADA, ETA, and UST patients.[20] In that study, discontinuation rates over a 12-month follow-up period post titration were lowest for UST (16%) and higher for ADA (27%) and ETA (35%). Another study used chart data to follow psoriasis patients for 4 years.[25] The UST group had the lowest discontinuation rate (39%) compared with 50% for ADA and 60% for ETA. Another study using administrative claims data included 8 patients with psoriasis treated with UST, 195 treated with ADA, and 369 treated with ETA.[26] Also in that study, discontinuation was evaluated among new initiators and existing users, and was defined as a gap ≥45 days of therapy without a restart or switch during the year. No UST patients discontinued treatment. Discontinuation rates were higher among initiators (ADA, 31%; ETA, 33%) than among existing users (ADA, 13%; ETA, 18%).

Figure 2. Number of Days Between Ustekinumab Doses

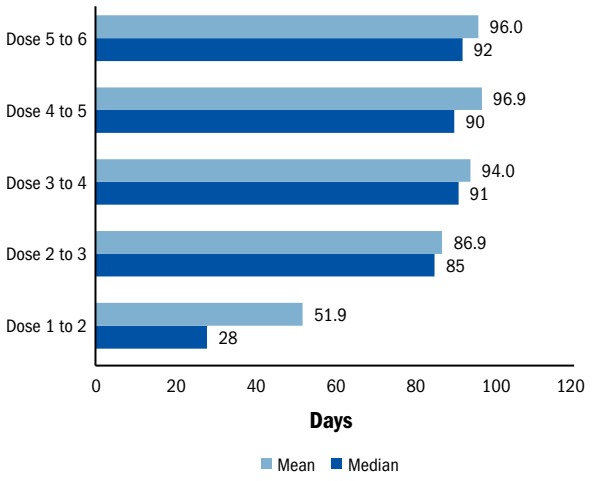
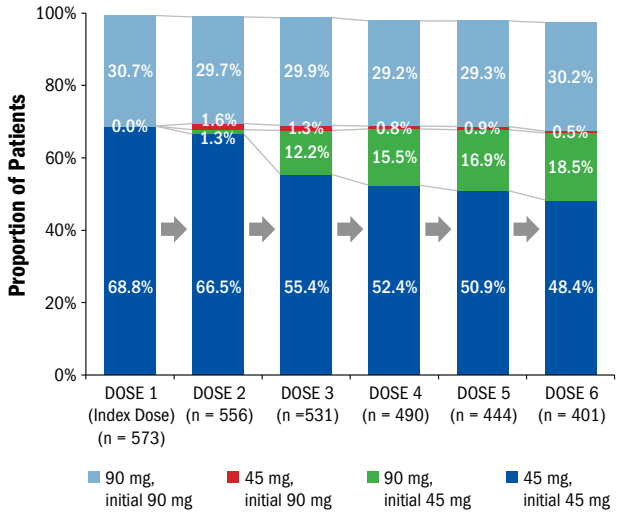


Figure 3. Ustekinumab Dose Changes by Index Dose



Note that in our study, all of the UST patients were initiators of UST (see Table 2), while in the weighted cohorts, 68% of ADA and 80% of ETA patients had received the index drug during the baseline year.

Studies comparing persistence with ADA and ETA reported results similar to those of our study. In our weighted cohorts, the percentages persistent at 1 year were 61.4% of UST, 46.7% of ADA, and 43.8% of ETA patients. Feldman and colleagues also found that the percentage persistent at 1 year was highest for UST (70.8%) and was lower for ADA (53.4%) and ETA (19.0%) patients.[20] Two studies of new users that defined persistence as no gaps ≥60 days reported 42.4% and 56.8% persistent on ADA compared with 40.4% and 46.4% persistent on ETA.[27,28] Two studies that defined persistence as no gaps ≥45 days reported 33% and 50% persistent on ADA and 22% and 33% persistent on ETA.[26,29] A study of existing users that defined persistence as no gaps ≥45 days reported 62.3% persistent on ADA and 47.7% persistent on ETA, which was higher than in our study.[26] Higher 1-year persistence with ADA (76%) was also found in a study conducted in a patient registry in the Netherlands that defined persistence as no gaps ≥90 days.[30]

Although continuous therapy is recommended for psoriasis treatment for all 3 study drugs, some clinical evidence has shown that these drugs can be effective among responders who are withdrawn and then re-treated after relapse.[18] Our study found that 17.5% of ADA and 23.1% of ETA patients had a therapy gap ≥90 days and then restarted during the year. Other studies comparing ADA and ETA defined pauses using shorter gaps and found higher proportions of patients with treatment pauses and restarts. Consistent with our study, pauses and restarts were more common among ADA than ETA patients. One study found restarts after a pause ≥45 days in 15.1% of ADA and 29.7% of ETA initiators and in 21.7% of existing ADA and 29.9% of existing ETA patients.[26] Another study reported 23.9% restarts in ADA patients and 32.3% in ETA patients.[29]

In our weighted cohorts, the percentages of patients switching to a nonindex biologic during 1 year, ADA (20.8%) and ETA (22.0%) were higher than reported in other claims studies. Rates of switching between ADA and ETA and among ADA, ETA, and infliximab during the first year, among drug initiators, ranged from 4.0% to 6.0% for ADA patients and 3.8% to 8% for ETA patients.[26,27,29] One study found that switch rates between ADA and ETA for existing users were 2.9% in the ADA cohort and 4.2% in the ETA cohort.[26] One explanation for our high rates of switching may be the time period of study: all of the follow-up time in our study was after February 8, 2010, when UST had recently become available, whereas most patients in the other studies were enrolled before UST became available.

Limitations

This study was subject to a number of limitations. First, discontinuation and restart rates depended on defined therapy gaps. This study relied on prescription dispensing dates and days of supply data, and we could not know when and whether patients actually took their medications. For UST, a gap of twice the dosing interval (≥168 days) was used to assess discontinuation and restarts and a gap of ≥90 days was used for ADA and ETA. Previous studies have used treatment gaps as low as 45 days.[26,29] Selection of longer treatment gaps may impact the rates of discontinuations and restarts.

Second, there was variability in the distribution of biologic experience across the cohorts. The multivariate model of the hazard of discontinuation adjusted for this by using variables for previous biologic therapy. However, there was no adjustment for the amount of time that the patients had been exposed to the index drug or to any other biologic therapy. Thirdly, a direct comparison of outcomes of UST with ADA and ETA may be confounded by the channeling of sicker patients to UST. To minimize the risk of this confounding, a recognized propensity score weighting method was used to adjust for the baseline patient differences. Also, this study used a population of patients diagnosed with psoriasis who had commercial insurance (including Medicare supplemental) and may not be generalizable to other populations.

Finally, other factors may influence prescriber dose selection, such as formulary guidelines regarding initiation of biologic therapy, or clinical information, such as a patient's weight. A payer may require a lower dose be administered to all patients regardless of weight or severity

prior to reimbursing a higher dose of the biologic. This type of information was not analyzed in our study.

CONCLUSIONS

This study showed considerable heterogeneity in baseline comorbid burden and treatment intensity among patients with psoriasis treated with subcutaneous biologic medications. Dose escalation during the maintenance period was observed for all biologics, but was less common among patients with psoriasis receiving UST compared with ADA or ETA. Discontinuations, restarts, and switches were significantly lower among patients with psoriasis receiving UST compared with those receiving ETA or ADA.

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Source of Funding: This study was funded by Janssen Scientific Affairs, LLC.

Author Disclosures: CC and SL are employees of Janssen Scientific Affairs and stockholders of Johnson & Johnson. KLW and DS are employees of Truven Health Analytics, which was paid by Janssen Scientific Affairs to conduct this study and to develop this manuscript.

Authorship Information: Concept and design (CC, KLW); acquisition of data (KLW); analysis and interpretation of data (SL, CC, KLW, DS); drafting of the manuscript (SL, CC, KLW); critical revision of the manuscript for important intellectual content (SL, CC, KLW, DS); administrative, technical, or logistic support (SL, CC).

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