Healthcare Resource Utilization and Costs of Commercially Insured US Patients with Atopic Dermatitis Switching from First-line to Second-line Systemic Targeted Therapies

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Abstract

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Background: The recent expansion of Food and Drug Administration (FDA)-approved treatment options for moderate-to-severe atopic dermatitis (AD) has notably improved clinical management options. With the availability of these novel therapies, data on frequency of therapy switching and differences in healthcare resource utilization (HCRU) and costs between switchers and non-switchers are limited.

Objective: To evaluate the frequency of treatment switching from first- to second-line systemic targeted therapies and compare HCRU and costs between switchers and non-switchers among commercially insured US patients with moderate-to-severe AD.

Methods: We conducted a retrospective cohort study using MarketScan health insurance claims data. Adult patients with AD initiating a first systemic targeted therapy (index date) between January 1, 2022 and December 31, 2022 were identified and followed for at least one year from index date. Two cohorts were classified based on whether switching occurred over follow-up, which was defined as discontinuation of first systemic targeted

therapy and initiation of second systemic targeted therapy. All-cause and AD-related HCRU outcomes, including hospitalizations, emergency department (ED) visits, and outpatient services, were compared between switchers and non-switchers during the follow-up period. Total healthcare costs were also evaluated, categorized by medical and drug costs. Statistical significance was defined as a two-sided p-value of < 0.05.

Results: After a year following the initiation of first-line systemic targeted therapy, 466 (5.8%) switched to second-line systemic targeted therapy among the 8,063 patients with moderate-to-severe AD included in this study. Nearly all switchers (96.4%) had at least one AD-related outpatient service compared to 82.8% for non-switchers ($p < 0.0001$), and the mean number of visits was higher among switchers compared to non-switchers (5.12 vs. 3.20, $p < 0.0001$). AD-related hospitalizations and ED visits were rare. Mean total AD-related healthcare costs also were significantly higher among switchers compared to non-switchers ($63,245 vs. $53,004; $p < 0.0001$), with drug costs accounting for approximately 99% of AD-related healthcare expenditures in both groups.

Discussion: We found a small proportion (5.8%) of patients switched from first- to second-line systemic targeted therapy after a median follow-up of approximately one year. Patients who switched therapies incurred significantly higher AD-related outpatient service use and total healthcare costs compared to non-switchers, which may potentially reflect either worsening disease severity or inadequate response or intolerability to first-line therapy. These findings emphasize the increased importance of personalized considerations for the selection of first-line systemic targeted therapy for patients with moderate-to-severe AD to reduce downstream economic burden. As additional therapies become available, future research exploring reasons for treatment switching and patient factors influencing response will be critical to guide clinical and formulary decision-making in this evolving treatment landscape.

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1. INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin condition characterized by intense itch and recurrent eczematous lesions.[1] It is the most common chronic inflammatory skin disease, with prevalence estimates ranging from 3.2 to 10.2% for adults in the United States (US).[2] AD is strongly associated with other atopic conditions (e.g., asthma and allergic rhinitis), significantly reducing quality of life.[3]

Many patients with AD can achieve adequate disease control with some combination of non-pharmacologic topical interventions (e.g., moisturizers and emollients) and/or pharmacologic topical therapies such as corticosteroids, calcineurin inhibitors, phosphodiesterase 4 inhibitors, and JAK inhibitors.[4] However, for the 40% of AD patients with uncontrolled moderate-to-severe disease, treatment with phototherapy or systemic oral or parenteral treatments is recommended by the American Academy of Dermatology (AAD).[4] Systemic treatments include non-targeted immunosuppressants (e.g., methotrexate, cyclosporine, azathioprine, and mycophenolate mofetil) as well as targeted therapies, such as biologics and JAK inhibitors.

The introduction of systemic targeted therapies with their improved efficacy and safety profiles has transformed the treatment landscape for patients with moderate-to-severe AD. Since the US Food and Drug Administration (FDA) approval of dupilumab for adults with AD in 2017, five additional systemic targeted therapies – two IL-13 inhibitors (tralokinumab and lebrikizumab), two JAK inhibitors (abrocitinib and upadacitinib), and one IL-31 inhibitor (nemolizumab) – have been approved for adults with moderate-to-severe AD.

Although the expanded range of treatment options benefits patients given the heterogeneity of AD and variability in treatment response, guidance on preferred sequencing of systemic targeted therapies remains inconsistent. On one hand, the 2024 AAD guidelines equally recommends dupilumab, tralokinumab, upadacitinib, and abrocitinib for the treatment of moderate-to-severe AD through shared decision-making between patients and clinicians.[4] On the other hand, the 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology

Joint Task Force strongly recommends dupilumab and tralokinumab, and only conditionally recommends the JAK inhibitors abrocitinib and baricitinib due to safety concerns.[5]

Furthermore, while trials such as HEADS UP and LEVEL UP have assessed the efficacy and safety of switching between systemic targeted therapies, real-world data on switching patterns are limited.[6,7] In particular, the frequency of switching and differences in healthcare resource utilization (HCRU) and costs between switchers and non-switchers remains poorly characterized. Switching may reflect clinical factors (e.g., inadequate response, adverse events, worsening disease) or non-clinical drivers (e.g., formulary changes, cost) that may result in higher HCRU and costs by patients. Real-world claims data on HCRU and costs can inform clinical and payer decision-making by highlighting the burden of moderate-to-severe AD and guiding strategies to better support patients.

In this study, we evaluated the frequency of treatment switching from first- to second-line systemic targeted therapies and compared HCRU and costs between switchers and non-switchers among commercially insured US patients with moderate-to-severe AD.

2. METHODS

2.1 Study Design and Data Source

We conducted a real-world retrospective observational cohort study to assess switch rates, HCRU, and associated costs among patients with moderate-to-severe AD as indicated by being treated with a systemic targeted therapy. Data from Merative MarketScan® Commercial Claims and Encounters (CCAE) Databases were used to identify patients and capture HCRU and costs. The CCAE databases include employees and dependents covered by employer-sponsored private health insurance plans in the US and captures claims across all settings of care and outpatient pharmacy. We collected all enrollment, inpatient, outpatient, and drug claim records within the study period from 1 January 2021 (the start of baseline period) to 31 December 2023 (the end of the follow-up period) (Figure 1).

2.2 Study Population

Patients were included if they had at least 2 medical claims with an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis of AD during the study period (Supplementary Table 1). Additional inclusion criteria required initiation of a new systemic targeted therapy (index date) between January 1, 2022, and December 31, 2022, and continuous medical and pharmacy coverage during both the 12-month baseline and a minimum 12-month follow-up period. Patients were excluded if they were <18 years old on the index date, had prescription drug claims for a targeted systemic therapy during the baseline period, or received more than two different targeted systemic therapies during follow-up. First-line systemic targeted therapy was defined as first ever initiated systemic targeted therapy and second-line systemic targeted therapy was defined as the second initiated systemic targeted therapy.

Within the overall population, two subgroups were created based on whether switching occurred over follow-up, which was defined as discontinuation of first systemic targeted therapy and initiation of second systemic targeted therapy. The study outcomes were assessed during the follow-up period, defined as the time from the index date to the end of the study period or the end of continuous enrollment, whichever occurred first.

2.3 Study Measures and Outcomes

Demographic and clinical characteristics were assessed during the baseline period. Information regarding sex, age, insurance plan type, geographic regions, Charlson Comorbidity Index (CCI) scores, atopic comorbidities (identified through ICD-10-CM codes in Supplementary Table 1), index therapy, and prior AD-related therapies were reported. Prior AD-related therapies included topical therapies, immunosuppressants, systemic corticosteroids, and phototherapy (Supplementary Table 2).

Switching from first-line to second-line systemic targeted therapy was assessed by switch rate, defined as the proportion of patients who initiated a new systemic targeted therapy following the initiation of the index treatment, and time to switch, defined as the duration from the index treatment initiation date to the start date of a subsequent systemic targeted therapy among patients who switched within the follow-up period.

HCRU outcomes included the number of hospitalizations, emergency department (ED) visits, and outpatient services during the follow-up period, stratified by switch status (switchers vs. non-switchers). HCRU outcomes were assessed from the index date across both cohorts. Health care settings were defined and categorized by the place of service variable in Marketscan, with codes adapted from prior literature (Supplementary Table 3).[8–10] HCRU was further categorized as all-cause or AD-related, which required the presence of a primary diagnosis code for AD.

Healthcare costs were estimated based on the total amount paid from adjudicated claims, including insurer and health plan payments as well as patient cost-sharing (copayments, deductibles, and coinsurance). Costs were categorized into medical and drug components. Medical costs included expenditures related to inpatient, ED, and outpatient HCRU, while drug costs reflected spending on prescription medications. Both types of costs were also further classified as all-cause and AD-related, which also required a primary diagnosis code for AD. Total healthcare costs during the follow-up period were defined as the sum of medical and drug costs from the index date. Costs were adjusted to 2023 US dollars using the medical care component of the US Consumer Price Index.[11]

2.4 Statistical Analysis

Baseline demographic and clinical characteristics, as well as treatment switch rates, were summarized descriptively. Statistical tests were conducted to compare HCRU and healthcare costs between switchers and non-switchers. Proportion of patients with at least one hospitalization, ED visit, or outpatient service, were independently compared using chi-square or Fisher's exact tests. Mean number of HCRU events among those with one or more events and medical, drug, and total costs were compared using independent t-tests.

As a secondary analysis, adjusted logistic regression models were used to estimate the probability of any hospitalizations and ED visits. Adjusted negative binomial regression was used to estimate the mean number of outpatient service visits. Medical, pharmacy, and total costs were modeled using gamma regression with a log link. All models adjusted

for baseline atopic comorbidities, CCI, prior AD-related therapies, index systemic targeted therapy, and baseline healthcare costs.

Statistical significance was defined as a two-sided p-value of < 0.05. Where applicable, 95% confidence intervals (CIs) were reported. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC) and R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

3. RESULTS

A total of 8,063 patients were included, with 466 (5.8%) identified as switchers and 7,597 (94.2%) as non-switchers (Table 1; Figure 2). The overall population consisted of primarily female (58.2%) patients living in the South (52.2%) with a mean age of 41.2 years. Patients had a mean CCI of 0.5 and had atopic comorbidities such as allergic rhinitis (24%) and asthma (18.8%). Many patients had prior claims 12 months before the index date for prescription topical therapies (45.4%) and systemic corticosteroids (28.5%), while few patients had prior claims for phototherapy (1.9%) and none had immunosuppressants. Nearly all patients initiated their first systemic targeted therapy with dupilumab (99.4%). Baseline demographic characteristics were similar between switchers and non-switchers. Use of prior AD-related therapies was observed more frequently among switchers than non-switchers. Compared to non-switchers, switchers were more frequently augmented with both prescription oral corticosteroids (27.7% vs. 15.8%) and topical corticosteroids (41.6% vs. 25.2%) after initiation of index therapy.

3.1 Switch Rates

Among the 466 switchers, the majority received dupilumab (n = 460) as first-line therapy while only a small number initiated abrocitinib (n = 3) or upadacitinib (n = 3); no patients initiated tralokinumab as first-line therapy (Supplementary Table 4). Total switch rate was determined to be 5.8% out of the overall population. The most common second-line therapy among dupilumab initiators was upadacitinib (56.3%), followed by tralokinumab (35.2%) and abrocitinib (8.5%). The overall mean time to switch from first-line to second-line therapy ranged from 186.3 days (1L = upadacitinib) to 395.7 days (1L = abrocitinib).

3.2 Healthcare Resource Utilization

Median follow-up duration was 381 and 379 days for switchers and non-switchers respectively. All-cause hospitalization rates were similar between groups, with 5.4% of switchers and 5.2% of non-switchers experiencing at least one hospitalization ($p = 0.83$) (Table 2). ED visits were significantly higher among switchers, with 31.8% having ≥1 ED visit versus 22.3% of non-switchers ($p < 0.0001$), although the mean number of ED visits among those with at least one visit did not differ significantly. While nearly all patients had at least one outpatient service use in both groups, switchers had a higher mean number of visits compared to non-switchers (28.43 vs. 22.83; $p < 0.0001$). AD-related hospitalizations and ED visits were rare across both groups. Nearly all switchers (96.4%) had at least one AD-related outpatient service compared to 82.8% of non-switchers ($p < 0.0001$), and the mean number of visits was higher among switchers compared to non-switchers (5.12 vs. 3.20, $p < 0.0001$). Results remained consistent after adjusting for baseline covariates. There were no significant differences in the odds of experiencing a hospitalization (all-cause or AD-related) between switchers and non-switchers (Supplementary Table 5). Switchers had higher odds of an all-cause ED visit (OR: 1.71; 95% CI: 1.38, 2.09); however, no difference was observed for AD-related ED visits, likely due to small event counts. Switchers had an estimated increase of 10 all-cause and 3.5 AD-related outpatient service visits compared to non-switchers.

3.3 Healthcare Costs

During the follow-up period, switchers incurred a $13,613 higher mean total all-cause healthcare cost compared to non-switchers ($83,335 vs. $69,722; $p < 0.0001$) (Table 3). Similarly, mean total AD-related healthcare costs were also significantly higher among switchers compared to non-switchers ($63,245 vs. $53,004; $p < 0.0001$). This difference was primarily driven by higher AD-related drug costs among switchers, who incurred an average of $62,579 (95% CI: $60,062 - $65,096) compared to $52,696 (95% CI: $52,096 - $53,296) for non-switchers ($p < 0.0001$). AD-related medical costs were also higher among switchers, with mean costs of $666 (95% CI: $592 - $739) versus $307 (95% CI: $280 - $335) in non-switchers ($p < 0.0001$). Differences in all-cause and AD-related costs

between switchers and non-switchers remained consistent with unadjusted results after adjusting for baseline covariates (Supplementary Table 6).

4. DISCUSSION

In this study of commercially insured patients with moderate-severe AD, we found that 5.8% of patients switched from first- to second-line systemic targeted therapy after a median follow-up of approximately one year, suggesting that first-line treatments may offer effective and well-tolerated disease control for most patients in the real-world setting. Almost all (99.4%) patients initiated their first-line systemic targeted therapy with dupilumab, which may be attributed to its earlier approval and limited uptake of more recently introduced systemic targeted therapies. Compared with non-switchers, patients who switched systemic targeted therapies incurred significantly higher AD-related outpatient service use and total healthcare costs. This may be expected as switching may reflect either worsening disease severity, inadequate response or intolerability to first-line therapy. Notably, drug costs accounted for approximately 99% of AD-related healthcare expenditures in both groups.

Our observed switch rate is consistent with a prior study using IQVIA's claims database from a similar time period, in which a switch rate of 5.1% was reported among 7,006 adults with AD initiating a first-line systemic targeted therapy.[12] To our knowledge, however, this is the first study comparing HCRU and costs between switchers and non-switchers following the approval of systemic targeted therapies beyond dupilumab. Previous research has established the substantial economic burden of AD in the US adult population. For instance, Shrestha et. al reported significantly higher HCRU and per-patient total costs among commercially insured adults with AD compared to matched controls ($10,461 vs. $7,187),[13] while Drucker et. al similarly estimated an adjusted annual incremental cost of $3,302 associated with AD.[14] Prior to the introduction of newer agents, patients commonly augmented dupilumab with systemic or topical corticosteroids, highlighting the difficulty of managing AD with the treatment options at the time.[15]

The recent expansion of FDA-approved systemic targeted therapies for moderate-to-severe AD has notably improved clinical management options. Our findings highlight that patients who switch therapies tend to use more healthcare resources and incur higher costs. With multiple targeted therapies now available, it is increasingly important to align initial treatment decisions with patient-specific clinical, economic, and contextual factors to reduce downstream healthcare burden.

4.1 Limitations

This study has several limitations. First, claims data do not capture the clinical reasons for treatment switching, nor do they include information on disease severity or response to therapy. We assumed systemic targeted therapies were prescribed on-label for patients with AD of moderate-to-severe severity. The number of patients receiving newer agents such as tralokinumab, abrocitinib, and upadacitinib was limited due to the timing of FDA approvals, and recently approved therapies such as lebrikizumab and nemolizumab are not captured within the current dataset. Total healthcare costs may be underestimated, as over-the-counter treatments and indirect costs are not included. Lastly, commercial patients included in the CCAE data may not be representative of all US commercial patients as the database under-represents smaller employers and excludes those with state-funded insurance. As with all retrospective studies using administrative claims data, results may be influenced by coding errors, misclassification, and variations in billing practices.

5. CONCLUSION

This study provides real-world insights into treatment patterns and economic burden among commercially insured patients with moderate-to-severe AD who initiated a systemic targeted therapy. We found that a small proportion of patients switch systemic targeted therapies, and those who switch experience higher healthcare resource use and costs. These findings underscore the increased importance of personalized considerations for the selection of first-line systemic targeted therapy for patients with moderate-to-severe AD to reduce downstream economic burden. As additional therapies become

available, future research exploring reasons for treatment switching and patient factors influencing response will be critical to guide clinical and formulary decision-making in this evolving treatment landscape.

6. TABLES AND FIGURES

Table 1. Baseline Characteristics

	Switchers (N = 466)	Non-Switchers (N = 7,597)	Overall (N = 8,063)
Age, years			
Mean (SD)	40.9 (14.3)	41.3 (14.2)	41.2 (14.2)
Sex, n (%)			
Male	201 (43.1)	3169 (41.7)	3370 (41.8)
Female	265 (56.9)	4428 (58.3)	4693 (58.2)
Insurance plan type, n (%)			
Comprehensive	18 (3.9)	175 (2.3)	193 (2.4)
EPO or PPO	206 (44.2)	3658 (48.2)	3864 (47.9)
HMO	56 (12.0)	962 (12.7)	1018 (12.6)
POS	35 (7.5)	700 (9.2)	735 (9.1)
CDHP or HDHP	147 (31.5)	1976 (26.0)	2123 (26.3)
Unknown	4 (0.9)	126 (1.7)	130 (1.6)
Geographic region, n (%)			
Northeast	64 (13.7)	1217 (16.0)	1281 (15.9)
North Central	86 (18.5)	1252 (16.5)	1338 (16.6)
South	253 (54.3)	3958 (52.1)	4211 (52.2)
West	62 (13.3)	1138 (15.0)	1200 (14.9)
Unknown	1 (0.2)	32 (0.4)	33 (0.4)
CCI, mean (SD)	0.5 (0.9)	0.5 (1.0)	0.5 (1.0)
Atopic comorbidities, n (%)			
Allergic rhinitis	99 (21.2)	1837 (24.2)	1936 (24.0)
Asthma	65 (13.9)	1447 (19.0)	1512 (18.8)
Chronic sinusitis	17 (3.6)	306 (4.0)	323 (4.0)
Nasal polyps	19 (4.1)	285 (3.8)	304 (3.8)
Food allergy	16 (3.4)	232 (3.1)	248 (3.1)
Allergic conjunctivitis	14 (3.0)	198 (2.6)	212 (2.6)
Atopic keratoconjunctivitis	7 (1.5)	97 (1.3)	104 (1.3)
Allergic urticaria	7 (1.5)	71 (0.9)	78 (1.0)
Eosinophilic esophagitis	0 (0)	51 (0.7)	51 (0.6)
Indexed 1L therapy, n (%)			

Dupilumab	460 (98.7)	7552 (99.4)	8012 (99.4)
Tralokinumab	0	0	0
Abrocitinib	3 (0.6)	10 (0.1)	13 (0.2)
Upadacitinib	3 (0.6)	35 (0.5)	38 (0.5)
Prior AD-related therapies, n (%)			
Topical therapies*	258 (55.4)	3405 (44.8)	3663 (45.4)
Immunosuppressants**	0	0	0
Systemic corticosteroids	167 (35.8)	2134 (28.1)	2301 (28.5)
Phototherapy	15 (3.2)	140 (1.8)	155 (1.9)
Baseline total cost ($USD), mean (SD)	31,379 (46,465)	29,483 (31,546)	29,593 (32,593)

*Topical corticosteroids, calcineurin inhibitors, PDE-4 inhibitors, JAK inhibitor

**Methotrexate, azathioprine, cyclosporine, mycophenolate mofetil

1L = first line; AD = atopic dermatitis; CCI = Charlson comorbidity index; CDHP = consumer driven health plan; EPO = exclusive provider organization; HDHP = high-deductible health plan; HMO = health maintenance organization; POS = point of service plan; PPO = preferred provider organization; SD = standard deviation

Table 2. All-Cause and Atopic Dermatitis-Related Healthcare Resource Utilization Among Switchers versus Non-Switchers Incurred During Follow-Up Period

	Switchers (N = 466)	**Non-switchers** (N = 7,597)	***P* value**
Follow-up duration in days, median (IQR)	381 (373, 388)	379 (371, 387)	-
All-cause HCRU			
Hospitalizations			
Total number of patients with ≥1 hospitalizations, n (%)	25 (5.4)	395 (5.2)	0.8302
Number of hospitalizations*, mean (SD)	2.08 (2.99)	1.34 (0.89)	0.229
ED Visits			
Total number of patients with ≥1 ED visit, n (%)	148 (31.8)	1696 (22.3)	<0.0001
Number of ED visits*, mean (SD)	1.77 (1.52)	1.84 (2.62)	0.6181
Outpatient Services			
Total number of patients with ≥1 outpatient service, n (%)	465 (99.8)	7538 (99.2)	0.2619
Number of outpatient services*, mean (SD)	28.43 (24.66)	22.83 (23.73)	<0.0001
AD-related HCRU			
Hospitalizations			
Total number of patients with ≥1 hospitalizations, n (%)	1 (0.2)	1 (0.01)	0.1123
Number of hospitalizations*, mean (SD)	1 (0)	1 (0)	-
ED Visits			
Total number of patients with ≥1 hospitalizations, n (%)	4 (0.9)	4 (0.1)	0.0006
Number of hospitalizations*, mean (SD)	1 (0)	1 (0)	-

Outpatient Services			
Total number of patients with ≥1 outpatient services, n (%)	449 (96.4)	6,293 (82.8)	<0.0001
Number of outpatient services*, mean (SD)	5.12 (5.25)	3.20 (5.73)	<0.0001

*Among patients with at least one event

AD = atopic dermatitis; ED = emergency department; HCRU = healthcare resource utilization; IQR = interquartile range; SD = standard deviation

Unadjusted results tested using chi-square and Fisher's exact tests.

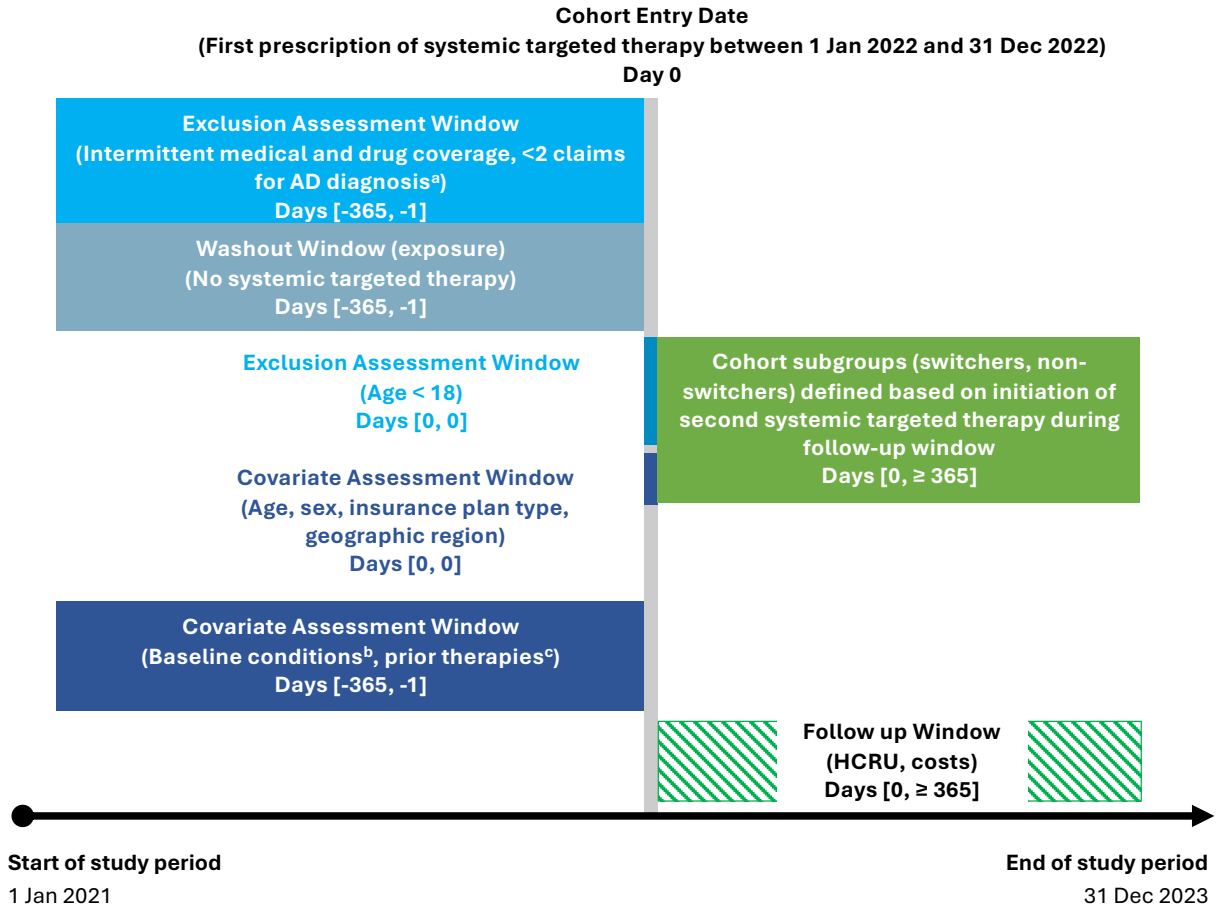
Table 3. All-Cause and Atopic Dermatitis-Related Costs Among Switchers versus Non-Switchers Incurred During Follow-Up Period

	Switchers (N = 466)	**Non-switchers** (N = 7,597)	**Difference**
All-cause Costs			
Medical costs, mean (95% CI)	$14,805 ($10,184 - $19,426)	$12,867 ($11,939 - $13,796)	$ 1,938 ($-6,651, $2,775) p = 0.4195
Drug costs, mean (95% CI)	$68,530 ($65,682 - $71,378)	$56,855 ($56,151 - $57,559)	$11,675 ($8,742, $14,608) p < 0.0001
Total healthcare costs, mean (95% CI)	**$83,335** ($77,973 - $88,698)	**$69,722** ($68,500 - $70,945)	**$13,613 ($8,113, $19,112)** p < 0.0001
AD-related Costs			
Medical costs, mean (95% CI)	$666 ($592 - $739)	$307 ($280 - $335)	$359 ($280, $437) p < 0.0001
Drug costs, mean (95% CI)	$62,579 ($60,062 - $65,096)	$52,696 ($52,096 - $53,296)	$9,883 ($7,296, $12,471) p < 0.0001
Total healthcare costs, mean (95% CI)	**$63,245** ($60,726 - $65,763)	**$53,004** ($52,401 - $53,606)	**$10,241 ($7,652, $12,830)** p < 0.0001

AD = atopic dermatitis; CI = confidence interval

Unadjusted results tested using independent two-sided t-tests.

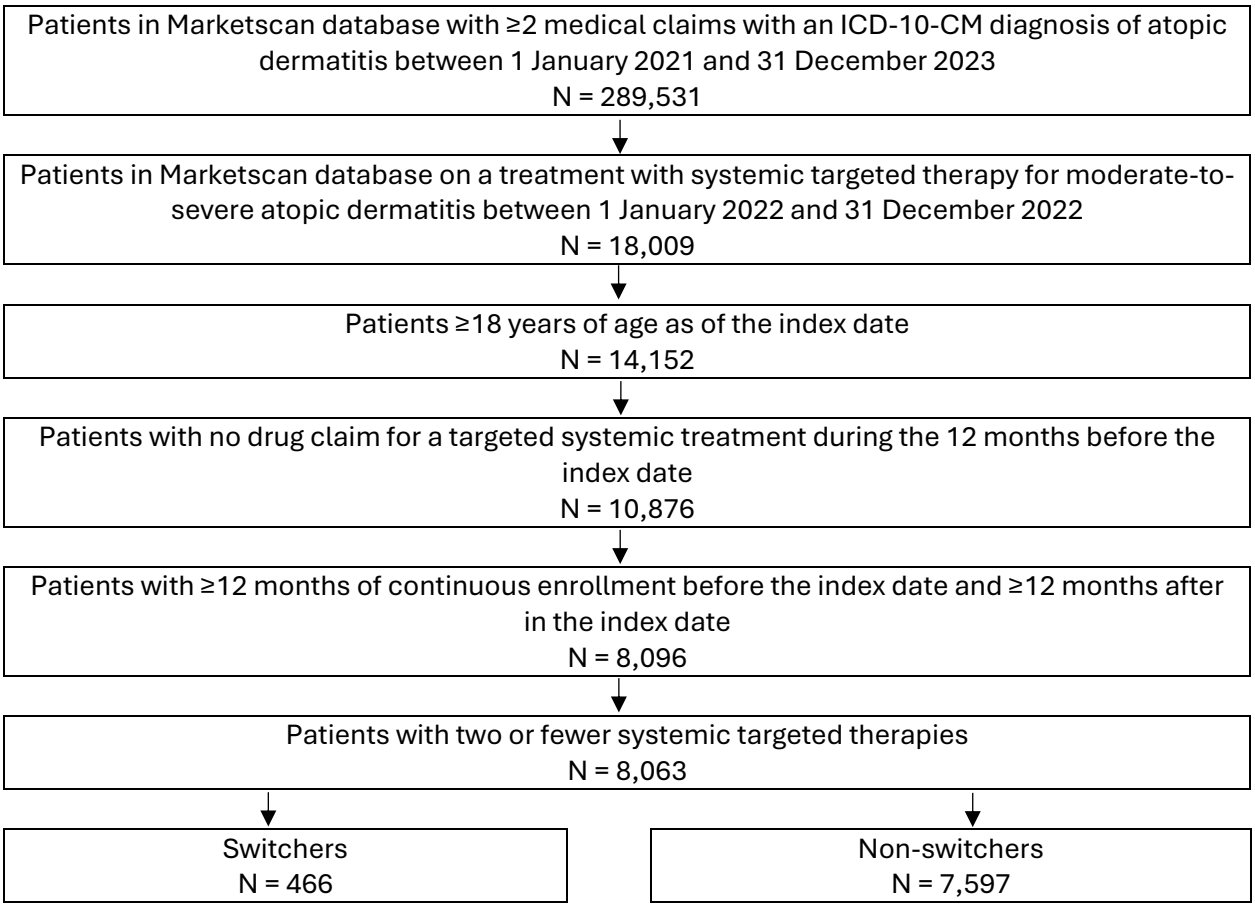
Figure 1. Study Design Schematic



a. 2 claims for AD diagnosis were searched throughout the full study period
b. Baseline conditions included: allergic rhinitis, asthma, chronic sinusitis, nasal polyps, food allergy, allergic conjunctivitis, atopic keratoconjunctivitis, allergic urticaria, eosinophilic esophagitis
c. Prior therapies included: topical therapies, immunosuppressants, systemic corticosteroids, phototherapy

AD = atopic dermatitis; HCRU = healthcare resource utilization

Figure 2. Patient Identification Flowchart



ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification

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8. SUPPLEMENT

Supplementary Table 1 ICD-10 Diagnosis Codes

Condition	ICD 10-CM Code	Description
Inclusion		
Atopic dermatitis	L20.0	Besnier's prurigo
	L20.8	Other atopic dermatitis
	L20.81	Atopic neurodermatitis
	L20.82	Flexural eczema
	L20.84	Intrinsic (allergic eczema)
	L20.89	Other atopic dermatitis
	L20.9	Atopic dermatitis, unspecified
Atopic Comorbidities		
Allergic rhinitis	J30.1	Allergic rhinitis due to pollen
	J30.2	Other seasonal allergic rhinitis
	J30.5	Allergic rhinitis due to food
	J30.8*	Other allergic rhinitis
	J30.9	Allergic rhinitis, unspecified
Asthma	J45.2*	Mild intermittent asthma
	J45.3*	Mild persistent asthma
	J45.4*	Moderate persistent asthma
	J45.5*	Severe persistent asthma
	J45.9*	Other and unspecified asthma
Chronic sinusitis	J32*	Chronic sinusitis
Allergic conjunctivitis	H10.1*	Acute atopic conjunctivitis
	H10.2	Other acute conjunctivitis
	H10.3	Unspecified acute conjunctivitis
Atopic keratoconjunctivitis	H16.2*	Keratoconjunctivitis
Nasal polyps	J33*	Nasal polyp
	J34*	Other and unspecified disorders of nose and nasal sinuses
Allergic urticaria	L50.0	Allergic urticaria
Eosinophilic esophagitis	K20.0	Eosinophilic esophagitis
Food allergy	Z91.010	Allergy to peanuts
	Z91.011	Allergy to milk products
	Z91.012	Allergy to eggs
	Z91.013	Allergy to seafood

	Z91.014	Allergy to mammalian meats
	Z91.018	Allergy to other foods

ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification

Supplementary Table 2 Codes for Therapies for Atopic Dermatitis

Therapy	NDC Codes
Systemic targeted therapies	
Dupilumab	00024-5914-01, 00024-5914-02, 00024-5918-01, 00024-5918-02, 00024-5915-02, 00024-5915-20, 00024-5919-02, 00024-5919-20, 00024-5911-02, 00024-5911-20
Tralokinumab	50222-0346-02, 50222-0346-04, 50222-0346-92, 50222-0350-01, 50222-0350-02, 50222-0350-91
Abrocitinib	00069-0235-30, 00069-0335-30, 00069-0435-30, 63539-0236-14, 63539-0336-14, 63539-0436-14
Upadacitinib	00074-2306-30, 00074-2306-70, 00074-2310-20, 00074-2310-30, 00074-1043-14, 00074-1043-28, 00074-2320-01, 00074-2320-70
Topical therapies	
Topical corticosteroids	
Alclometasone	Available upon request.
Amcinonide	Available upon request.
Betamethasone	Available upon request.
Clobetasol propionate	Available upon request.
Desonide	Available upon request.
Desoximetasone	Available upon request.
Diflorasone diacetate	Available upon request.
Fluocinolone acetonide	Available upon request.
Fluocinonide	Available upon request.
Flurandrenolide	Available upon request.
Fluticasone propionate	Available upon request.
Halcinonide	Available upon request.
Halobetasol propionate	Available upon request.
Hydrocortisone	Available upon request.
Hydrocortisone acetate	Available upon request.
Hydrocortisone butyrate	Available upon request.
Hydrocortisone probutate	Available upon request.

Hydrocortisone valerate	Available upon request.
Mometasone furoate	Available upon request.
Triamcinolone acetonide	Available upon request.
Topical calcineurin inhibitors	
Pimecrolimus	00078037540, 00078037546, 00078037549, 00078037563, 00187510001, 00187510102, 00187510203, 00187510304, 00591294430, 00591294460, 00591294487, 12280007930, 35356022300, 54569550200, 54868487800, 54868487801, 54868487802, 68462060935, 68462060965, 68462060994, 68682011001, 68682011102, 68682011203, 70518229200
Tacrolimus	00093342810, 00093342830, 00093342892, 00093342910, 00093342930, 00093342992, 00168041630, 00168041660, 00168041699, 00168041730, 00168041760, 00168041799, 00469520102, 00469520111, 00469520130, 00469520160, 00469520202, 00469520211, 00469520230, 00469520260, 16729042101, 16729042110, 16729042112, 16729042201, 16729042210, 16729042212, 35356023500, 45802039000, 45802039001, 45802039002, 45802070000, 45802070001, 45802070002, 50222020310, 50222020330, 50222020360, 50222021110, 50222021130, 50222021160, 54569525800, 54868523300, 54868523301, 68308070301, 68308070360, 68462053435, 68462053465, 68462053494, 72934209602, 72934209702, 72934217402, 72934417308, 72934434908, 72934515802, 72934515902, 82160012401, 82160012402
Topical PDE-4 inhibitor	
Crisaborole	55724021111, 55724021121, 55724021123, 55724021142
Topical JAK inhibitor	
Ruxolitinib	50881000704, 50881000705, 50881000707
Immunosuppressants	
Methotrexate	38779003503, 38779003504, 38779003506, 38779003510, 38779003511, 38779003515, 38779003525, 49452460001, 49452460002, 49452460003, 49452460101, 49452460102, 49452460103, 49452460104, 51552105401, 51552105409, 51927156500, 62991120001, 62991120002, 62991120004, 63370015410, 63370015415, 63370015425
Azathioprine	38779031203, 38779031204, 38779031206, 38779031211, 38779031215, 38779031225, 49452078201, 49452078202, 49452078203, 49452078301, 49452078302, 49452078303, 49452078304, 49452078305, 51552077902, 51552077904, 51552077905, 51927225800, 52372072801, 52372072802, 52372072803, 52372072804
Cyclosporine	00395810819, 00395810835, 00395810862, 38779066001, 38779066003, 38779066004, 38779066005, 38779066006, 38779066008, 46144032325, 49452241102, 51552066301, 51552066302, 51552066304, 51552066305, 51552066306, 51552066309, 51927319600, 63307013101, 63307013105, 63307013111, 63307013115, 63307013137, 63370005710, 70457982601, 70457982602, 70457982603, 71052042310, 71052042325
Mycophenolate mofetil	51927512500, 71052031700
Oral systemic corticosteroids	

Dexamethasone	Available upon request.
Hydrocortisone	Available upon request.
Prednisolone	Available upon request.
Prednisone	Available upon request.
Methylprednisolone	Available upon request.
Phototherapy	
CPT Codes	96900, 96910, 96912, 96913, 96921, 96922, 96999
HCPCS Codes	E0691, E0692, E0693, E0694

CPT = current procedural terminology; HCPCS = healthcare common procedure coding system; NDC = national drug code

Supplementary Table 3 Codes and Description of Place of Service Variables for Health Care Settings

Place of Service Code Value	Place of Service Name	Place of Service Description (CMS 2024)
Inpatient Setting		
21	Inpatient Hospital	A facility, other than psychiatric, which primarily provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services by, or under, the supervision of physicians to patients admitted for a variety of medical conditions.
Emergency Department		
23	Emergency Room – Hospital	A portion of a hospital where emergency diagnosis and treatment of illness or injury is provided.
Outpatient/Ambulatory Setting		
Office Visits		
11	Office	Location, other than a hospital, skilled nursing facility (SNF), military treatment facility, community health center, State or local public health clinic, or intermediate care facility (ICF), where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.
17	Walk-in Retail Health Clinic	A walk-in health clinic, other than an office, urgent care facility, pharmacy or independent clinic and not described by any other Place of Service code, that is located within a retail operation and provides, on an ambulatory basis, preventive and primary care services.
49	Independent Clinic	A location, not part of a hospital and not described by any other Place of Service code, that is organized and

		operated to provide preventive, diagnostic, therapeutic, rehabilitative, or palliative services to outpatients only.
50	Federally Qualified Health Center	A facility located in a medically underserved area that provides Medicare beneficiaries preventive primary medical care under the general direction of a physician.
71	Public Health Clinic	A facility maintained by either State or local health departments that provides ambulatory primary medical care under the general direction of a physician.
72	Rural Health Clinic	A certified facility which is located in a rural medically underserved area that provides ambulatory primary medical care under the general direction of a physician.
Urgent Care		
20	Urgent Care Facility	Location, distinct from a hospital emergency room, an office, or a clinic, whose purpose is to diagnose and treat illness or injury for unscheduled, ambulatory patients seeking immediate medical attention.
41	Ambulance – Land	A land vehicle specifically designed, equipped and staffed for lifesaving and transporting the sick or injured.
42	Ambulance – Air or Water	An air or water vehicle specifically designed, equipped and staffed for lifesaving and transporting the sick or injured.
Other Outpatient Services		
15	Mobile Unit	A facility/unit that moves from place-to-place equipped to provide preventive, screening, diagnostic, and/or treatment services.
19	Off Campus - Outpatient Hospital	A portion of an off-campus hospital provider-based department which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.
22	On Campus - Outpatient Hospital	A portion of a hospital's main campus which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.

24	Ambulatory Surgical Center	A freestanding facility, other than a physician's office, where surgical and diagnostic services are provided on an ambulatory basis.
53	Community Mental Health Center	A facility that provides the following services: outpatient services, including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the CMHC's mental health services area who have been discharged from inpatient treatment at a mental health facility; 24 hour a day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to State mental health facilities to determine the appropriateness of such admission; and consultation and education services.
55	Residential Substance Abuse Treatment Facility	A facility which provides treatment for substance (alcohol and drug) abuse to live-in residents who do not require acute medical care. Services include individual and group therapy and counseling, family counseling, laboratory tests, drugs and supplies, psychological testing, and room and board.
56	Psychiatric Residential Treatment Center	A facility or distinct part of a facility for psychiatric care which provides a total 24-hour therapeutically planned and professionally staffed group living and learning environment.
57	Non-residential Substance Abuse Treatment Facility	A location that provides treatment for substance (alcohol and drug) abuse on an ambulatory basis. Services include individual and group therapy and counseling, family counseling, laboratory tests, drugs and supplies, and psychological testing.
61	Comprehensive Inpatient Rehabilitation Facility	A facility that provides comprehensive rehabilitation services under the supervision of a physician to inpatients with physical disabilities. Services include physical therapy, occupational therapy, speech pathology, social or psychological services, and orthotics and prosthetics services.
62	Comprehensive Outpatient Rehabilitation Facility	A facility that provides comprehensive rehabilitation services under the supervision of a physician to outpatients with physical disabilities. Services include physical therapy, occupational therapy, and speech pathology.
95	Outpatient (NEC)	Outpatient setting, not elsewhere classified (NEC).

Supplementary Table 4 Switch Rates by Index Drug

	1L (Index) Therapy (n = 466)			
	Dupilumab (N = 460)	**Tralokinumab (N = 0)**	**Abrocitinib (N = 3)**	**Upadacitinib (N = 3)**
Overall switch rate (2L therapy), n (%)				
Dupilumab	-	0	2 (66.6)	1 (33.3)
Tralokinumab	162 (35.2)	-	0	1 (33.3)
Abrocitinib	39 (8.5)	0	-	1 (33.3)
Upadacitinib	259 (56.3)	0	1 (33.3)	-
Days to switch, mean (SD)	380.3 (141.7)	-	395.7 (211.2)	186.3 (81.8)
Dupilumab	-	-	517.5 (10.6)	129
Tralokinumab	401.0 (132.6)	-	0	150
Abrocitinib	380.9 (182.3)	-	-	280
Upadacitinib	367.3 (139.3)	-	152	-

1L = First line; 2L = second line; SD = standard deviation

Supplementary Table 5 Adjusted Estimated All-Cause and Atopic Dermatitis-Related Healthcare Resource Utilization Among Switchers versus Non-Switchers Incurred During Follow-Up Period

	Switchers (N = 466)	**Non-switchers** (N = 7,597)	**Difference**
All-cause HCRU			
Hospitalizations			
Odds ratio (95% CI)	1.12 (0.71, 1.70)	Ref	p = 0.5942
Predicted probability (95% CI)	~0	~0	
ED Visits			
Odds ratio (95% CI)	1.71 (1.38, 2.09)	Ref	p < 0.0001
Predicted probability (95% CI)	0.49 (0.32, 0.66)	0.36 (0.22, 0.53)	
Outpatient Services			
Estimated mean (95% CI)	42.5 (32.5, 55.7)	32.4 (24.9, 42.0)	10.2 (6.0, 14.4); p < 0.0001
AD-related HCRU			
Hospitalizations			
Odds ratio (95% CI)	13.5 (0.37, 654)	Ref	p = 0.1206
Predicted probability (95% CI)	~0	~0	
ED Visits			
Odds ratio (95% CI)	7.84 (0.92, 53.6)	Ref	p = 0.0359
Predicted probability (95% CI)	~0	~0	
Outpatient Services			
Estimated mean (95% CI)	7.67 (5.46, 10.77)	4.19 (3.01, 5.83)	3.48 (2.15, 4.81); p < 0.0001

AD = atopic dermatitis; CI = confidence intervals; ED = emergency department; HCRU = healthcare resource utilization
Adjusted for covariates total baseline cost, atopic comorbidities, CCI, prior AD-related therapies, and index systemic targeted therapy. Logistic regression used to predict rare events (e.g., hospitalizations and ED visits) and negative binomial regression used to compare mean outpatient services. Wide CIs reflect small event count.

Supplementary Table 6 Adjusted Estimated All-Cause and Atopic Dermatitis-Related Costs Among Switchers versus Non-Switchers Incurred During Follow-Up Period

	Switchers (N = 466)	**Non-switchers** (N = 7,597)	**Difference**
All-cause Costs			
Medical costs, mean (95% CI)	$15,993 ($5,845 - $43,760)	$14,555 ($5,490 - $38,590)	$1,819 ($-3,982 - $7,619) p = 0.5351
Drug costs, mean (95% CI)	$75,287 ($63,981 - $88,592)	$61,680 ($52,685 - $72,210)	$11,619 ($8,801 - $14,437) p < 0.0001
Total healthcare costs, mean (95% CI)	**$92,571** ($74,276 - $115,374)	**$76,907** (62,134 - $95,193)	**$13,440 ($8,703 - $18,176)** p < 0.0001
AD-related Costs			
Medical costs, mean (95% CI)	$3,144 ($1,769 - $5,588)	$1,714 ($977 - $3,007)	$240 ($177 - $303) p < 0.0001
Drug costs, mean (95% CI)	$69,756 ($59,609 - $81,629)	$58,771 ($50,471 - $68,437)	$9,189 ($6,687 - $11,691) p < 0.0001
Total healthcare costs, mean (95% CI)	**$70,747** ($60,438 - $82,815)	**$59,487** ($51,070 - $69,291)	**$9,336 ($6,823 - $11,850)** p < 0.0001

AD = atopic dermatitis; CI = confidence interval
Adjusted for covariates total baseline cost, atopic comorbidities, CCI, prior AD-related therapies, and index systemic targeted therapy using gamma regression with log link. Statistical comparisons tested using Wald's test are based on model's link scale, while means are shown on natural scale.