Real-World Effectiveness of Systemic Therapies for Atopic Dermatitis in the United States: Retrospective Analysis of a US Claims Database

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BACKGROUND

- Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense pruritus and recurrent eczematous lesions[1]
- In 2017, it was estimated that moderate-to-severe AD affected up to 6.6 million people in the United States[2]
- AD is associated with decreased health-related quality of life for patients and caregivers,[3-5] as well as significant economic burden to patients, payers, and society[4,6,7]
- As systemic therapies rapidly evolve, it is necessary to understand the effectiveness of current systemic AD treatments, using evidence that reflects real-world practice

OBJECTIVE

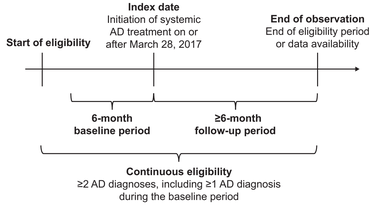
- To evaluate the real-world effectiveness of current systemic treatments for moderate-to-severe AD in the United States among patients newly initiating these therapies

METHODS

Study Design

- A retrospective cohort analysis was conducted using data from the IQVIA Health Plan Claims data set
- The study period spanned September 29, 2016 (6 months before US approval of dupilumab [March 28, 2017]) to December 31, 2019 (**Figure 1**)
  - The index date was defined as the initiation date of a systemic immunosuppressant (SIS) or dupilumab
  - The baseline period was defined as the 6-month period before the index date
  - The follow-up period was ≥6 months and spanned the index date to the earliest date of the end of insurance eligibility or data availability

Figure 1. Study Design



AD, atopic dermatitis.

Patient Inclusion Criteria

- At least 2 claims for the same systemic treatment (based on American Academy of Dermatology clinical guidelines and reviews of treatments for moderate-to-severe AD) on March 28, 2017, or later
  - First claim defined as the index date
- Newly initiated (ie, no claim during the baseline period) on SIS (ie, azathioprine, cyclosporine, methotrexate, mycophenolate) or dupilumab
  - Patients who had >1 treatment at the index date were classified into only 1 of the treatment cohorts using the following hierarchy:
    - Dupilumab
    - SIS
- ≥2 AD diagnoses (*ICD-9/10-CM*: 691.8/L20.x) during continuous eligibility, including 1 AD diagnosis during the baseline period
- Age ≥12 years on the index date
- ≥6 months continuous enrollment before and after a patient's first systemic therapy claim (index date)

Outcomes

- Baseline demographic and clinical characteristics
- Index treatment
- Treatment nonresponse, defined as a composite endpoint based on any of the following indicators observed after the index date:
  - Adding/switching to a different therapy for moderate-to-severe AD (ie, dupilumab, phototherapy, SIS, systemic corticosteroid)
  - AD-related inpatient or emergency room visit
  - Presence of incident staphylococcal or group A streptococcal skin infection
- All-cause healthcare resource utilization (HCRU) evaluated in the follow-up period (excluding the index date):
  - Inpatient visits
  - Emergency room visits
  - Outpatient visits
  - Other visits

Analysis

- Demographics and clinical characteristics were described using mean, SD, and median for continuous variables; frequency and proportion were used for categorical variables (overall and by index treatment) and compared using χ^2 tests
- AD treatments received on and after the index date were described using frequencies and proportions, overall and by index treatment
- Rates of nonresponse were compared between index treatment cohorts:
  - The proportion of patients meeting the composite nonresponse measure was reported overall and by index treatment
  - Time to nonresponse across index treatments was measured using Kaplan-Meier curves and compared using log-rank tests
- The number of HCRU visits per year was calculated by dividing the total number of visits in the follow-up period by the total number of follow-up years per patient

RESULTS

Patient Demographics and Clinical Characteristics

- Demographics and clinical characteristics of the overall patient population (n=3249; **Table 1**) were comparable between the SIS (n=794) and dupilumab (n=2455) treatment cohorts; mean age (SD) was 40.6 (16.1) years, and 54.2% of patients were female
- Atopic march conditions were the most prevalent types of comorbidity (35.5%; including allergic rhinitis [26.6%] and asthma [20.7%]) followed by psychological conditions (27.8%); uncomplicated hypertension (18.5%); infection (17.9%); and AD-related conditions, including conjunctivitis (16.1%) (**Table 1**)

Table 1. Baseline Demographics and Clinical Characteristics Among Patients New to Systemic AD Treatments

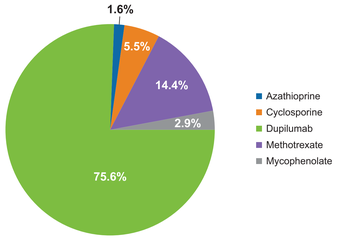
Patient Characteristics	Overall n=3249	Index Treatment	
		Dupilumab n=2455	SIS n=794
Demographics			
Age on index date, mean ± SD, y	40.6 ± 16.1	39.8 ± 15.5	43.4 ± 17.4
Age categories on index date, n (%)			
12-17 years	203 (6.2)	97 (4.0)	106 (13.4)
≥18 years	3046 (93.8)	2358 (96.0)	688 (86.6)
Female, n (%)	1761 (54.2)	1321 (53.8)	440 (55.4)
Region, n (%)			
South	1510 (46.5)	1169 (47.6)	341 (42.9)
Northeast	688 (21.2)	521 (21.2)	167 (21.0)
Midwest	700 (21.5)	544 (22.2)	156 (19.6)
West	351 (10.8)	221 (9.0)	130 (16.4)
Payer type, n (%)			
Commercial–fully insured	1811 (55.7)	1333 (54.3)	478 (60.2)
Commercial–self-insured	1417 (43.6)	1104 (45.0)	313 (39.4)
Medicaid	14 (0.4)	13 (0.5)	1 (0.1)
Medicare	5 (0.2)	3 (0.1)	2 (0.3)
Unknown	2 (0.1)	2 (0.1)	0 (0.0)
Year of index date, n (%)			
2017	953 (29.3)	673 (27.4)	280 (35.3)
2018	1570 (48.3)	1193 (48.6)	377 (47.5)
2019	726 (22.3)	589 (24.0)	137 (17.3)
Clinical characteristics			
Comorbidities, n (%)			
Atopic march conditions	1155 (35.5)	917 (37.4)	238 (30.0)
Allergic rhinitis	865 (26.6)	696 (28.4)	169 (21.3)
Asthma	673 (20.7)	547 (22.3)	126 (15.9)
Food allergies	46 (1.4)	37 (1.5)	9 (1.1)
Psychological conditions	902 (27.8)	653 (26.6)	249 (31.4)
Anxiety	438 (13.5)	328 (13.4)	110 (13.9)
Depression	365 (11.2)	257 (10.5)	108 (13.6)
Sleep disorders	343 (10.6)	233 (9.5)	110 (13.9)
Uncomplicated hypertension	600 (18.5)	399 (16.3)	201 (25.3)
Infection[a]	583 (17.9)	396 (16.1)	187 (23.6)
Viral infection	293 (9.0)	215 (8.8)	78 (9.8)
Fungal infection	191 (5.9)	116 (4.7)	75 (9.4)
Bacterial infection	125 (3.8)	78 (3.2)	47 (5.9)
AD-related conditions	523 (16.1)	335 (13.6)	188 (23.7)

AD, atopic dermatitis; SIS, systemic immunosuppressant.
[a]Percentages add up to >100% because some patients had multiple infections.

Treatment Patterns

- Patients initially treated with an SIS were more likely to have used systemic corticosteroids at baseline than those in the dupilumab cohort (57.9% vs 48.3%; *P*<0.001)
- Similarly, baseline use of high-potency topical corticosteroids was more common in the SIS cohort (49.2% vs 44.5%; *P*=0.019)
- The distribution of index treatments among the 3249 patients initiating systemic therapy was dupilumab, 75.6%; methotrexate, 14.4%; cyclosporine, 5.5%; mycophenolate, 2.9%; azathioprine, 1.6% (**Figure 2**)

Figure 2. Index Treatments Among Patients With AD New to Systemic Therapy

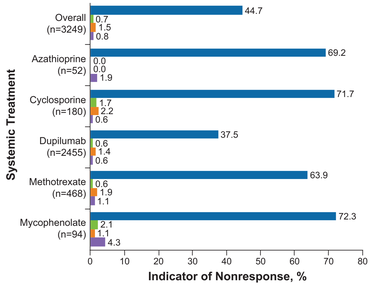


AD, atopic dermatitis.

Treatment Nonresponse

- During follow-up, 45.4% of patients overall exhibited ≥1 indicator of nonresponse
  - Overall, adding/switching to another moderate-to-severe AD therapy (44.7%) was the most common outcome; the rate was highest for the patients who were treated with mycophenolate (72.3%) and lowest for the patients treated with dupilumab (37.5%) (**Figure 3**)

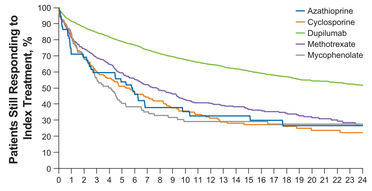
Figure 3. Nonresponse Outcomes for Patients New to Systemic Treatments for AD[a]



AD, atopic dermatitis; GAS, group A streptococcus; HCRU, healthcare resource utilization.
[a]All measures were evaluated during the follow-up period, excluding the index date.

- Kaplan-Meier rates of nonresponse at 12 months varied by index therapy
  - The rate for dupilumab was lowest (35.4%) compared with that of azathioprine (67.4%), cyclosporine (68.7%), methotrexate (59.6%), and mycophenolate (70.9%); *P*<0.01 for all comparisons versus dupilumab (**Figure 4**)

Figure 4. Kaplan-Meier Curve: Continuation of Treatment Response



Healthcare Resource Utilization

- The most common type of HCRU in the follow-up period was outpatient visit (**Table 2**)
- Most patients (99.5%) had ≥1 outpatient visit in the follow-up period (mean visits per year ± SD, 18.3 ± 20.8; **Table 2**)
- Across index treatments, mean number of all-cause inpatient (0.1 ± 0.3 vs 0.1 ± 0.5), outpatient (17.3 ± 20.7 vs 21.6 ± 21.0), and emergency room (0.5 ± 1.2 vs 0.7 ± 2.9) visits per year occurred less frequently in the dupilumab subgroup than in the SIS subgroup (**Table 2**)
- Mean all-cause healthcare costs per year were $34,483 ± $32,484 in the follow-up period; pharmacy costs were on average $27,075 ± $21,950 per year; outpatient visit costs were $5133 ± $15,702 per year; and inpatient visit costs were $1727 ± $11,788 per year

Table 2. Follow-Up All-Cause HCRU Among Patients New to Systemic AD Treatments

HCRU Measures	Overall n=3249	Dupilumab n=2455	SIS n=794
Follow-up period (excluding index date), mean ± SD [median], days	472.3 ± 213.7 [433.0]	460.9 ± 211.0 [412.0]	507.5 ± 218.1 [477.0]
Inpatient visits			
Patients with ≥1 visit, n (%)	218 (6.7)	141 (5.7)	77 (9.7)
Visits per year, mean ± SD [median]	0.1 ± 0.3 [0.0]	0.1 ± 0.3 [0.0]	0.1 ± 0.5 [0.0]
Emergency room visits			
Patients with ≥1 visit, n (%)	944 (29.1)	692 (28.2)	252 (31.7)
Visits per year, mean ± SD [median]	0.5 ± 1.7 [0.0]	0.5 ± 1.1 [0.0]	0.7 ± 2.9 [0.0]
Outpatient visits			
Patients with ≥1 visit, n (%)	3234 (99.5)	2441 (99.4)	793 (99.9)
Visits per year, mean ± SD [median]	18.3 ± 20.8 [11.9]	17.3 ± 20.7 [10.3]	21.6 ± 21.0 [15.6]
Other visits			
Patients with ≥1 visit, n (%)	510 (15.7)	385 (15.7)	125 (15.7)
Visits per year, mean ± SD [median]	0.2 ± 0.8 [0.0]	0.2 ± 0.9 [0.0]	0.2 ± 0.7 [0.0]

AD, atopic dermatitis; HCRU, healthcare resource utilization; SIS, systemic immunosuppressant.

CONCLUSION

- This study highlights the challenges of treating patients with AD who require systemic treatment
- A substantial proportion of patients who initiated systemic treatment did not continue therapy; this was especially true for patients in the SIS cohort
- Time-on-therapy differences between cohorts, in addition to the lack of efficacy, could partly be explained by differences in safety, although more research is necessary
- A limitation of the study is the lack of information on the specific reasons a patient switched or discontinued therapy

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