A Real-World Study Evaluating AdeQUacy of Existing Systemic Treatments for Patients with Moderate-to-Severe Atopic Dermatitis (AD-QUEST): Baseline Treatment Patterns and Unmet Needs Assessment

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INTRODUCTION

- Atopic dermatitis (AD) is a relapsing, chronic, pruritic, inflammatory skin disease associated with gene-environment interactions, immune dysregulation, and skin barrier dysfunction.[1]
  - AD affects around 3.2% of adults in the USA.[2]
- Severe disease is often associated with significant disability, leading to high socioeconomic costs including: psychological problems, significant sleep loss, and impaired quality of life.[3]
- The current treatment approach for AD is to reactively treat flares.
  - Topical corticosteroids are most frequently prescribed for the treatment of AD;[4] however, in patients with moderate-to-severe disease and inadequate response to topical therapy, more aggressive systemic therapies are medically necessary.[5]
- At present, the real-world treatment patterns and unmet needs of adult patients with moderate-to-severe AD are poorly quantified for patients treated with systemic therapies.

OBJECTIVE

- To evaluate from a patient perspective the adequacy of systemic treatment and to document potential unmet needs in the treatment of moderate-to-severe AD.

METHODS

- The study was a longitudinal prospective observational study of adult patients with moderate-to-severe AD, receiving a systemic medication for the treatment of AD in the previous 6 months.
- Study subjects were adult commercial health plan enrollees with AD, identified from the Optum Research Database.
- AD was defined using International Classification of Disease, Ninth or Tenth Revision, Clinical Modification (ICD-9-CM or ICD-10-CM).
- Eligible study participants were invited by mail to participate in a baseline paper survey, followed by web-based surveys at 3, 6, 9, and 12 months. Monthly abbreviated web-based surveys were also included.
- Diagnosis of AD, moderate-to-severe AD (during the previous 12 months), and systemic medication use was verified by patients at the time they completed the baseline survey.
- An informed consent statement was provided with the paper survey, and consent for study participation was implied when the survey was returned.

Inclusion criteria

- Aged ≥18 years.
- At least one medical claim with an ICD-9-CM diagnosis code for AD (691.8) or ICD-10-CM diagnosis code (L200, L2081, L2082, L2083, L2084, L2089, L209) from a dermatologist or allergist/immunologist over the last 5 years; or
- At least one medical claim with a diagnosis code for contact dermatitis due to an unspecified condition (ICD-9: 692.9, ICD-10: L259) or rash and other non-specific skin eruption (ICD-9: 782.1, ICD-10: R21) from a dermatologist or allergist/immunologist over the last 5 years; *and* at least two non-diagnostic medical claims at least 30 days apart with a diagnosis code for asthma, food allergies, or allergic rhinitis.
- At least one pharmacy claim or medical claim over the last 6 months for: at least one oral corticosteroid; at least one injectable corticosteroid; at least one phototherapy treatment; or any immunosuppressant.
- Continuous enrollment with both medical and pharmacy benefits in a large commercial US health plan affiliated with Optum during the past 6 months.
- Able and willing to complete surveys.
- Self-reported AD diagnosis in the patient survey.
- Moderate-to-severe AD over the past 12 months using the Rajka and Langeland criteria.[6]

Exclusion criteria

- Participation in a clinical trial for AD in the last 6 months.
- At least two non-diagnostic medical claims at least 30 days apart with a diagnosis code for conditions that may be treated with systemic steroids during the last 5 years.
- At least one pharmacy or medical claim for an immunosuppressant in the last 5 years and at least two non-diagnostic medical claims at least 30 days apart with a diagnosis code for conditions that may be treated with immunosuppressants.
- At least two non-diagnostic medical claims at least 30 days apart with a diagnosis code that may be treated with systemic immunosuppressants within the past 5 years.
- At least two non-diagnostic claims at least 30 days apart with a code indicating a solid organ transplant over the last 5 years.
- Surveys that were partially completed, ineligible, returned too late, or had non-responses were excluded.

Survey outcomes

- The baseline paper survey collected the following from patients:
  - Sociodemographic characteristics: race, ethnicity, marital status, education level, and household income level.
  - Medical history: patient confirmation of AD diagnosis by a healthcare professional, age at AD diagnosis, and self-reported disease severity using the Rajka and Langeland criteria.[6]
  - Signs and symptoms of AD: patient-reported flares, Patient-Orientated Eczema Measure (POEM)[7] and the pruritus Numeric Rating Scale (NRS).[8]
  - Disease-specific quality of life assessed using the Dermatology Life Quality Index (DLQI)[9] and work productivity assessed by the Work Productivity and Activity Impairment Scale (WPAI).[10]
  - Prior and ongoing medications for AD: systemic immunosuppressants and corticosteroids, topical corticosteroids and immunomodulators, phototherapy, antibiotics, and antihistamines.
  - Treatment satisfaction using the Treatment Satisfaction Questionnaire for Medication (TSQM-II).[11]

Statistical analysis

- Chi-square tests and *t*-tests were used for bivariate comparisons of demographics and outcome measures based on the distribution of the measure. Spearman's rank-order correlation analyses were conducted to examine the relationship between number of flares and select patient-reported outcome measures.
  - Unless otherwise specified, tests of significance were two-tailed and carried out at the 5% level of significance.

RESULTS

Demographics, AD history and medication use

- From 6000 potential study participants, 5199 patients were excluded and 801 (13.4%) were included in the analysis.
  - Mean age of patients was 45.2 years; 71.8% were female; 83.7% were Caucasian (**Table 1**).
- Many patients (66.3%) reported that they were diagnosed with AD after the age of 20.
  - Per the self-completed Rajka and Langeland criteria, 73.7% of patients had moderate AD and 26.3% had severe AD.
  - In the 12 months prior to baseline, 38.3% of patients reported no remission, 35.8% reported <3 months of remission, and 25.8% reported 3 or more months of remission (Table 1).

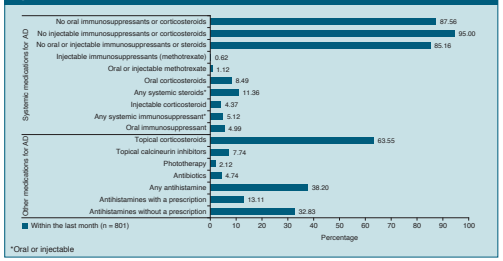
Table 1. Baseline demographic characteristics and AD diagnosis and severity.

Characteristics		Total (N = 801)	
Age (years), mean (SD)		45.21 (13.84)	
		n	%
Age group			
	18–44	363	45.32
	45–64	396	49.44
	65+	42	5.24
Gender			
	Male	226	28.21
	Female	575	71.79
Geographic region			
	Northeast	72	8.99
	Midwest	185	23.10
	South	402	50.19
	West	142	17.73
Hispanic			
	Yes	67	8.48
	No	723	91.52
Race*			
	White or Caucasian	665	83.65
	Black or African American	66	8.30
	American Indian or Alaska Native	15	1.89
	Asian or Pacific Islander	41	5.16
	Other	31	3.90
	Missing	6	–
Employed†			
	Yes	631	78.78
	No	170	21.22
Age at AD diagnosis			
	Under 5 years	99	12.41
	5–10 years	59	7.39
	11–20 years	111	13.91
	21 years or older	529	66.29
	Missing	3	–
AD severity categories (Rajka and Langeland grading system)			
	Moderate (4.5–7.5)	590	73.66
	Severe (8–9)	211	26.34
AD severity score (Rajka and Langeland grading system), mean (SD)		6.67 (1.21)	
Total time patients experienced remission from AD			
	No remission during last 12 months	307	38.33
	<3 months of remission during the last 12 months	287	35.83
	3 or more months of remission during the last 12 months	207	25.84

SD, standard deviation. *Respondent could select more than one response; †Employment status (working for pay) was derived from the first question in the WPAI

- Medication used within the last month included: topical corticosteroids, 63.6%; topical calcineurin inhibitors, 7.7%; oral corticosteroids, 8.5%; and oral immunosuppressants, 5.0% (**Figure 1**).

Figure 1. Baseline AD medication used within the last month.



Patient reported flares, POEM, and pruritus NRS

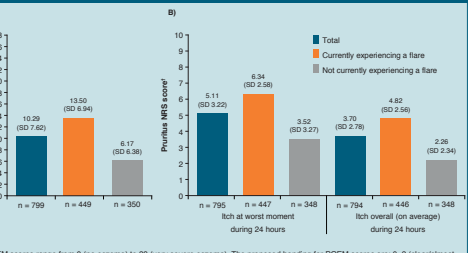
- A total of 56.2% patients were currently experiencing a flare, and 38.3% experienced more than two flares over the past month.
  - Of those experiencing at least one flare over the last month, 65.1% and 21.9% had partial or no recovery of their most recent flares (**Table 2**).

Table 2. Baseline AD flares.

AD flares	Total (N = 801)	
	n	%
Are you currently experiencing a flare of your AD?		
Yes	449	56.20
No	350	43.80
Missing	2	–
Over the past month, how many flares have you experienced?		
0	149	18.70
1	186	23.34
2	157	19.70
>2	305	38.27
Missing	4	–
Over the past month, on average, approximately how long did each flare(s) last?		
<1 week	145	22.34
1 week to <2 weeks	205	31.59
2 weeks to <3 weeks	117	18.03
3 or more weeks	182	28.04
Have you recovered from your most recent flare?		
I have completely recovered	84	12.96
I have partially recovered	422	65.12
I have not recovered at all	142	21.91
Over the past month, how often did you worry about having a flare of your AD		
Always	170	21.30
Often	188	23.56
Sometimes	237	29.70
Rarely	136	17.04
Never	67	8.40
Missing	3	–
Over the past month, on average, how worried were you about your next flare?		
Extremely worried	74	9.28
Very worried	115	14.43
Somewhat worried	283	35.51
Not very worried	228	28.61
Not at all worried	97	12.17
Missing	4	–

- Mean POEM score over the last week was 10.3 (POEM scores range from 0–28, with higher scores indicating more severe eczema), with 57.6% reporting moderate to very severe symptoms based on POEM scores of 8 or greater. 23.3% of patients reported sleep disturbance for at least 3 days out of 7 days. The mean pruritus NRS score for the worst itch during the previous 24 hours was 5.1 (pruritus NRS scores range from 0 (no itch) to 10 (worst itch imaginable).
- At baseline, the number of flares correlated with the POEM categories and POEM sleep disruption days, pruritus NRS itch at worst moment, and pruritus NRS overall itch (correlation coefficient 0.5172, 0.4061, 0.4250 and 0.4694, respectively; all $P < 0.001$).
- Mean POEM and pruritus NRS scores for worst itch and itch overall were significantly higher in those experiencing a flare versus those not experiencing a flare (all $P < 0.001$) (Figure 2). Among those experiencing a flare, 33.2% of patients reported sleep disturbance for at least 3 out of 7 days.

Figure 2. Baseline AD patient-reported outcomes by current AD flare status: A) POEM score; B) Pruritus NRS score.



*POEM scores range from 0 (no eczema) to 28 (very severe eczema). The proposed banding for POEM scores are: 0–2 (clear/almost clear); 3–7 (mild); 8–16 (moderate); 17–24 (severe); 25–28 (very severe).[7]
†Pruritus NRS scores range from 0 (no itch) to 10 (worst itch imaginable). The proposed banding for NRS scores are: <3 (mild itch); >6.9 (severe itch); >9.0 (very severe itch).[8]

DLQI, TSQM and WPAI

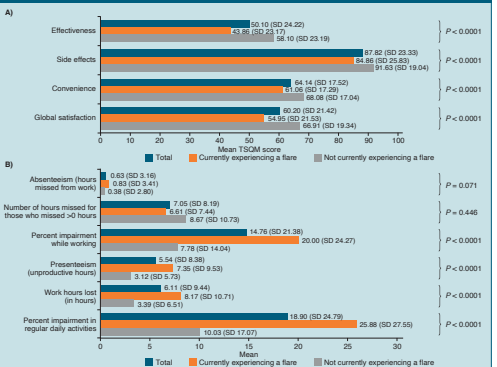
- Twenty-two percent of patients reported that AD had a very or extremely large effect on quality of life (QoL), while the TSQM score for global satisfaction was 60.2 (TSQM scores range from 0–100, with higher scores representing better satisfaction). Among working patients (78.8%), work productivity loss in the past 7 days was 6.1 hours (Table 3).
- Outcomes were worse for patients experiencing flares compared with those not experiencing flares according to DLQI (8.60 vs 3.67, respectively; $P < 0.001$), all four TSQM domains and WPAI, except for hours missed from work for all patients and patients who missed work (**Figure 3**).

Table 3. Baseline AD patient-reported outcomes.

		Total (N = 801)	
		n	Mean (SD)
DLQI score*		789	6.44 (6.28)
		n	%
DLQI categories	No effect on QoL	180	22.81
	Small effect on QoL	263	33.33
	Moderate effect on QoL	176	22.31
	Very large effect on QoL	131	16.60
	Extremely large effect on QoL	39	4.94
	Missing	12	–
		n	Mean (SD)
TSQM score†	Effectiveness	800	50.08 (24.20)
	Side effects	799	87.85 (23.31)
	Convenience	796	64.09 (17.53)
	Global satisfaction	797	60.17 (21.47)
WPAI score‡	Absenteeism (hours missed from work in the past 7 days due to AD)	625	0.63 (3.16)
	Number of hours missed for those who missed >0 hours (due to AD)	56	7.05 (8.19)
	Percent impairment while working in the past 7 days due to AD	559	14.74 (21.35)
	Presenteeism (unproductive hours in the past 7 days due to AD)	559	5.53 (8.37)
	Work productivity loss (in hours) in past 7 days (absenteeism + presenteeism) due to AD	558	6.11 (9.43)
	Percent impairment in regular daily activities in the past 7 days due to AD	792	18.88 (24.76)
		n	%
	Work time missed due to AD	564	2.11

*DLQI scores range from 0 (no effect on QoL) to 30 (extremely large effect on QoL). †TSQM scores range from 0–100 where higher scores represent better satisfaction.
‡Higher WPAI scores indicate greater impairment.

Figure 3. Baseline AD patient-reported outcomes by current AD flare status A) Mean TSQM score*; B) Mean WPAI score†.



*TSQM scores range from 0–100 where higher scores represent better satisfaction. †Higher WPAI scores indicate greater impairment and are for over the past 7 days due to AD.

LIMITATIONS

- This study was a patient survey where recall bias was a limitation.
- Additionally, in the current baseline analysis, patients' assessment of outcomes like DLQI were based on the past 7 days and may not capture the comprehensive impact of change to AD, given the fluctuation of the disease.
- Since AD-QUEST was a longitudinal survey, the follow-up survey should provide more comprehensive understanding of the disease burden.

CONCLUSIONS

- Despite standard-of-care treatments, adults with moderate-to-severe AD report high disease burden from disease symptoms, recurrent flares and impaired QoL, suggesting significant unmet therapeutic needs.

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Disclosures

Wenhui Wei is a former employee and current stockholder of Sanofi and an employee of Regeneron Pharmaceuticals, Inc. Eric Ghorayeb and James Schnitzer are employees of and stockholders in Sanofi. Michael Andria, Jingdong Chao, Martha Kennedy and Zhen Chen are employees of and stockholders in Regeneron Pharmaceuticals, Inc. Valery Walker, Angela Belland and John White are employees of Optum, a company that received research funding for the current study. Jonathan Silverberg is a member of an institution that received research funding for the current study.

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