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ORIGINAL RESEARCH

Baseline Characteristics and Treatment Patterns of Patients with Atopic Dermatitis Treated with Oral Systemic Therapies: An Interim Analysis of the AD-REAL Study

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ABSTRACT

Introduction: AD-REAL is an ongoing 1-year multinational observational cohort study evaluating oral systemic therapies in the management of adults with atopic dermatitis (AD) in a real-world practice across four European countries. Herein, we provide insights on baseline disease characteristics and treatment patterns of patients treated with oral systemic therapies, including baricitinib.

Methods: AD-REAL included adults with moderate-to-severe AD for ≥ 6 months, who were initiated on an oral systemic treatment in clinical practice and enrolled either in the baricitinib or the other oral systemic (OOS) cohort. Here, we report baseline characteristics, including clinician-assessed outcomes (Eczema Area and Severity Index [EASI]) and patient-reported outcomes (PROs), and explore AD subgroups based on body surface area (BSA) ≤ 40% and Itch numerical rating scale (NRS) ≥ 7. Continuous outcomes were reported using mean and standard deviation (SD) and categorical variables using frequencies. Baseline continuous variables with missing data were imputed using the multiple imputation method.

Results: Baseline demographics were consistent across both baricitinib and OOS cohorts. Patients showed long disease duration (26.2 years), refractory to several systemic options,

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and a moderate EASI mean (SD) score of 17.5 (10.7). The majority (53.7%) presented with severe Validated Investigator Global Assessment (vIGA) and highly impacted Dermatology Life Quality Index (DLQI) score (14.0 [7.1]). At baseline, patients were predominantly female, with AD mainly affecting face/neck (89.4%) and upper extremities (90.3%). About 68.4% presented with BSA ≤ 40 and 33.8% with BSA ≤ 40 and Itch NRS ≥ 7. From those with BSA ≤ 40% and Itch NRS ≥ 7, 63.9% were treated with Janus kinase inhibitors (JAKi).

Conclusion: This analysis provides key information on baseline disease characteristics of patients treated with oral systemics, including baricitinib. Most patients treated with oral systemics in AD-REAL had long-lasting disease, refractory to systemic therapies, with moderate skin affectation but severe itch and impact on quality of life. AD-REAL is the first study to show many patients in real-world practice who are treated with oral systemics present with BSA ≤ 40 and Itch NRS ≥ 7, and most of these patients were treated with JAKi.

Keywords: Atopic dermatitis; Oral systemic treatments; Severe itch

Key Summary Points

Why carry out the study?

Atopic dermatitis is one of the most prevalent skin diseases and affects 10–25% of children and 7–10% of adults [1, 2]

Itch is the most burdensome and impairing symptom, and chronic itching occurs in 87–100% of patients with AD [3, 4]

What was learned from the study?

AD-REAL is an ongoing 1-year multinational observational cohort study evaluating oral systemic therapies in the management of adults with atopic dermatitis in a real-world practice across four European countries

This interim analysis aims to describe baseline characteristics such as body surface area and itch severity of atopic dermatitis patients treated with oral systemic therapies in real-world clinical practice

INTRODUCTION

Atopic dermatitis (AD) is one of the most prevalent skin diseases and affects 10–25% of children and 7–10% of adults [1, 2]. The signs and symptoms of the disease can have a profound impact on a patient's quality of life (QoL) [5]. Itch is the most burdensome and impairing symptom, and chronic itching occurs in 87–100% of patients with AD [3, 4]. Itch has a strong negative impact on a patient QoL; patients frequently report sleep disturbances, which affect the patient's daytime attention and performance levels at work. In addition, itch can also affect a patient's relationship with others, putting patients with severe itch at a higher risk of developing psychological disorders [4].

Due to the clinical heterogeneity found in patients with AD, diagnosing patients and optimizing treatment courses are difficult. AD treatment is accompanied by a multifaceted stepwise approach that can be customized depending on disease severity [6]. The consensus-based European guidelines for treatment of AD recommends using systemic treatments for patients with Scoring of AD score > 50 and those who feel they are unable to participate in daily life activities while receiving an adequate treatment regimen or have failed to respond to topical therapy [7].

Work carried out by Chovatiya et al. determined that combined itch and lesional severity best described the clinical phenotypes of AD. Phenotypes were characterized by different combinations of mild-to-severe itch and mild-to-severe lesions. It was determined that most patients in the study were in the 'mild-to-moderate' category for both itch and lesions; patients who presented with severe itch and mild-to-moderate lesions (SI-ML) accounted for the second largest subgroup. The authors described this

subgroup as 'itch-dominant' and observed the inconsistency in the identification of the high disease burden between patients and healthcare providers (HCPs) [3].

The recent work by Thyssen et al. showed how baseline disease characteristics can predict patients' response to treatment with baricitinib in different subgroups categorized by body surface area (BSA) and itch severity. This work determined that BSA involvement of ≤ 40% was the strongest baseline disease variable for predicting response to baricitinib 4 mg in both monotherapy (BREEZE-AD1/2) and in combination with TCS (BREEZE-AD7) and that patients with BSA ≤ 40% and Itch numerical rating scale (NRS) ≥ 7 were the subgroup most likely to respond to baricitinib 4 mg [8]. Identifying patient's characteristics associated with treatment response helps HCPs to tailor treatment strategies and to provide the most effective treatment to each individual patient [9]. Clinical tailoring approaches, such as the one proposed by Thyssen et al., are gaining importance with the emergence of new therapies [10], although they are not yet widely adopted in AD management. Conducting randomized controlled trials stratified by subgroups, alongside reconfirmation from observational studies and AD registries, will provide critical data sources for reconfirmation [8].

Before modern targeted systemic agents (such as biologics and Janus kinase inhibitors [JAKi]) became available for the treatment of AD in recent years, cyclosporine was the only oral systemic treatment approved in the EU for the treatment of AD. While cyclosporine is only approved for patients with severe AD, and its long-term use is limited due to side effects, other oral systemic (OOS) treatments that were and are still being prescribed in clinical practice are used off-label, such as methotrexate, mycophenolate mofetil or azathioprine [11]. Overall, data for these therapies from randomized clinical trials (RCTs) and from prospective observational studies are very limited. In contrast, targeted systemic therapies including biologics and JAKis are approved for patients with moderate-to-severe AD who are candidates for systemic therapy and have proven high levels of efficacy with acceptable safety profiles in placebo-controlled clinical trials [12, 13]. However, limited data are available from real-world evidence, which are critical for HCPs to make the most informed decisions when deciding on treatment strategies. The goal of AD-REAL is to provide evidence on using oral systemics in real-world practice. This study includes data on new treatments entering the market and on established therapies where data are limited. The observational study AD-REAL aims to bridge this knowledge gap by elucidating treatment patterns of patients prescribed baricitinib and OOS treatments in real-world practice.

The objective of this interim analysis of AD-REAL from patients enrolled across four European countries (France, Germany, Spain and the UK) is to describe baseline characteristics such as BSA and itch severity of patients with AD treated with oral systemic therapies in real-world clinical practice. This analysis also aims to elucidate the frequency and severity of those with itch-dominant (BSA ≤ 40% and Itch NRS ≥ 7) phenotype.

METHODS

Study Design and Patient Eligibility

AD-REAL is a 12-month prospective, multicenter, international, observational cohort study reflecting treatment within clinical practice settings of patients with AD who initiate an oral systemic treatment. In this study, data collection occurred at baseline, at post-baseline visits at Weeks 4 (± 1 week), 12 (± 2 weeks) and 24 (± 4 weeks) and then at Month 12. This study includes four European countries (France, Germany, Spain and the UK). Eligible participants had to be ≥ 18 years with moderate-to-severe AD for ≥ 6 months who presented during routine medical care. All adult patients who initiated oral systemic treatment for AD based on country-specific regulations were eligible to participate, independent of whether they were systemic treatment-naïve or had previously received oral and/or biologic systemic treatments for AD (systemic experienced).

This interim analysis evaluated baseline data of participants who were initiated on baricitinib and OOS in AD-REAL, including conventional

systemics (azathioprine, azathioprine + prednisone, cyclosporine, cyclosporine + prednisolone, methotrexate, methotrexate + prednisolone, mycophenolate mofetil), systemic corticosteroids (betamethasone, dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone, other systemic corticosteroids), other oral JAKis (abrocitinib and upadacitinib) and other (OOS AD treatments according to country-specific guidelines). Patients were also stratified based on BSA and Itch NRS.

Disease Characteristic Analysis

This analysis investigated physician-assessed clinical measures; Eczema Area Severity Index (EASI), BSA, validated Investigator's Global Assessment (vIGA-AD) and patient-reported outcomes (PROs); Itch NRS, Atopic Dermatitis Sleep Scale (ADSS), Patient Oriented Eczema Measure (POEM) and Dermatology Life Quality Index (DLQI) at baseline.

Statistical Analysis

Continuous outcomes were reported using mean and standard deviation (SD) and categorical variables were reported using frequencies. SAS statistical software was used to prepare the data. Baseline continuous variables with missing data were imputed using the multiple imputation method. This method provided imputed baseline values for those with missing baseline values. The imputed data were used for the analysis of the outcome variables. Missing clinical outcome data at baseline were imputed using the SAS PROC MI procedure. Given the relatively small amount of missing data, the expectation maximization (EM) method was applied for single imputation. For missing data during follow-up visits, multiple imputation was applied using Rubin's method. The process assumed data were missing at random (MAR) and addressed intermittent missingness using SAS PROC MI with a Markov Chain Monte Carlo (MCMC) method to impute missing values, transforming the dataset into a monotone missing pattern. A single value for each outcome of interest was imputed in the monotone dataset.

Ethics

Prior to enrollment, patients provided written informed consent. The study was conducted with the approval of each center's institutional review board or independent ethics committee and in accordance with the guiding principles of the Declaration of Helsinki.

RESULTS

Baseline Demographics

In this interim analysis, 320 patients with moderate-to-severe AD were analyzed. Of these, 88 patients were in the baricitinib treatment cohort and 232 patients in the OOS treatment cohort, which included 53.0% patients ($n = 123$) treated with conventional systemics (of the $n = 123$ patients receiving conventional systemics, 69.9% [$n = 86$] received cyclosporine and 25.2% [$n = 31$] received methotrexate), 39.7% of patients ($n = 92$) treated with other oral JAKis (14.7% of patients [$n = 34$] treated with abrocitinib and 25.0% of patients [$n = 58$] treated with upadacitinib), 5.2% of patients ($n = 12$) treated with systemic corticosteroids and 2.2% of patients ($n = 5$) treated with OOS. The enrollment of patients across the different countries was consistent; 29.7% of patients ($n = 95$) enrolled from the UK, 25.0% of patients ($n = 80$) from Germany, 22.8% of patients ($n = 73$) from France and 22.5% of patients ($n = 72$) from Spain. The average age of the overall study population was 35.2 (SD = 13.6) years with treatment cohorts averages ranging from 30.0 (SD = 10.4) to 38.4 (SD = 15.8) years. However, patients in the baricitinib cohort were slightly older (38.4 years). About 50.9% ($n = 163$) of patients were females, with most female patients (59.1%) being treated with baricitinib. Disease duration was consistent across treatment cohorts, ranging between 25.0 (SD = 11.3) to 28.6 (SD = 11.6) years. For the overall population, 59.7% ($n = 191$) were exposed to systemic treatment at baseline. Of those patients treated with systemic medications, dupilumab and cyclosporine were the

most commonly used (24.7%, *n* = 79 for both). Patients who received baricitinib (*n* = 40, 45.5%), upadacitinib (*n* = 28, 48.3%) and abrocitinib (*n* = 14, 41.2%) reported numerically more failures to prior systemic therapies at baseline (Table 1). There were 185 patients (57.8%) in the overall population who received monotherapy, and 135 patients (42.2%) received concomitant topical steroid use at baseline. As expected, 46.6% (*n* = 149) of the overall population had atopic comorbidities.

Table 1 Baseline demographics for the overall population

	Baricitinib (*n* = 88)	**Other oral systemics (*n* = 232)**					**Overall population (*N* = 320)**
		Conventional systemics (*n* = 123)	**Other oral JAKi**		**Systemic corticosteroids (*n* = 12)**	**Other (*n* = 5)**	
			Abrocitinib (*n* = 34)	**Upadacitinib (*n* = 58)**			
Country, *n* (%)							
France	17 (19.3)	36 (29.3)	7 (20.6)	13 (22.4)	0	0	73 (22.8)
Germany	38 (43.2)	2 (1.6)	21 (61.8)	18 (31.0)	0	1 (20.0)	80 (25.0)
Spain	12 (13.6)	35 (28.5)	5 (14.7)	11 (19.0)	6 (50.0)	3 (60.0)	72 (22.5)
UK	21 (23.9)	50 (40.7)	1 (2.9)	16 (27.6)	6 (50.0)	1 (20.0)	95 (29.7)
Age (years)	38.4 (15.8)	33.9 (12.9)	37.8 (12.6)	32.9 (12.0)	31.0 (8.5)	30.0 (10.4)	35.2 (13.6)
Female, *n* (%)	52 (59.1)	72(58.5)	13 (38.2)	22 (37.9)	2 (16.7)	2 (40.0)	163 (50.9)
Duration since AD diagnosis (years)	26.6 (14.7)	25.9 (14.3)	26.6 (15.3)	26.1 (13.5)	25.0 (11.3)	28.6 (11.6)	26.2 (14.1)
BMI (kg/m^2)	25.7 (5.1)	25.0 (4.9)	26.6 (5.5)	25.4 (4.9)	25.6 (4.6)	25.2 (5.2)	25.5 (5.0)
Failure of previous systemic therapy							
No, *n* (%)	48 (54.5)	108 (87.8)	20 (58.8)	30 (51.7)	9 (75.0)	2 (40.0)	217 (67.8)
Yes, *n* (%)	40 (45.5)	15 (12.2)	14 (41.2)	28 (48.3)	3 (25.0)	3 (60.0)	103 (32.2)
Monotherapy	48 (54.5)	70 (56.9)	23 (67.6)	36 (62.1)	5 (41.7)	3 (60.0)	185 (57.8)
Concomitant use of topical steroids, *n* (%)	40 (45.5)	53 (43.1)	11 (32.4)	22 (37.9)	7 (58.3)	2 (40.0)	135 (42.2)

Data reported as mean (standard deviation) unless otherwise stated

Abbreviations: *AD* atopic dermatitis, *BMI* body mass index

Baseline Disease Characteristics

Mean BSA at baseline for the overall study population was 36.1 (SD = 24.4), with 219 (68.4%) of patients reporting BSA ≤ 40%. Mean BSA was 27.9 (SD = 19.7) for patients treated with baricitinib, 43.3 (SD = 25.3) for patients treated with conventional systemics, 34.7 (SD = 23.1) for patients treated with abrocitinib, 34.5 (SD = 25.8) for patients treated with upadacitinib, 35.9 (SD = 31.3) for patients treated with systemic corticosteroids and 33.3 (SD = 25.9) for patients treated with OOS (Table 2). For the overall study population, specific body region involvement was most prevalent in the

Table 2 Baseline disease characteristics for the overall population

	Baricitinib (*n* = 88)	Other oral systemics (*n* = 232)					Overall population (*N* = 320)
		Conventional systemics (*n* = 123)	Other oral JAKi		Systemic corticosteroids (*n* = 12)	Other (*n* = 5)	
			Abrocitinib (*n* = 34)	Upadacitinib (*n* = 58)			
BSA	27.9 (19.7)	43.3 (25.3)	34.7 (23.1)	34.5 (25.8)	35.9 (25.9)	33.3 (31.3)	36.1 (24.5)
EASI	16.9 (11.7)	20.2 (12.7)	15.0 (7.6)	17.9 (11.3)	17.9 (15.3)	15.0 (9.4)	18.2 (11.8)
Itch NRS	5.9 (2.2)	6.9 (5.6)	7.4 (1.9)	6.0 (2.5)	6.8 (2.8)	6.6 (0.9	6.5 (3.9)
ADSS Item 2	1.9 (1.9)	2.6 (3.3)	2.3 (2.6)	2.8 (2.8)	4.8 (8.4)	0.5 (0.9	2.4 (3.2)
POEM	13.7 (7.0	19.1 (10.3)	17.5 (7.4)	18.6 (7.5)	22.3 (4.6)	16.3 (3.5)	17.5 (8.8)
DLQI	15.0 (6.7)	14.1 (7.3)	12.5 (6.2)	12.8 (7.4)	18.0 (5.6)	7.8 (6.3)	14.0 (7.1)
vIGA, *n* (%)	*n* = 86	*n* = 116	*n* = 33	*n* = 55	*n* = 12	*n* = 5	*n* = 307
3	48 (55.8)	59 (50.9)	20 (60.6)	30 (54.5)	7 (58.3)	1 (20.0)	165 (53.7)
4	20 (23.3)	46 (39.7)	9 (27.3)	17 (30.9)	4 (33.3)	3 (60.0)	99 (32.2)
Specific body region involvement, *n* (%)							
Hands	52 (59.1)	89 (72.4)	25 (73.5)	41 (70.7)	9 (75.0)	3(60.0)	219 (68.4)
Feet	29 (33.0)	59 (48.0)	14 (41.2)	29 (50.0)	7 (58.3)	2 (40.0)	140 (43.8)
Face/neck	82 (93.2)	109 (88.6)	29 (85.3)	50 (86.2)	11 (91.7)	5 (100.0)	286 (89.4)
Scalp	41 (46.6)	57 (46.3)	21 (61.8)	33 (56.9)	8 (66.7)	2 (40.0)	162 (50.6)
Genitals	15 (17.0)	26 (21.1)	10 (29.4)	15 (25.9)	3 (25.0)	1 (20.0)	70 (21.9)
Trunk	66 (75.0)	112 (91.1)	27 (79.4)	48 (82.8)	11 (91.7)	3 (60.0)	267 (83.4)
Upper extremities	73 (83.0)	118 (95.9)	28 (82.4)	54 (93.1)	12 (100.0)	4 (80.0)	289 (90.3)
Lower extremities	67 (76.1)	110 (89.4)	27 (79.4)	52 (89.7)	11 (91.7)	5 (100.0)	272 (85.0)

Data reported as mean (standard deviation) unless otherwise stated

Abbreviations: *BSA* body surface area, *EASI* Eczema Area and Severity Index, *NRS* numerical rating scale, *ADSS* Atopic Dermatitis Sleep Scale, *POEM* Patient Oriented Eczema Measure, *DLQI* Dermatology Life Quality Index, *vIGA-AD* validated Investigator Global Assessment

upper extremities ($n = 289$, 90.3%) and in the face and neck ($n = 286$, 89.4%), with patients in the baricitinib cohort reporting the highest percentage of face/neck involvement ($n = 82$, 93.2%). Mean EASI at baseline for the overall study population was 18.2 (SD = 11.8). Mean EASI was 16.9 (SD = 11.7) for patients treated with baricitinib, 20.2 (SD = 12.7) for patients treated with conventional systemics, 15.0 (SD = 7.6) for patients treated with abrocitinib, 17.9 (SD = 11.3) for patients treated with upadacitinib, 17.9 (SD = 15.3) for patients treated with systemic corticosteroids and 15.0 (SD = 9.4) for patients treated with OOS. However, the EASI scores reported were within the moderate range for all cohorts. The overall proportion of patients with vIGA-AD 4 (severe) was 32.2% ($n = 99$); these patients also reported a mean POEM score of 17.5 (SD = 8.8), which was in the severe range as well. Mean Itch NRS at baseline for the overall study population was 6.5 (SD = 3.9); the Itch NRS scores for all treatments ranged from 5.9 (SD = 2.2) to 7.4 (SD = 1.9).

Baseline Demographics and Disease Characteristics for BSA and Itch Subgroups

The 320 participants enrolled in the study were stratified into subgroups by BSA (≤ 40% and > 40%) and Itch NRS (< 7 and ≥ 7) at baseline. A total of 108 patients were in the BSA ≤ 40%/Itch NRS ≥ 7 subgroup, 111 in the BSA ≤ 40%/Itch NRS < 7, 57 in the BSA > 40%/Itch NRS ≥ 7 and 44 in the BSA > 40%/Itch NRS < 7 subgroup. At baseline, the average age for the subgroups ranged between 33.1 (SD = 12.5) and 40.5 (SD = 16.7) years. Disease duration was consistent across the subgroups ranging from 24.9 (SD = 12.4) and 29.7 (SD = 17.1). Patients with BSA ≤ 40% were more systemic experienced than patients with BSA > 40% at baseline. Across all subgroups, the most common AD treatments reported prior to baseline were cyclosporine and dupilumab ($n = 79$, 24.7% for both). Patients in the BSA ≤ 40%/Itch NRS ≥ 7 subgroup reported a numerically higher number of failures to previous systemics (Supplemental Table 1). Despite patients with BSA ≤ 40%/Itch NRS ≥ 7 who had mean BSA and EASI scores of 22.9 and 15.0, respectively, which fell within the moderate range, they reported high DLQI (15.1) and POEM (17.6) scores, indicating high disease burden which may be associated with the severe itch (mean NRS 8.2) they experienced (Supplemental Table 2). Patients in the BSA ≤ 40%/Itch NRS ≥ 7 subgroup mostly reported upper extremities ($n = 99$, 91.7%) and face/neck ($n = 96$, 88.9%) as the specific body regions affected with AD. The disease involvement experienced by these patients is reflected in the vIGA-AD scores reported; most patients within the BSA ≤ 40% and Itch NRS ≥ 7 reported scores of 3 ($n = 61$, 58.7%) and 4 ($n = 29$, 27.9%), which were in the moderate-to-severe range. Patients with BSA ≤ 40% were the predominant group, and the subgroup BSA ≤ 40%/Itch NRS ≥ 7 was mostly treated with JAKis (63.9% of patients). From the patients treated with abrocitinib, baricitinib and upadacitinib, 50.0%, 38.6% and 31.0% had BSA ≤ 40%/Itch NRS ≥ 7 at baseline, respectively (Fig. 1).

DISCUSSION

Currently, a vast landscape of therapies is available for the treatment of AD. Therefore, the prediction of treatment efficacy is becoming more important in an effort to understand which patients are most likely to benefit from a specific treatment option [14]. A means of determining which patients are most suited to each therapy can be achieved by establishing the factors that are associated with treatment selection. Due to the limited data available on oral systemic treatments in AD real-world clinical practice, AD-REAL focuses on describing treatment patterns of baricitinib and OOS treatments in real-world practice. AD-REAL is also the first real-world study which highlights the frequency within patients with AD treated with oral systemics and disease burden experienced by patients with itch-dominant AD (BSA ≤ 40%/Itch NRS ≥ 7). In this interim analysis of baseline data from four European countries, we observed that Germany was the only country to reimburse JAKi as first-line systemics

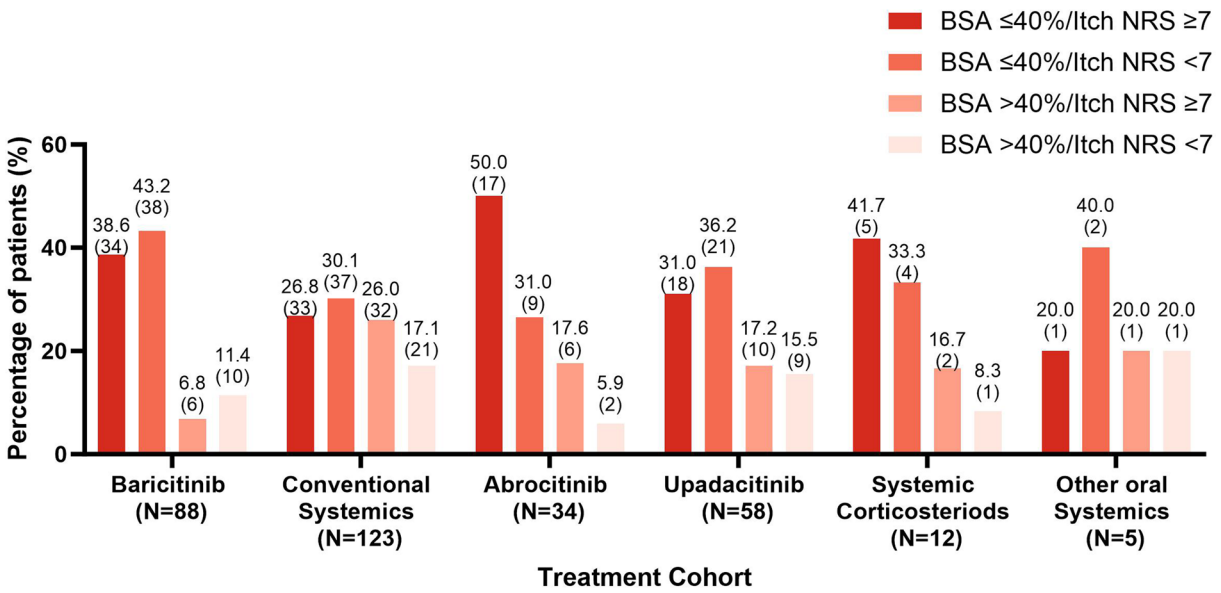

Fig. 1 Atopic disease severity for all treatment cohorts at baseline. Data reported as percentage (number). Conventional systemics included azathioprine, azathioprine + prednisone, cyclosporine, cyclosporine + prednisolone, methotrexate, methotrexate + prednisolone, mycophenolate mofetil; systemic corticosteroids included betamethasone, dexamethasone, methylprednisolone, prednisolone, prednisone, triamcinolone, other systemic corticosteroids; other oral JAKis included abrocitinib and upadacitinib; other included OOS AD treatments according to country-specific guidelines

[15]. Consequently, a numerically higher number of patients enrolled in Germany received JAKis, whereas conventional systemics were more frequently used in the other countries. AD-REAL found that most patients treated with oral systemic therapies previously had received other systemic treatments, which might be reflective of reimbursement requirements and their impact on AD management. The baseline demographics were relatively consistent across treatment cohorts. Baricitinib patients tended to be slightly older with refractory disease to previous systemics, and their disease presented in the upper moderate range based on EASI. Their vIGA-AD showed that most (77.3%) had a vIGA-AD 3–4, and BSA indicated that around a third of their body surface was affected by AD, predominantly in the head/neck area. This indicates that while these patients might not have extensive disease, they have significant inflammatory activity and involvement of visible areas, which are known to negatively impact the patients' lives. This was reflected by high DLQI scores, and POEM scores in the severe range also showed high symptom burden in these patients. We also found that the proportion of patients reporting BSA ≤ 40% (68.4%) was contrary to the findings from previous RCTs [16, 17]. The results from this study are in line with the limited previous real-world evidence reporting mean BSA [8]. In terms of AD severity and treatment selection, most patients with BSA ≤ 40% and Itch NRS ≥ 7 received JAKis mainly as abrocitinib, baricitinib and updacitinib for treatment of women and those with head/neck affectation, while patients with higher BSA and EASI scores mostly initiated conventional systemics at baseline. This study indicates that current treatments, including biologics, are not effective for all patients, highlighting a significant unmet need for effective management of AD, despite moderate skin affectation. Therefore, it is crucial to have a variety of treatment options available that can be tailored to individual patients. The limitations of this study are that it is an interim analysis, the small sample size

of patients and missing data for some of these patients.

CONCLUSION

This interim analysis from the AD-REAL study provides key information on baseline and disease characteristics of patients treated with oral systemic therapies, including baricitinib, in real-world clinical practice across four European countries. This analysis is also the first to describe patients with BSA ≤ 40% and Itch NRS ≥ 7 treated with oral systemic therapies in real-world clinical practice. Most of the patients in the BSA ≤ 40% and Itch NRS ≥ 7 subgroup received abrocitinib, baricitinib and upacitinib at baseline.

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Data Availability. Eli Lilly and Company provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available on request 6 months after the indication studied has been approved in the US and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

Declarations

Conflict of Interest. Matthias Augustin served as a consultant or paid speaker for clinical trials sponsored by companies that manufacture drugs used for the treatment of alopecia areata including AbbVie, Almirall, Eli Lilly and Company, and Pfizer and received support for attending meetings/travel from Eli Lilly and Company. Anthony Bewley reports royalties from Practical Pyschodermatology (Wiley 2014); ad hoc consulting fees from AbbVie, Almirall, BMS, Eli Lilly and Company, Galderma, Incyte, Leo-Pharma, Janssen, Novartis, Pfizer, Sanofi, UCB; ad hoc lecturing fees from AbbVie, Almirall, BMS, Eli Lilly and Company, Galderma, Incyte, Leo-Pharma, Janssen, Novartis, Pfizer, Sanofi, UCB; support for attending meetings/travel from Novartis, Galderma, UCB, Janssen, Sanofi and other financial or non-financial interests including Immediate Past President of ESDaP, Medical Advisory

Board for National Eczema Society, Ichthyosis Support Group and Psoriasis Association. Julien Seneschal reports personal consulting fees from AbbVie, Almirall, Leo-Pharma, Eli Lilly and Company, Pfizer, La Roche Posay; honoraria from AbbVie, Almirall, Leo-Pharma, Eli Lilly and Company, Pfizer. Esther Seera-Baldrich reports payment/honoraria from Amgen, Leo-Pharma, Sanofi, Eli Lilly and Company, Pfizer, Novartis, AbbVie, Incyte, Almirall and Galderma; support for attending meetings/travel from Eli Lilly and Company, Sanofi, Pfizer, Novartis and Leo-Pharma. Andrew Pinter reports payment/honoraria from Eli Lilly and Company; support for attending meetings and/or travel from Eli Lilly and Company and participation on Data Safety Monitoring/Advisory Boards from Eli Lilly and Company. Susanne Grond, Anastasia Lampropoulou, Mohamed Elrayes, Samuel Ogwu and Inmaculada De La Torre are employees and minor shareholders of Eli Lilly and Company.

Ethics. Protocols for all studies included in this analysis were approved by the Institutional Review Board or Ethics Committee at each participating site. All studies included in this analysis were conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all eligible participants before undergoing study-related procedures.

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