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Real-world effectiveness and safety of lebrikizumab in adults with moderate-to-severe atopic dermatitis: a retrospective observational study with focus on head and neck involvement

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Conflict of interest: Marco Galluzzo and Marina Talamonti declare to have acted as speakers and/or consultants for AbbVie, Almirall, Eli-Lilly, Johnson & Johnson, LeoPharma, Novartis and Sanofi, outside the submitted work; Luca Bianchi declares to have acted as a speaker and/or consultant for AbbVie, Almirall, Eli-Lilly, Johnson & Johnson, LeoPharma, Novartis, Pfizer, Sanofi and UCB outside the submitted work. The other authors declare no conflict of interest.

Ethics approval and consent to participate: the study was conducted in accordance with the ethical principles outlined in the 1975 Declaration of Helsinki and its subsequent amendments. In line with Italian regulations, no formal ethical committee approval was required for this type of retrospective observational study. All patients provided written informed consent to participate.

Availability of data and materials: the data that support the findings of this study are available on request from the corresponding author.

Abstract

Lebrikizumab, an anti-interleukin (IL)-13 monoclonal antibody, is a promising treatment for moderate-to-severe atopic dermatitis (AD). We conducted a single-center, retrospective study in 21 adults with moderate-to-severe AD who were biologic-naïve and had failed or were intolerant to conventional systemic therapies. Patients received lebrikizumab 500 mg at weeks 0 and 2, then 250 mg every 2 weeks; those achieving complete remission at week 16 transitioned to monthly dosing. Assessments at baseline, weeks 6, 16, and 24 showed significant improvement in Eczema Area and Severity Index (EASI), pruritus and sleep Numeric Rating Scale (NRS), and Dermatology Life Quality Index (DLQI) scores (all $p<0.001$). At week 16, 77.7% achieved EASI-75 and 27.7% reached EASI-90. Three patients transitioned to monthly dosing after remission. Only two mild cases of keratoconjunctivitis were reported, with no treatment interruptions. These findings support lebrikizumab as an effective, well-tolerated option for biologic-naïve patients with moderate-to-severe AD, including those with challenging head and neck involvement.

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder characterized by eczematous lesions, intense pruritus, and substantial impairment in quality of life. While it primarily affects children, a significant proportion of cases persist into or manifest during adulthood.[1] The disease is driven by a combination of epidermal barrier dysfunction and immune dysregulation, particularly involving Th2 cytokines such as interleukin (IL)-4 and IL-13.[2] The head and neck region is frequently affected in adults with AD, representing a therapeutic challenge due to its visibility, sensitivity, and tendency for treatment resistance.[3] Among the latest therapeutic innovations, lebrikizumab – a monoclonal antibody targeting IL-13 – has emerged as an effective treatment option for moderate-to-severe AD. By blocking the IL-13Rα1/IL-4Rα receptor complex formation, lebrikizumab interrupts IL-13-mediated signaling and helps restore skin barrier function, reduce inflammation, and alleviate pruritus.[4] Phase 3 clinical trials (ADvocate 1 and 2, ADhere, and ADore) have demonstrated its significant efficacy and safety, including improvements in Eczema Area and Severity Index (EASI) and Investigator's Global Assessment (IGA) scores, as well as itch and sleep quality, even in difficult-to-treat areas such as the head and neck.[5-7] However, randomized controlled trials do not always reflect the complexity of real-life clinical scenarios. To address this gap, we conducted a single-center, retrospective study focused on adult patients with moderate-to-severe AD to provide real-world evidence on the effectiveness and tolerability of lebrikizumab in clinical practice.

Materials and Methods

We conducted a single-center, retrospective observational study involving adult patients with moderate-to-severe AD, defined as having a baseline EASI score greater than 24. All patients included in the study had previously experienced therapeutic failure or had contraindications to conventional systemic treatments. At baseline, routine laboratory tests were performed, including complete blood count, liver and kidney function panels, and total serum IgE levels. During the treatment course, all adverse events and any treatment discontinuations were accurately recorded. Clinical assessments were carried out at four time points: baseline, week 6, week 16, and week 24. The following parameters were evaluated at each visit: overall EASI score, EASI specific to the head and neck region, Dermatology Life Quality Index (DLQI), Numeric Rating Scale (NRS) for pruritus, and NRS for sleep disturbance. Continuous variables are expressed as mean ± standard deviation, while categorical variables are presented as absolute numbers and percentages. Data reported at each time point correspond to the mean of the patients evaluated at that specific visit. Longitudinal changes in EASI, NRS pruritus, NRS sleep disturbance, and DLQI scores were analyzed, and statistical comparisons with baseline values were performed using the Wilcoxon signed-rank test for paired samples. A p-value of less than 0.05 was considered statistically significant. Additionally, the proportion of patients with a peak pruritus NRS (PP-NRS) score equal to or greater than 4 was assessed at each observation point. All patients received lebrikizumab according to the recommended dosing regimen: an initial dose of 500 mg (two 250 mg injections) at week 0 and week 2, followed by 250 mg every 2 weeks until week 16 or later, when adequate clinical response was achieved. Maintenance dosing was 250 mg every 4 weeks in accordance with the product label. The study was conducted in accordance with the ethical principles outlined in the 1975 Declaration of Helsinki and its subsequent amendments. In line with Italian regulations, no formal ethical committee approval was required for this type of retrospective observational study. The analysis was conducted on an “as-treated” basis. Since patients initiated therapy at different time points, the data represent a real-world cross-sectional snapshot of patients treated up to January 2026.

Results

A total of 21 adult patients with moderate-to-severe AD were enrolled in the study. All patients received lebrikizumab at a dosing interval of every two weeks according to the recommended schedule. The baseline characteristics are summarized in Table 1. Clinical assessments were conducted at baseline (n=21), week 6 (n=19), week 16 (n=18), and week 24 (n=13). Longitudinal evaluations revealed significant improvements in all measured parameters. The mean EASI score decreased from

22.3±8.2 at baseline to 7.4±6.3 at week 6, 4.2±4.2 at week 16, and 5.3±3.6 at week 24 ($p<0.0001$ at weeks 6 and 16, $p=0.001$ at week 24). The head and neck EASI followed a similar trend, declining from 5.9±1.1 at baseline to 2.9±1.8, 1.7±1.4, and 2.6±1.7 at weeks 6, 16, and 24 respectively ($p<0.0001$ at weeks 6 and 16, $p=0.001$ at week 24). Pruritus NRS scores improved significantly from 8.4±2.5 at baseline to 2.8±1.8 at week 6, 1.7±1.9 at week 16, and 2.7±2.4 at week 24 (all $p<0.001$). Sleep disturbance NRS scores decreased from 5.1±3.3 at baseline to 0.2±1.9 at week 6, 1.1±2.1 at week 16, and 0.2±0.8 at week 24 (all $p<0.001$). The DLQI score improved markedly from 16.8±7.5 at baseline to 1.8±3.4 at week 6, 0.9±2.4 at week 16, and 1.2±3.1 at week 24 (all $p<0.001$). The proportion of patients achieving EASI-50, EASI-75, and EASI-90 responses increased progressively. At week 6, 84.2% achieved EASI-50, 36.8% achieved EASI-75, and 15.7% achieved EASI-90. At week 16, 100% of patients achieved EASI-50, 77.7% achieved EASI-75, and 27.7% achieved EASI-90. By week 24, 100% maintained EASI-50, with 61.5% reaching EASI-75 and 23.1% EASI-90 (Figure 1). Considering only the head and neck area, EASI-50 responses were achieved by 63.1% at week 6, 82.3% at week 16, and 76.9% at week 24. EASI-75 and EASI-90 responses were 21.0%, 44.4%, and 46.1%, and 5.2%, 22.2%, and 23.1%, respectively (Figure 2). Among patients with a baseline PP-NRS≥4, 73.6% achieved a ≥4-point reduction by week 6, 76.4% by week 16, and 69.2% by week 24. At week 16, three patients who had achieved complete remission transitioned to a monthly dosing schedule (250 mg every 4 weeks), in accordance with the product label. Regarding safety, two cases of keratoconjunctivitis were reported during the treatment course. Both were managed with topical therapy prescribed by an ophthalmologist and did not result in treatment discontinuation. One patient discontinued lebrikizumab at week 16 due to primary inefficacy.

Discussion

This single-center, retrospective study provides real-world evidence on the effectiveness and tolerability of lebrikizumab in adults with moderate-to-severe AD, with a particular focus on head and neck involvement – a region often challenging to manage due to its visibility, sensitivity, and treatment resistance. Our results demonstrate significant clinical improvement across multiple domains, including disease severity (EASI), pruritus, sleep quality, and quality of life. At week 16, 77.7% of patients achieved EASI-75 and 27.7% achieved EASI-90. These EASI-75 results are notably higher than those reported in the pivotal trials ADvocate 1 and ADvocate 2,[5] where EASI-75 responses at week 16 were 58.8% and 52.1%, respectively ($p<0.001$ for both), and EASI-90 responses were 38.3% and 30.7%. A possible contributing factor to the higher EASI-75 response rate in our cohort is that most patients were biologic-naïve, which may have resulted in a more favorable response to treatment.

Conversely, the lower EASI-90 response relative to the trials (27.7% *vs.* 38.3%-30.7%) can likely be attributed to the involvement of the head and neck region in all our patients. This area is particularly difficult to treat due to its visibility, sensitivity, and frequent resistance to therapy, which may limit the achievement of complete skin clearance despite substantial overall improvement. Our findings align with other recent real-world studies. In the study by Hagino *et al.*, EASI-50, EASI-75, and EASI-90 response rates at week 16 were 81.8%, 63.5%, and 18.8%, respectively, closely paralleling our own outcomes.[8] Additionally, another real-world study reported EASI-75 and EASI-90 rates of 75.6% and 58.5% at week 24, consistent with those observed in our population,[9] particularly among long-term responders. These observations are further supported by the multicenter study by Avallone *et al.*, which included 78 adults with moderate-to-severe AD, 80.8% of whom had head and neck involvement. At week 16, EASI-75, EASI-90, and EASI-100 responses were 61.5%, 28.2%, and 9.0%, respectively, with significant improvements in EASI head and neck scores.[10] Compared with our cohort, both studies report similar challenges related to head and neck involvement, which likely explains the relatively lower EASI-90 and EASI-100 responses despite high overall efficacy. Notably, our study showed slightly higher EASI-75 rates at week 16 (77.7% *vs.* 61.5%), which may reflect differences in baseline patient characteristics, such as a higher proportion of biologic-naïve patients in our cohort. Conversely, EASI-90 responses were similar (27.7% *vs.* 28.2%), consistent with the difficulty of achieving complete skin clearance in the head and neck region. Lebrikizumab also showed favorable efficacy in the head and neck region, with 76.9% of patients achieving EASI-50 and nearly half of patients reaching EASI-75 at week 24 – an encouraging finding for an area often refractory to treatment. These results echo those from the ADvocate 1 and 2 trials, where improvements across body regions were evident as early as week 16.[11] Pruritus improved rapidly and significantly, with 73.6% of patients achieving a ≥4-point reduction in PP-NRS by week 6, and remained stable through week 24 – highlighting the central role of IL-13 in pruritic pathways and supporting lebrikizumab's mechanism of action. The safety profile was consistent with clinical trials and other real-world data.[12] Only two mild cases of keratoconjunctivitis were reported and managed without treatment discontinuation. One patient discontinued due to primary inefficacy. Limitations of this study include its retrospective design, small sample size, and patient attrition at later time points. Nevertheless, the consistency of our findings with both trial data and real-world studies supports lebrikizumab as an effective and well-tolerated treatment for moderate-to-severe AD.

Conclusions

Our real-world data confirm lebrikizumab as an effective and well-tolerated treatment option for adults with moderate-to-severe AD, including those with significant head and neck involvement. The high EASI-75 response rate, likely related to a predominantly biologic-naïve population, supports its use early in the treatment pathway. Further prospective studies with larger cohorts are needed to validate these findings and inform clinical practice.

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Table 1. Baseline clinical characteristics of AD patients receiving lebrikizumab therapy. Data are presented as mean ± standard deviation for continuous variables and number and percentage for categorical variables.

Clinical characteristics	**Total (N=21)**
General characteristics	
Female/male	15 (71.4)/6 (28.6)
Age (years)	32.1±12.7
BMI (kg/m^2)	22.3±6.4
Age disease onset (years)	8.1±14.8
Atopic comorbidities	
Allergic rhinitis	15 (71.4)
Asthma	4 (19)
Allergic conjunctivitis	11 (52.3)
Previous systemic therapy	
Systemic steroid	14 (66.6)
Cyclosporine	3 (14.2)
Dupilumab	3 (14.2)
JAK inhibitors	3 (14.2)
Predominant phenotype	
Classic/flexural	2 (9.5)
Head and neck eczema	10 (47.6)
Hand eczema	2 (9.5)
Diffuse	7 (33.3)
Disease localization	
Head and neck	21 (100)
Hands	12 (57.1)
Genitalia	2 (9.5)

BMI, body mass index; JAK, Janus kinases.
Predominant phenotype refers to the main clinical pattern of AD observed in each patient. Disease localization indicates all anatomical sites involved at the time of assessment; patients may have involvement limited to specific areas even if their predominant phenotype is diffuse or classic/flexural.

Figure 1. Proportion of patients achieving EASI 50, 75, and 90 responses during treatment with lebrikizumab.

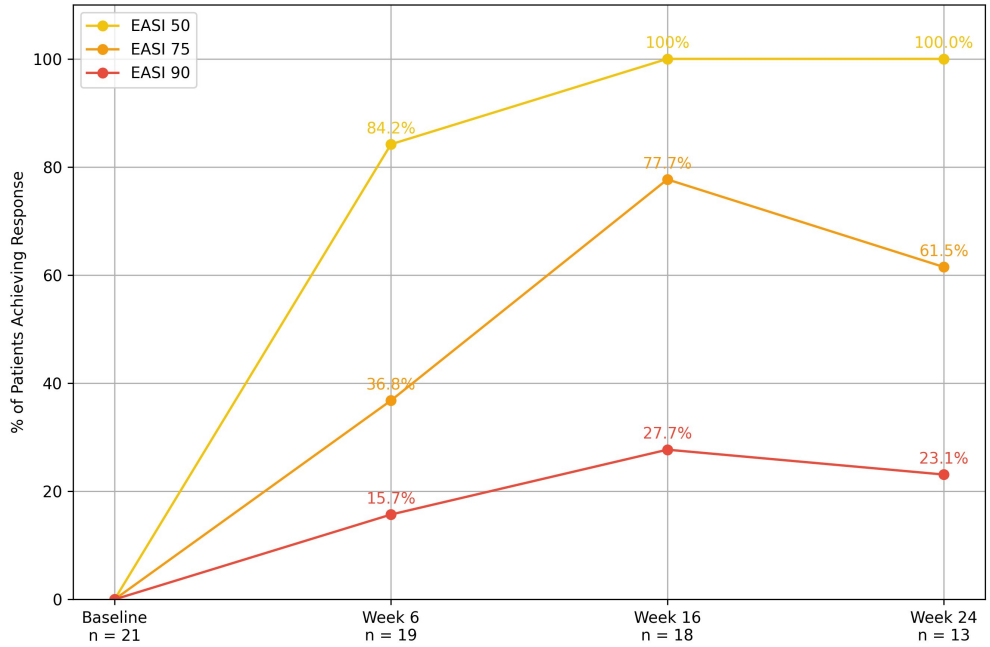

Figure 2. Proportion of patients achieving EASI 50, 75, and 90 responses limited to the head and neck area during treatment with lebrikizumab.