Dermatol Ther (Heidelb)
https://doi.org/10.1007/s13555-026-01726-w

ORIGINAL RESEARCH

Real-World Effectiveness and Safety of Lebrikizumab in Adults and Adolescents with Moderate-to-Severe Atopic Dermatitis: A 52-Week Retrospective Italian Study Focusing on Head and Neck Involvement

Luigi Gargiulo · Luciano Ibba · Matteo Bianco · Sara Di Giulio · Mario Valenti · Gianluca Avallone · Martina Zussino · Paolo Calzari · Angelo Valerio Marzano · Antonio Costanzo · Silvia Mariel Ferrucci · Alessandra Narcisi

Received: December 19, 2025 / Accepted: March 10, 2026

ABSTRACT

***Introduction*:** Lebrikizumab, a monoclonal antibody targeting interleukin (IL)-13, has demonstrated efficacy and safety in phase III trials for moderate-to-severe atopic dermatitis (AD). However, long-term real-world evidence, particularly in European populations and in difficult-to-treat areas such as the head and neck, remains limited. This study evaluated the 52-week real-world effectiveness and safety of lebrikizumab in patients with moderate-to-severe AD.

***Methods*:** This retrospective, two-center study included adults and adolescents treated with lebrikizumab according to the approved label. Clinical assessments were performed at baseline and weeks 16, 24, and 52. Effectiveness outcomes included the Eczema Area and Severity Index (EASI) 75/90/100, absolute EASI thresholds, Investigator's Global Assessment (IGA) 0/1, patient-reported outcomes (Peak Pruritus Numerical Rating Scale [PP-NRS] and Sleep Disturbance Numerical Rating Scale [S-NRS]), and minimal disease activity (MDA) defined as the combined endpoint EASI 90 plus PP-NRS 0/1. Head and neck involvement was specifically analyzed. Safety was assessed by recording adverse events (AEs).

***Results*:** A total of 123 patients were included (116 adults, 7 adolescents). EASI 75 was achieved by 65.0%, 68.9%, and 82.6% of patients at weeks 16, 24, and 52, respectively. EASI 90 increased from 43.9% at week 16 to 69.6% at week 52, while EASI 100 was observed in 56.5% at week 52. IGA 0/1 was achieved by 82.6% of patients at week 52. Clinically meaningful pruritus improvement (ΔPP-NRS ≥ 4) was observed in 65.2% of patients at week 52, and MDA was achieved by 56.6%. Patients with head and neck AD showed comparable clinical responses

Luigi Gargiulo and Luciano Ibba contributed equally to this article and share first authorship.

Silvia Mariel Ferrucci and Alessandra Narcisi contributed equally to this article and share senior authorship.

L. Gargiulo (✉) · L. Ibba · M. Bianco · S. Di Giulio · M. Valenti · A. Costanzo · A. Narcisi
Dermatology Unit, Scientific Institute for Research, Hospitalization and Healthcare (IRCCS) Humanitas Research Hospital, Rozzano, Milan, Italy
e-mail: luigi.gargiulo@humanitas.it

L. Gargiulo · L. Ibba · M. Bianco · S. Di Giulio · M. Valenti · A. Costanzo · A. Narcisi
Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy

G. Avallone · M. Zussino · A. V. Marzano · S. M. Ferrucci
Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Pace, 9, 20122 Milan, Italy

G. Avallone · P. Calzari · A. V. Marzano
Department of Pathophysiology and Transplantation, Università Degli Studi di Milano, Milan, Italy

Published online: 28 March 2026

to those without involvement of this area, with a marked reduction in head and neck EASI (H&N EASI) over time. Overall, 5.7% of patients reported at least one AE, most commonly mild-to-moderate conjunctivitis, with no new safety signals.

Conclusions: In this real-world European cohort, lebrikizumab demonstrated sustained effectiveness and a favorable safety profile over 52 weeks, including in patients with head and neck involvement, supporting its long-term use in routine clinical practice.

Keywords: Anti-IL-13; Atopic dermatitis; Biologics; Lebrikizumab; Real-life

Key Summary Points
Why carry out this study?
Long-term real-world data on lebrikizumab, particularly in European populations and in difficult-to-treat areas such as the head and neck, are currently limited.
Understanding long-term effectiveness, maintenance dosing, and patient-reported outcomes is essential to define the place of lebrikizumab in clinical practice.
What was learned from the study?
Lebrikizumab showed sustained effectiveness and a favorable safety profile over 52 weeks in a real-world setting.
Clinical responses were maintained with maintenance dosing every 4 weeks (Q4W) and were comparable in patients with and without head and neck involvement.

INTRODUCTION

Atopic dermatitis (AD) is among the most prevalent inflammatory skin diseases worldwide [1]. AD can affect infants, children, adolescents, and adults, strongly impairing patients' quality of life because of continuous itch and chronic-relapsing cutaneous lesions [1]. It can also be associated with other diseases, most commonly allergic rhinitis, allergic asthma, conjunctivitis, and food allergy [1]. While mild cases of AD are managed with topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI), moderate-to-severe patients usually require a systemic approach [2]. In particular, according to the most recent version of the EuroGuiDerm guidelines for the management of AD, several drugs are approved for the treatment of severe patients, such as cyclosporin A (CsA), biologic agents (dupilumab, tralokinumab, and lebrikizumab), and Janus kinase (JAK) inhibitors (upadacitinib, baricitinib, and abrocitinib) [2].

Lebrikizumab is the most recently approved biological drug for the treatment of severe AD in both adults and adolescents aged 12 years or older [3]. Lebrikizumab is a humanized monoclonal antibody that selectively targets interleukin (IL) 13, a key driver of Type II inflammation, blocking its ability to form a functional receptor complex with IL-4 receptor alpha (IL-4Rα) and IL-13 receptor alpha 1 (IL-13Rα1). This drug was approved following evaluation in two pivotal phase III clinical trials, Advocate 1 and Advocate 2, which demonstrated superior efficacy in monotherapy compared with placebo [4]. Also, the clinical trial Advantage demonstrated the efficacy of lebrikizumab in combination with TCS compared with placebo plus TCS in adults and adolescents with moderate-to-severe AD who had a contraindication to CsA or a history of inadequate response to CsA [5]. Despite their fundamental role, however, clinical trials often do not completely represent the real-world clinical patient populations, due to their strict inclusion and exclusion criteria. Thus, real-world evidence (RWE) is crucial to further evaluate the role of new drugs, such as lebrikizumab. Long-term real-world data on lebrikizumab are currently very limited, and in particular, most of the studies have focused on Asian populations, with small patient cohorts [6–9].

For these reasons, we conducted a retrospective analysis involving two referral AD centers in Northern Italy, including both adult and adolescent patients treated with lebrikizumab for moderate-to-severe AD to provide more data on its effectiveness and safety in a real-world

setting, with patients followed for 52 weeks of continuous treatment.

METHODS

We enrolled adult and adolescent patients in our retrospective study, all treated with lebrikizumab at the Scientific Institute for Research, Hospitalization and Healthcare (IRCCS) Humanitas Research Hospital, Rozzano (Milan), Italy, or at Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. All patients received lebrikizumab according to the summary of product characteristics (SmPC), with two 250 mg subcutaneous injections at weeks 0 and 2, followed by one 250 mg injection every other week until week 16. Some of these patients were previously evaluated in a multicenter retrospective study until week 16 [8]. After that, patients received one injection every 4 weeks (Q4W), while patients who achieved only partial disease control continued with one injection every 2 weeks (Q2W) until week 24, according to the SmPC of lebrikizumab. The eligibility of patients for the treatment was assessed in compliance with the Italian and European guidelines for atopic eczema [2, 10]. Demographic characteristics are shown in Table 1, and disease features at baseline and at each observation were retrieved from electronic medical records with a retrospective, observational approach. Clinical phenotypes were evaluated according to the clinical criteria described in the literature [11]. Patients that were previously exposed to at least one innovative treatment (biologics, JAK inhibitors) were defined as bio-experienced. Patients were evaluated at weeks 0, 16, 24, and 52, as per our routine clinical practice, between 1 January 2024 and 30 November 2025. For some patients, clinical data at week 8 were also recorded; however, not every patient was assessed at this time point. During the treatment with lebrikizumab, patients were able to apply short courses of TCS and/or TCI when needed. Due to the retrospective nature of the study, not all follow-ups were available for analysis at the moment of the data cut-off.

The effectiveness of lebrikizumab was evaluated at all visits in terms of percentage reduction of Eczema Area and Severity Index (EASI) compared with baseline, in particular as EASI 75, EASI 90, and EASI 100 (improvement of at least 75%, 90%, 100%, respectively). Additional endpoints were the proportion of patients achieving an absolute EASI of 7 or less, an absolute EASI of 3 or less, and IGA 0/1 (with an improvement of at least 2 points compared with baseline). Patients achieving optimal disease control with low residual disease activity and minimal symptoms were generally switched to Q4W dosing, whereas patients with residual clinically relevant signs or symptoms were more frequently maintained on Q2W dosing until week 24. Partial disease control was defined as per routine clinical practice as an incomplete but clinically meaningful improvement in disease severity and symptoms, characterized by failure to achieve optimal treatment targets (such as EASI 90, IGA 0/1, or near-complete symptom control), despite a clear improvement from baseline. The decision to maintain Q2W dosing or switch to Q4W dosing after week 16 was guided by a physician's global judgment, with a multidimensional assessment integrating validated clinical scores, patient-reported outcomes. Given the high involvement of the head/neck district in our population, we also evaluated the mean reduction in Head and Neck EASI (H&N EASI) at all visits. We also compared the effectiveness of lebrikizumab in patients with and without head and neck involvement in terms of EASI 75, EASI 90, and EASI 100. This comparison was conducted up to week 24, due to the small sample size at week 52. We also assessed the impact of lebrikizumab on patients' reported outcomes (PROs), such as Peak Pruritus Numerical Rating Scale (PP-NRS) and Sleep Disturbance Numerical Rating Scale (S-NRS). For both endpoints, we recorded both the percentage of patients achieving a reduction of at least 4 points compared with baseline and the percentage of those reporting PP-NRS and S-NRS of 0/1 at each visit. Finally, the proportion of those achieving a combined response (EASI 90 and PP-NRS 0/1) was evaluated at each visit. Pruritus intensity was assessed using the Peak

Table 1 Demographic and disease characteristics at baseline of our patients

Total patients	**123**
	N (%)
Female	70 (56.9)
Male	53 (43.1)
Adolescent	7 (5.7)
AD phenotype	
Classic	106 (86.2)
Prurigo-nodularis-like	6 (4.9)
Generalized inflammatory	3 (2.4)
Generalized lichenoid	2 (1.6)
Head and neck	2 (1.6)
Nummular eczema	2 (1.6)
Portrait dermatitis	1 (0.8)
Psoriasiform	1 (0.8)
At least one AD sensitive area	107 (87)
Previous exposure to at least one innovative therapy	47 (38.2)
Previous exposure to at least two innovative therapies	17 (13.8)
At least one cardiometabolic comorbidity	18 (14.6)
At least one atopic comorbidity	58 (47.2)
	Mean ± SD
Age, years	38 ± 18
BMI, kg/m^2	22.4 ± 3
Age of onset, years	12.8 ± 18.3
EASI at baseline	18.3 ± 9.4
PP-NRS at baseline	7 ± 2.3
S-NRS at baseline	4.8 ± 3.6

AD, atopic dermatitis; BMI, body mass index; EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale; SD, standard deviation; S-NRS, Sleep Disturbance Numerical Rating Scale

Pruritus Numerical Rating Scale (PP-NRS© 2019 Regeneron Pharmaceuticals, Inc. and SAR&D, used with permission). Sleep disturbance was evaluated using the Sleep Disturbance Numerical Rating Scale (SD-NRS© Galderma Holding SA, used with permission).

The safety was assessed by investigating for adverse events (AEs) at each visit, with special emphasis on severe AEs and AEs leading to discontinuation of the drugs.

Statistical Analyses

Categorical variables were expressed as absolute numbers and percentages, while continuous variables were reported as mean and standard deviation (SD).

For the subgroup analysis comparing patients with and without head involvement, we performed the chi-squared test or Fisher's exact test when appropriate.

Statistical significance was defined as $p < 0.05$.

Statistical analysis was conducted using an "as observed" basis and was performed using STATA/SE 18.0. We used Microsoft Excel and GraphPad Prism 10.2.3. to generate tables and figures, respectively.

Ethical Approval

Ethical approval was granted by an institutional review board (Ethics Approval Committee Lombardia 3, protocol number Lebri-AD-2024). All patients received lebrikizumab, as per standard clinical practice, in accordance with European and Italian guidelines for the management of atopic eczema. For some of the included patients, Almirall provided the drug lebrikizumab through a Compassionate Use Program activated according to the Decreto Ministerial (DM) 7/9/2017. The study was conducted following the principles of the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws, regulations, and guidance regarding patient protection, including patient privacy. All patients provided written informed consent to participate in the study and for publication.

RESULTS

Patient Population

In total, 123 patients were included in our retrospective study, with 116 adults and 7 adolescents. All included patients had completed at least 16 weeks of treatment with lebrikizumab, with 61 patients reaching week 24, and 23 completing 1 year of observation. Of these, 70 (56.9%) were female, and the mean age of our cohort was 38 years old (SD 18). Regarding clinical phenotypes, most of the patients (106) presented classic flexural AD (86.2%), while six (4.9%) were affected by prurigo-nodularis-like AD. At least one sensitive area (including head/neck, hands, or genitalia) was involved in 107 patients (87%). Regarding concomitant diseases, at least one other atopic condition was reported by 58 patients (47.2%), while cardiometabolic comorbidities were previously diagnosed in 18 patients (14.6%). In all, 47 patients were bio-experienced (38.2%) and in 17 patients, multiple treatments had failed (13.8%). The most common previous drug was dupilumab, which had failed in 35 patients, followed by upadacitinib (12). At baseline, mean EASI was 18.3 (SD 9.4), mean PP-NRS was 7 (SD 2.3), and mean S-NRS was 4.8 (SD 3.6). A total of 100 patients had involvement of the head and neck area, and their mean H&N EASI was 2.85 (SD 1.38). Regarding the maintenance phase of the treatment, 98 patients continued with lebrikizumab Q2W until week 24, while 25 patients were switched to lebrikizumab Q4W starting from week 16. This decision was made by each physician individually on the basis of both clinical scores and PROs at week 16. Due to the real-world retrospective nature of the study, no standardized criteria were defined a priori to assess the response. Additional characteristics of our patient population are represented in Table 1.

Effectiveness of Lebrikizumab

An overview of all effectiveness outcomes at weeks 16, 24, and 52 is provided in Fig. 1 and Fig. 2. At week 16, EASI 75 was achieved by 65% of our patients. This proportion was higher at subsequent visits, as 68.9% and 82.6% of patients reached EASI 75 at weeks 24 and 52. Regarding EASI 90, this was obtained by 43.9%, 57.4% and 69.6% of patients at weeks 16, 24, and 52, respectively. We also observed complete skin clearance (EASI 100) in 19.5%, 26.2% and 56.5% of our population at the same time points. In terms of absolute EASI, the optimal target of absolute EASI ≤ 3 was achieved by 57.7%

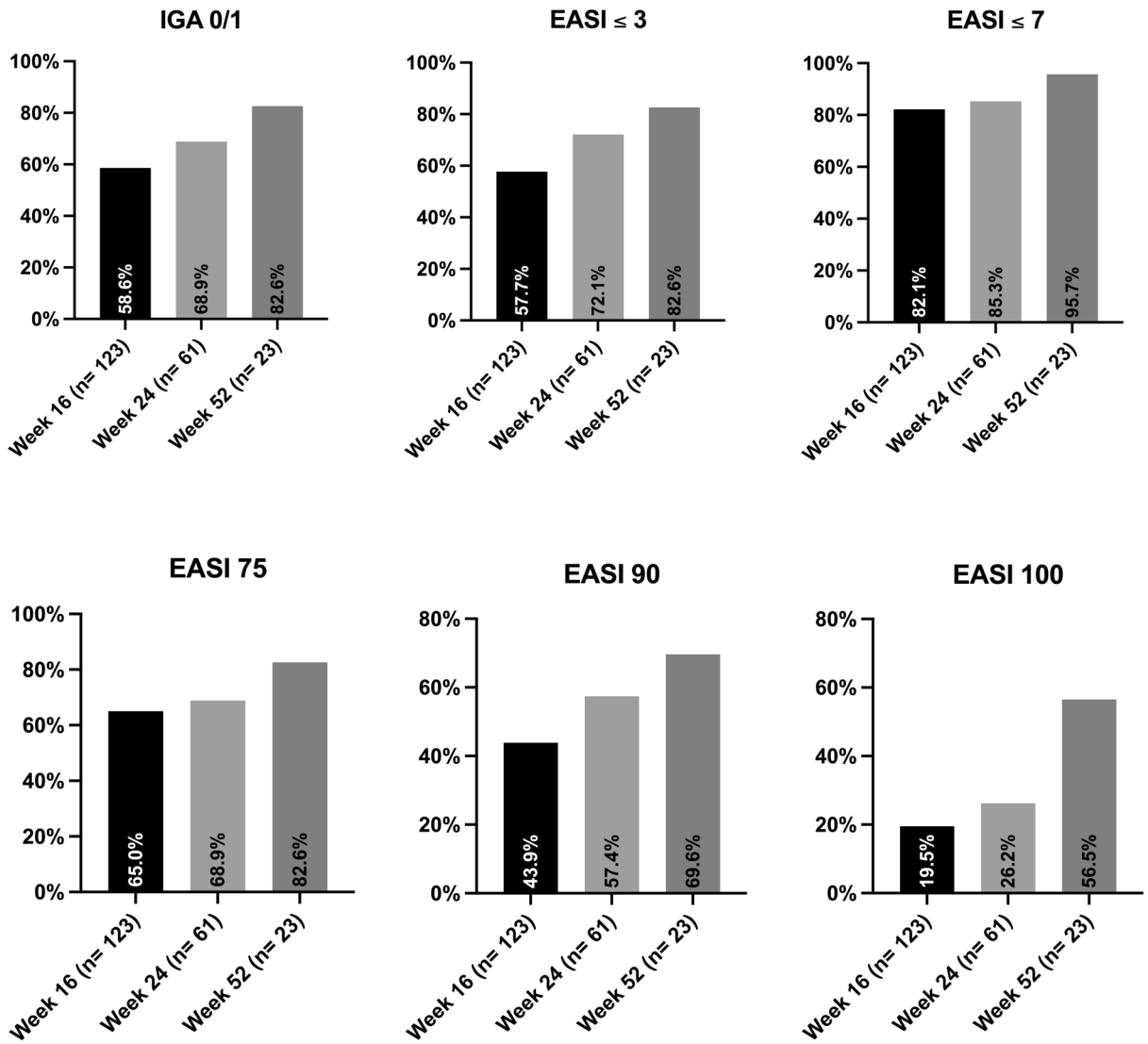


Fig. 1 Effectiveness of lebrikizumab in terms of IGA 0/1, EASI ≤ 3, EASI ≤ 7, EASI 75, EASI 90, and EASI 100 throughout the study period. EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment

of patients at week 16, 72.1% at week 24, and 82.6% at week 52. Also, IGA 0/1 was observed in 58.9%, 68.9%, and 82.6% of patients at each visit. We also observed significant improvement in terms of PROs, as ΔPP-NRS ≥ 4 was reported by 58.8%, 52.5%, and 65.2% of patients at weeks 16, 24, and 52, respectively. The optimal target of PP-NRS 0/1 was reached by 41.5%, 44.3%, and 56.5% of our cohort at the same visits.

An additional endpoint was the achievement of minimal disease activity, defined as concomitant achievement of EASI 90 and PP-NRS 0/1, as defined by Silverberg et al. [12]. Lebrikizumab achieved MDA in 30.1% of patients at week 16, 39.3% at week 24, and 56.6% at week 52 (Fig. 3). Four patients discontinued the treatment before week 52 due to loss of effectiveness.

Impact of Lebrikizumab on Head and Neck AD

Lebrikizumab also showed marked effectiveness in patients with head and neck dermatitis, as mean H&N EASI decreased to 0.75 (SD 0.92) at week 16, to 0.46 (SD 0.66) at week 24, and to 0.35 (SD 0.76) at week 52 (Fig. 4). Comparing patients with and without head and neck involvement, we observed comparable responses in terms of EASI 75 and EASI 90 at both week 16 and 24 (Fig. 5). In particular, 63.3% and 64.7% of those with head and neck dermatitis achieved EASI 75 at weeks 16 and 24, respectively, compared with 73.9% and 90% of the other group at the same time points ($p = 0.322$ and $p = 0.114$, respectively). EASI 90 at week 16 was reached by 40% of those with head and neck AD (versus 60.9%) at week 16 and by 52.9% (versus 80%) at week 24 ($p = 0.069$ and $p = 0.114$). We observed significantly higher rates of EASI 100 at both time points for patients without head and neck AD (34.8% versus 16% at week 16 [$p = 0.04$], and 60% versus 19.6% at week 24 [$p = 0.008$]) (Fig. 5). In terms of itch, the effectiveness of lebrikizumab was comparable between the two groups, as ΔPP-NRS ≥ 4 was achieved by 56% of participants with head and neck involvement at week 16 (compared with 69.6%, [$p = 0.234$]) and by 51% (compared with 60%) at week 24 ($p = 0.602$) (Fig. 5).

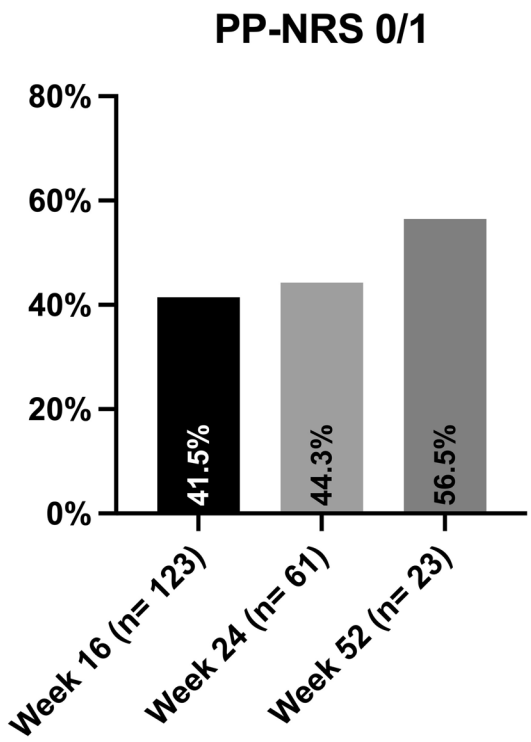
Safety

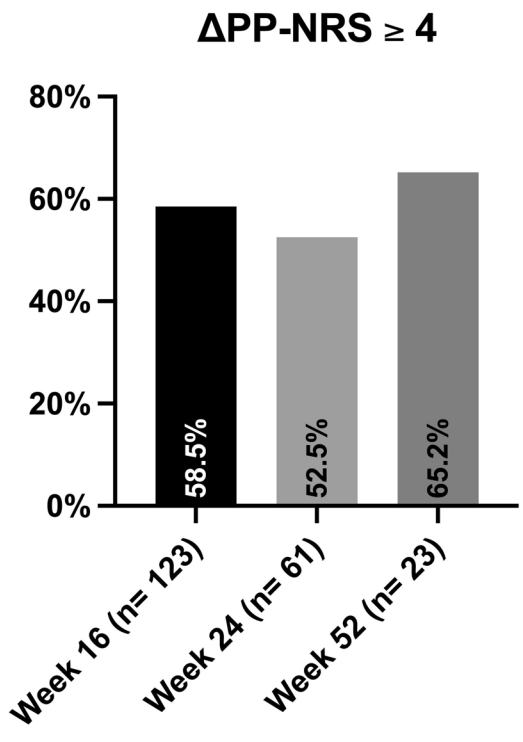
In our 52-week study, we did not observe any new significant safety findings (Table 2). Seven patients reported at least one AE (5.7%). The most common AE was conjunctivitis (five patients, 4.1%). None of our patients discontinued lebrikizumab due to conjunctivitis, as all cases were mild to moderate and were managed with topical treatments. Also, two patients (1.6%) experienced worsening of head and neck AD, which led to treatment discontinuation in both cases (Table 2). No severe AEs were reported.

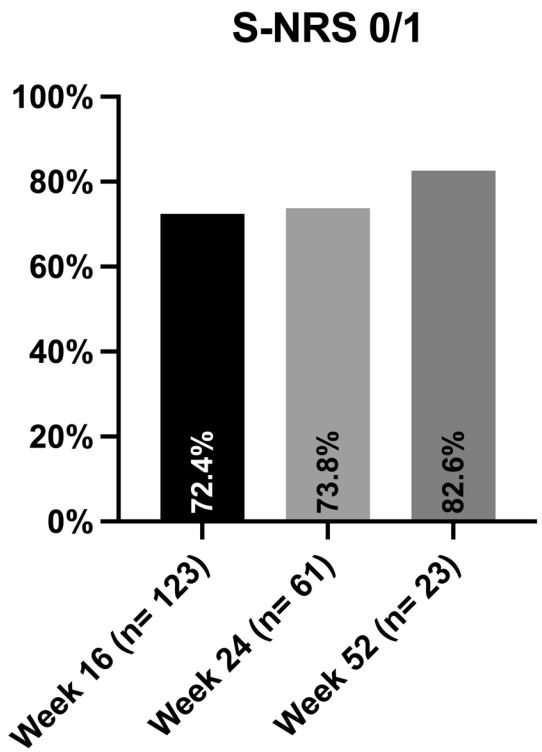
DISCUSSION

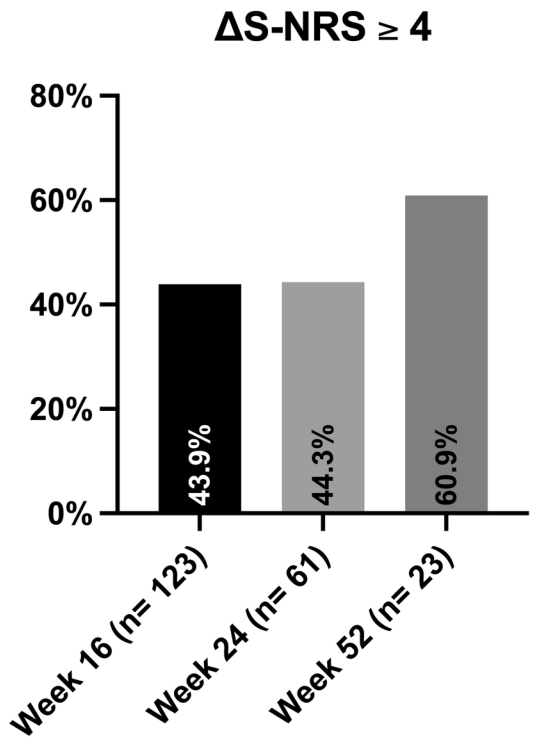
Real-world evidence has gained crucial relevance when assessing the effectiveness and safety of new drugs for the management of chronic conditions, such as moderate-to-severe AD. The results of our study offer new insights into the use of lebrikizumab for a year of continuous treatment, filling a current gap in knowledge, as long-term data on this drug are very limited and are mostly focused on Japanese populations. At week 52, the proportion of patients achieving EASI 75 was comparable with pooled data from the phase III clinical trials Advocate 1 and Advocate 2 (82.6% in our study versus 81.7% of patients receiving lebrikizumab Q4W in clinical trials) [4]. Regarding other endpoints, at week 52, an IGA 0/1 with a 2-point improvement from baseline was reached by 82.6% of our patients compared with 76.9% in the Advocate studies [4].

As previously stated, our patients were able to use TCS when needed, resembling the design of the Advantage clinical trial [5]. At week 52 in that study, 64.4% of patients treated with lebrikizumab Q2W with/without TCS achieved IGA 0/1 response, and 71.3% achieved a ≥ 4-point improvement in pruritus NRS. This is particularly relevant since, in our study, all patients received the maintenance dosage of lebrikizumab Q4W after week 24, achieving similar responses at week 52 compared with those enrolled in the ADvantage study (82.6% for IGA 0/1 and 65.2% for ΔPP-NRS ≥ 4). Comparable effectiveness at week 52 was also observed in terms of EASI 75 and EASI 90, as the proportions of patients treated with lebrikizumab with/without TCS who achieved these endpoints in the Advantage trial were 88.9% and 71.7%, respectively (compared with 82.6% and 69.6% in our cohort) [5]. Our experience supports the effectiveness of the Q4W dosage in the maintenance phase of the treatment, in accordance with the SmPC of lebrikizumab [3]. The continuous improvement in clinical endpoints we observed in our study is also consistent with a recent analysis of the Czech BIOREP registry [13]. In this study, the authors found that lebrikizumab Q2W from week 16 to week 24 provided better disease


PP-NRS 0/1
80%
60%
40%
20%
0%
41.5%
44.3%
56.5%
Week 16 (n= 123)
Week 24 (n= 61)
Week 52 (n= 23)


ΔPP-NRS ≥ 4
80%
60%
40%
20%
0%
58.5%
52.5%
65.2%
Week 16 (n= 123)
Week 24 (n= 61)
Week 52 (n= 23)


S-NRS 0/1
100%
80%
60%
40%
20%
0%
72.4%
73.8%
82.6%
Week 16 (n= 123)
Week 24 (n= 61)
Week 52 (n= 23)


ΔS-NRS ≥ 4
80%
60%
40%
20%
0%
43.9%
44.3%
60.9%
Week 16 (n= 123)
Week 24 (n= 61)
Week 52 (n= 23)

◂**Fig. 2** Effectiveness of lebrikizumab in terms of patient-reported outcomes (PP-NRS 0/1, ΔPP-NRS ≥ 4, S-NRS 0/1, and ΔS-NRS ≥ 4) throughout the study period. PP-NRS, Peak Pruritus Numerical Rating Scale; S-NRS, Sleep Disturbance Numerical Rating Scale

control for patients who did not achieve it at week 16, whereas Q4W dosing maintained the clinical response [13]. Similarly, in our experiment the lebrikizumab administration schedule from week 16 to week 24 was decided on the basis of the clinical picture, taking into account both clinical scores (EASI/IGA response) and PROs (Dermatology Life-Quality Index [DLQI], pruritus), allowing to achieve higher rates of EASI 75, EASI 90, and EASI 100 at week 24. The "clinical picture" included the extent and severity of skin lesions, residual inflammatory activity, involvement of sensitive areas, pruritus intensity, sleep disturbance, and the patient's perceived disease burden, as evaluated during routine clinical visits. This strategy helped achieve better EASI 75 and EASI 90 responses at week 24 compared with week 16, as stated in the text. Unfortunately, a comparison between the Q2W and Q4W groups was not possible due to the small sample size.

Finally, we also evaluated the percentage of patients achieving a combined endpoint (EASI 90 and PP-NRS 0/1), in accordance with the recently published Aiming High in Eczema/Atopic Dermatitis (AHEAD) recommendation that supports the evaluation of both clinician-reported measures and patient-reported outcomes [12]. We chose to evaluate EASI 90 and PP-NRS 0/1 since they are the most common endpoints in clinical trials. At weeks 16, 24, and 52, 30.1%, 39.3%, and 56.5% of our patients, respectively, achieved EASI 90 and PP-NRS of 0/1 simultaneously, reaching an optimal disease control. Very limited data are available in the literature regarding this combined endpoint [14, 15]. In the Level Up study, at week 16, a simultaneous EASI 90 and PP-NRS 0/1 response was achieved by 19.9% of patients receiving

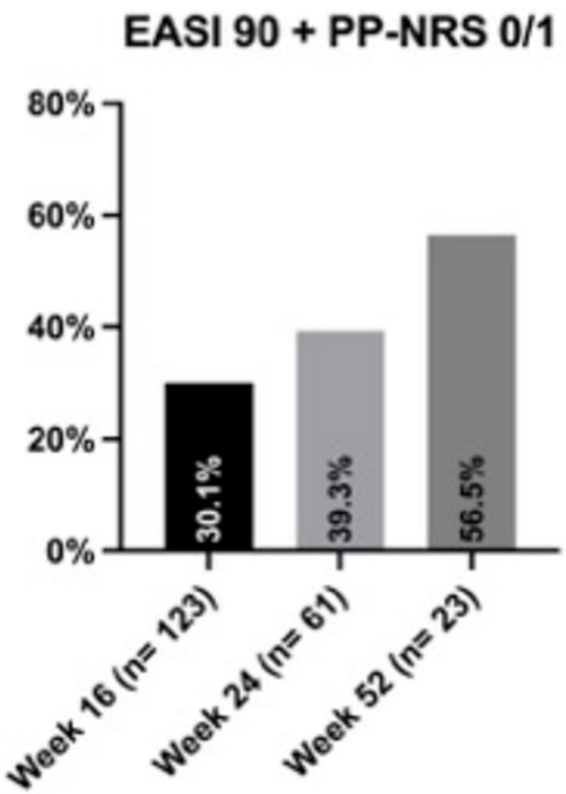


Fig. 3 Proportion of patients achieving minimal disease activity, defined as simultaneous achievement of EASI 90 and PP-NRS 0/1, at weeks 16, 24, and 52. EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale

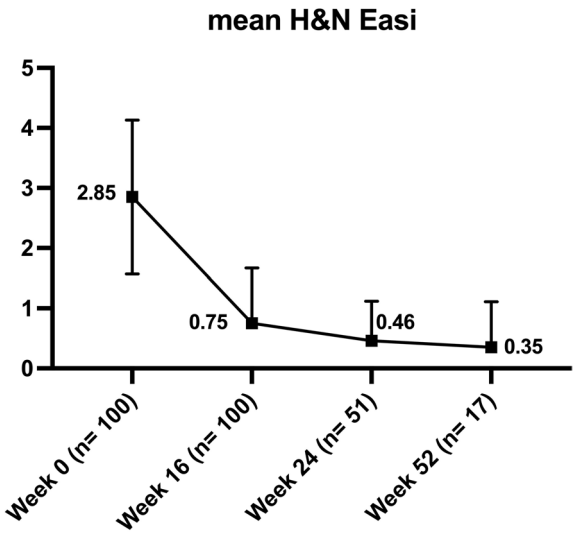
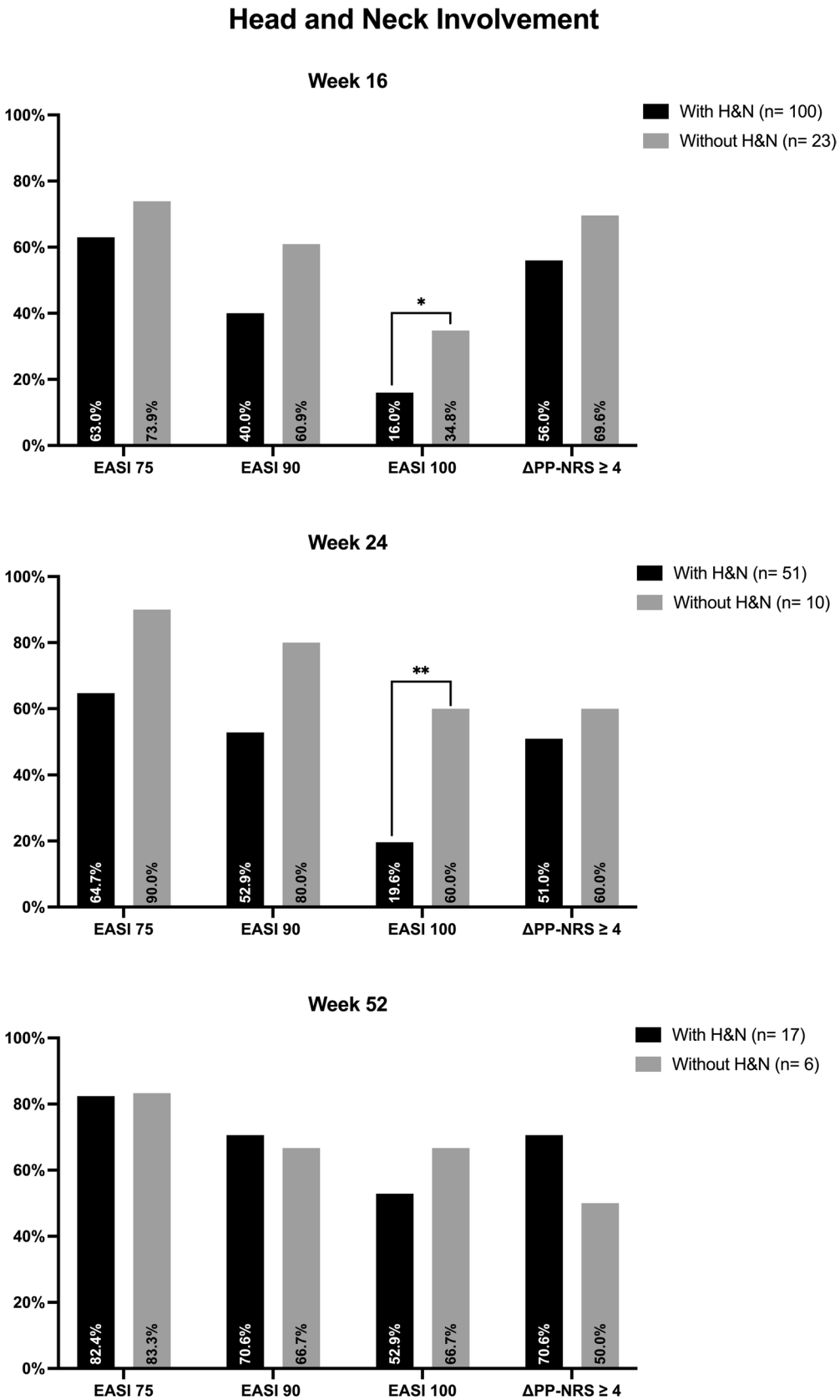


Fig. 4 Mean Head and Neck EASI (H&N EASI) values at baseline and during treatment with lebrikizumab at weeks 16, 24, and 52. Error bars indicate standard deviation. H&N EASI, Head and Neck Eczema Area and Severity Index


Head and Neck Involvement
Week 16
With H&N (n= 100)
Without H&N (n= 23)
100%
80%
60%
40%
20%
0%
63.0%
73.9%
40.0%
60.9%
16.0%
34.8%
56.0%
69.6%
*
EASI 75
EASI 90
EASI 100
ΔPP-NRS ≥ 4
Week 24
With H&N (n= 51)
Without H&N (n= 10)
64.7%
90.0%
52.9%
80.0%
19.6%
60.0%
51.0%
60.0%
**
Week 52
With H&N (n= 17)
Without H&N (n= 6)
82.4%
83.3%
70.6%
66.7%
52.9%
66.7%
70.6%
50.0%

◂**Fig. 5** Comparison of lebrikizumab effectiveness in patients with and without head and neck involvement at weeks 16, 24, and 52 in terms of EASI 75, EASI 90, EASI 100, and ΔPP-NRS ≥ 4. EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale. H&N, Head and Neck involvement. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$

upadacitinib versus 8.9% of those treated with dupilumab [14]. Despite different conditions and patients' characteristics, we observed similar, or even higher, percentages for lebrikizumab in our study, with continuous improvement during the period of observation. Compared with other European real-world experiences, we observed similar clinical response in the short-term for dupilumab and tralokinumab, and JAK inhibitors, although indirect comparisons are limited by very different patients' characteristics at baseline [15–17].

Our study also focused on head and neck AD, which is commonly referred to as a both sensitive and difficult-to-treat area [18]. Our findings support the effectiveness of lebrikizumab on different anatomical sites, as no significant differences emerged between patients with and without head and neck AD in terms of EASI 75, EASI 90, and ΔPP-NRS ≥ 4. Also, mean H&N EASI decreased throughout the study, consistent with earlier week 16 data from Avallone et al. [8]. Although raw rates of EASI 100 were lower in patients with head/neck AD, overall responses (EASI 75, EASI 90, and PP-NRS improvement) were comparable, confirming that lebrikizumab remains effective even in this historically difficult-to-treat area. Our findings are also consistent with post hoc analyses of the Advocate studies, which showed that, in both studies, patients treated with lebrikizumab showed significantly greater percent improvement in EASI across all body regions versus placebo at week 16 [19].

Table 2 Safety profile of lebrikizumab throughout the study period

	N (%)
Patients with AEs	7 (5.7)
Conjunctivitis	5 (4.1)
Head and neck dermatitis	2 (1.6)
Patients with SAEs	0
Permanent discontinuations due to AEs	2 (1.6)

AE, adverse event; SAE, severe adverse event

Regarding the safety profile of lebrikizumab, our data are comparable with both previous short-term studies and phase III clinical trials, with no new safety signals [4–9].

Our study has a few limitations that should be acknowledged and that could limit the generalizability of our findings. First, the retrospective two-center nature of our analysis is intrinsically limited by the impossibility of retrieving missing data and by the possible heterogeneity of clinical assessments. Second, not all patients had already completed 52 weeks of treatment at the time of data cutoff, because they started the treatment with lebrikizumab at different times. Third, the effectiveness at week 52 could be overestimated due to a possible survival bias of the cohort at this time point. Finally, the safety data should be interpreted with caution since, in real-world clinical practice, it is very common not to report every AE, especially the mild ones. Despite these limitations, our study is one of the first real-world experiments on lebrikizumab with a year of follow-up, providing long-term data on both effectiveness and safety, along with a comparison between patients who were bio-naïve and those who were bio-experienced.

CONCLUSIONS

We believe that, in the current landscape of AD treatment, with several drugs being approved, it is crucial to assess the place in therapy of new drugs, such as lebrikizumab, in different subpopulations.

Our experience, despite the aforementioned limitations, supports data from both clinical trials and other shorter real-life studies. We observed sustained effectiveness of lebrikizumab during 52 weeks of continuous treatment, in the absence of new significant safety findings. The maintenance dosing was not associated with loss of clinical response in our study, supporting data

from phase III clinical trials. Lebrikizumab also showed effectiveness in patients with involvement of the head and neck, with comparable clinical responses. Multicenter prospective studies with a larger cohort should be carried out to further assess our preliminary results.

ACKNOWLEDGEMENTS

We thank the participants of the study.

Declarations

Author Contributions. All authors contributed to the conception and design of the study. Material preparation and data analysis were conducted by Luigi Gargiulo, Luciano Ibba, Matteo Bianco, and Sara Di Giulio. Data collection was performed by Mario Valenti, Gianluca Avallone, Martina Zussino, and Paolo Calzari. The first draft of the manuscript was written by Luigi Gargiulo and Luciano Ibba, and all authors commented on previous versions of the manuscript. Alessandra Narcisi and Silvia M. Ferrucci performed the review and the editing of the final draft of the manuscript. Alessandra Narcisi, Silvia M. Ferrucci, Antonio Costanzo, and Angelo V. Marzano supervised the study. All authors read and approved the final manuscript.

Funding. No funding or sponsorship was received for this study or publication of this article.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest. Luigi Gargiulo has been a consultant and/or speaker and has served as an advisory board member for AbbVie, Almirall, Amgen, BMS, Eli Lilly, Galderma, Johnson and Johnson, Incyte, LEO Pharma, Novartis, Pierre Fabre, Pfizer, Sanofi, and UCB Pharma. Luciano Ibba has been a consultant and/or speaker and has served as an advisory board member for Almirall and LEO Pharma. Matteo Bianco has been a speaker for BMS. Mario Valenti has been a consultant and/or speaker for Sanofi, Leo Pharma, Eli Lilly, Novartis, Janssen, AbbVie, and Boehringer Ingelheim. Mario Valenti is an Editorial Board member of *Dermatology and Therapy*. Mario Valenti was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. Angelo V. Marzano has conflict of interest with AbbVie, Boehringer Ingelheim, Bristol Myers, Squibb, Incyte, Leopharma, Novartis, Pfizer, Sanofi and UCB. Antonio Costanzo has served as an advisory board member and as consultant and has received fees and speaker's honoraria or has participated in clinical trials for AbbVie, Almirall, Biogen, Leo Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma. Silvia M. Ferrucci has been principal investigator in clinical trials for AbbVie, Almirall, Galderma, Leo Pharma, Sanofi, Amgen, and Novartis, Bayer, and received honoraria for lectures for Novartis and Menarini. Alessandra Narcisi has served on advisory boards, received honoraria for lectures, and research grants from Almirall, AbbVie, Leo Pharma, Celgene, Eli Lilly, Janssen, Novartis, Sanofi Genzyme, Amgen, and Boehringer Ingelheim. Sara Di Giulio, Gianluca Avallone, Martina Zussino, and Paolo Calzari have nothing to declare. Luigi Gargiulo and Mario Valenti are Editorial Board members of *Dermatology and Therapy*. Luigi Gargiulo and Mario Valenti were not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

Ethical Approval. Ethical approval was granted by an institutional review board (Ethics Approval Committee Lombardia 3, protocol number Lebri-AD-2024). All patients received lebrikizumab, as per standard clinical practice, in accordance with European and Italian guidelines for the management of atopic eczema. For some of the included patients, Almirall provided the drug lebrikizumab through a Compassionate Use Program activated according to the DM 7/9/2017. The study was conducted following the principles of the Helsinki Declaration of 1964 and its later amendments. Data collection and handling complied with applicable laws,

regulations, and guidance regarding patient protection, including patient privacy. All patients provided written informed consent to participate in the study and for publication.

REFERENCES

1. Guttman-Yassky E, Renert-Yuval Y, Brunner PM. Atopic dermatitis. Lancet. 2025;405:583–96.

2. Wollenberg A, Kinberger M, Arents B, et al. European guideline (EuroGuiDerm) on atopic eczema: living update. Acad Dermatol Venereol. 2025;39(9):1537–66. https://doi.org/10.1111/jdv.20639.

3. European Medicines Agency Ebglyss (Lebrikizumab): summary of product characteristics. 2023. https://www.ema.europa.eu/en/medicines/human/EPAR/ebglyss. Accessed 6 Dec 2025.

4. Blauvelt A, Thyssen JP, Guttman-Yassky E, et al. Efficacy and safety of lebrikizumab in moderate-to-severe atopic dermatitis: 52-week results of two randomized double-blinded placebo-controlled phase III trials. Br J Dermatol. 2023;188:740–8.

5. Warren RB, de Bruin-Weller M, Tsianakas A, et al. Efficacy and safety of lebrikizumab in adult and adolescent patients with moderate-to-severe atopic dermatitis inadequately controlled with or ineligible for ciclosporin A: a placebo-controlled, randomized phase IIIb clinical study (Advantage). Br J Dermatol. 2025;193(5):876–88. https://doi.org/10.1093/bjd/ljaf285.

6. Hagino T, Uchiyama A, Kosaka K, et al. Thirty-six-week real-world effectiveness of lebrikizumab for different anatomical sites and clinical signs in atopic dermatitis: results from a prospective Japanese study. Dermatitis. 2025. https://doi.org/10.1177/17103568251361920.

7. Gargiulo L, Bianco M, Ibba L, et al. Reply to Hagino et al.: "Importance of Upadacitinib dose escalation prior to switch to lebrikizumab." J Eur Acad Dermatol Venereol. 2025. https://doi.org/10.1111/jdv.70089.

8. Avallone G, Bombelli A, Gargiulo L, et al. Effectiveness, safety, and health-related quality of life in moderate-to-severe atopic dermatitis treated with lebrikizumab: a 16-week nationwide retrospective cohort study. Dermatol Ther. 2025;15(12):3671–88. https://doi.org/10.1007/s13555-025-01550-8.

9. Hagino T, Uchiyama A, Onda M, et al. 24-week real-world effectiveness and safety of lebrikizumab for atopic dermatitis in Japan: an analysis stratified by prior systemic therapy. Dermatitis. 2025. https://doi.org/10.1089/derm.2025.0045.

10. Argenziano G, Cusano F, Corazza M, et al. Italian S3-Guideline on the treatment of atopic eczema - Part 1: Systemic therapy, adapted from EuroGuiDerm by the Italian Society of Dermatology and STD (SIDEMAST), the Italian Association of Hospital Dermatologists (ADOI) and the Italian Society of Allergological and Environmental Dermatology (SIDAPA). Ital J Dermatol Venereol. 2024;159:223–50.

11. Silvestre Salvador JF, Romero-Pérez D, Encabo-Durán B. Atopic dermatitis in adults: a diagnostic challenge. J Investig Allergol Clin Immunol. 2017;27(2):78–88. https://doi.org/10.18176/jiaci.0138.

12. Silverberg JI, Gooderham M, Katoh N, Aoki V, Pink AE, Binamer Y, et al. Combining treat-to-target principles and shared decision-making: international expert consensus-based recommendations with a novel concept for minimal disease activity criteria in atopic dermatitis. J Eur Acad Dermatol Venereol. 2024;38(11):2139–48.

13. Rob F, Kojanová M, Hercogová JT, et al. Efficacy and safety evaluation of different lebrikizumab dosages in atopic dermatitis patients over 16 to 24 weeks: a BIOREP registry analysis. Int J Dermatol. 2025. https://doi.org/10.1111/ijd.70180.

14. Silverberg JI, Bunick CG, Hong HC, et al. Efficacy and safety of upadacitinib versus dupilumab in adults and adolescents with moderate-to-severe

atopic dermatitis: week 16 results of an open-label randomized efficacy assessor-blinded head-to-head phase IIIb/IV study (Level Up). Br J Dermatol. 2024;192(1):36–45. https://doi.org/10.1093/bjd/ljae404.

15. Ibba L, Gargiulo L, Vignoli CA, et al. Practical use of upadacitinib in patients with severe atopic dermatitis in a real-world setting: a systematic review. Clin Cosmet Investig Dermatol. 2024;17:593–604. https://doi.org/10.2147/CCID.S329442. (**Published 2024 Mar 12**).

16. Izu Belloso RM, Juliá Manresa M, Martínez Peña N, et al. Real-world clinical practice evaluation of tralokinumab in atopic dermatitis: a 52-week multi-center retrospective study in the Basque Country. J Clin Med. 2025;14(16):5727. https://doi.org/10.3390/jcm14165727. (**Published 2025 Aug 13**).

17. Waligóra-Dziwak K, Dańczak-Pazdrowska A, Jenerowicz D. Long-term real-world effectiveness of dupilumab vs. upadacitinib in early treatment responders with atopic dermatitis: results from Central European health fund registry. Int J Mol Sci. 2025;26(9):4230. https://doi.org/10.3390/ijms26094230. (**Published 2025 Apr 29**).

18. Lio PA, Wollenberg A, Thyssen JP, et al. Impact of atopic dermatitis lesion location on quality of life in adult patients in a real-world study. J Drugs Dermatol. 2020;19(10):943–8. https://doi.org/10.36849/JDD.2020.5422.

19. Simpson EL, de Bruin-Weller M, Hong HC, et al. Lebrikizumab provides rapid clinical responses across all Eczema Area and Severity Index body regions and clinical signs in adolescents and adults with moderate-to-severe atopic dermatitis. Dermatol Ther (Heidelb). 2024;14(5):1145–60. https://doi.org/10.1007/s13555-024-01158-4.