Lebrikizumab as monotherapy improves the signs of moderate-to-severe atopic dermatitis across different body regions including head and neck over one year of treatment

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BACKGROUND & OBJECTIVE

- Some areas of the body, and some individual signs may be more resistant to treatment in atopic dermatitis (AD).
- The efficacy of lebrikizumab (LEB), a high-affinity monoclonal antibody targeting interleukin-13, in improving body signs, such as erythema, edema/papulation, excoriation, and lichenification, by anatomical region at Week 16 has already been published for moderate-to-severe AD.[1]
- The aim of this analysis was to determine the efficacy of LEB as monotherapy for AD across four clinical signs by anatomical region in two phase 3 clinical trials ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967A) up to one year of treatment.

CONCLUSION

- Lebrikizumab in monotherapy consistently reduced the severity of AD and the extent of involvement across all body regions, including head and neck, and the response was sustained from Week 16 up to Week 52.
- Lebrikizumab also reduced the severity of all four clinical signs of AD, including lichenification, in all body regions, and the response was sustained from Week 16 up to Week 52.

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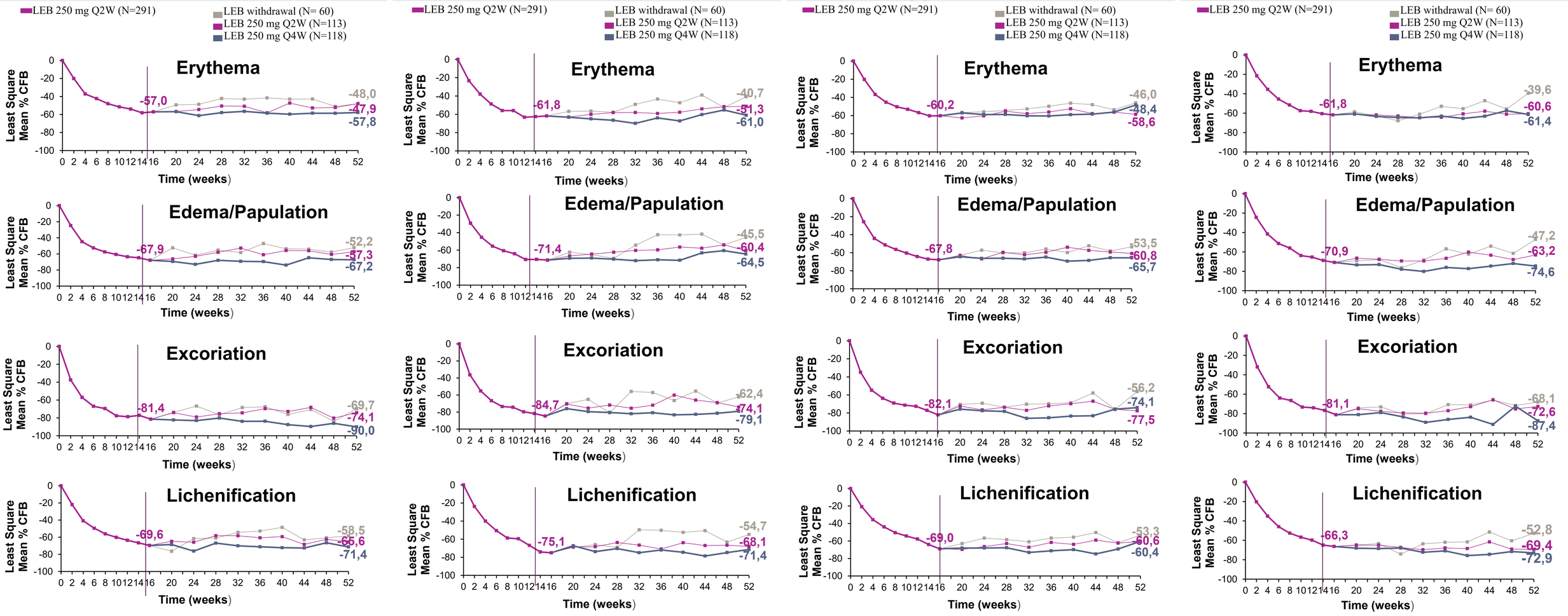
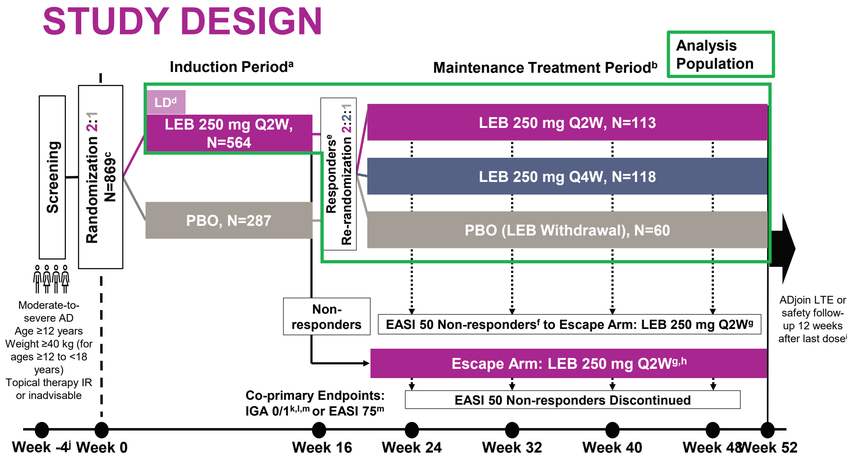
KEY FINDINGS

EASI % Change From Baseline (CFB) by sign and body region up to Week 52 (MMRM)



- In Week 16 LEB responders, improvement of moderate-to-severe AD across body regions -including head and neck-, and across signs, -including lichenification- was maintained through Week 52.

STUDY DESIGN



[a] Use of topical/systemic treatments for AD prohibited; [b] Use of intermittent topical rescue medications for AD permitted. Responders who received PBO during induction who were re-randomized to LEB received an LD of either 500 mg given at Week 16 or 500 mg given at Week 16 and Week 18; [c] 424 patients (ADvocate1) and 445 patients (ADvocate2) with moderate-to-severe AD; [d] 500 mg LD at Week 0 and Week 2; [e] Responders achieving EASI 75 or IGA 0/1 with ≥2-point improvement at Week 16, without rescue medication use; [f] Patients who did not maintain ≥EASI 50 were assigned to the Escape Arm; [g] Maintenance of response assessed by EASI 50 at Week 24, Week 32, Week 40, and Week 48, respectively. Patients who received systemic rescue medication were required to washout for 5 half-lives prior to initiating treatment in the Escape Arm; [h] Participants who were eligible for the Escape Arm at Week 16 received blinded LD at Week 16 and Week 18, based on their prior treatment assignment; [i] Patients completing ADvocate1/2 were offered treatment in ADjoin; otherwise, patients participated in a safety follow-up 12 weeks after their last dose; [j] ≤30-day screening period; [k] IGA 0/1 with ≥2-point improvement from baseline; [l] FDA primary endpoint; [m] EMA co-primary endpoint.

Key eligibility criteria

- Adults and adolescents (≥12 to <18 years weighting ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having at the baseline visit:
  - Eczema Area and Severity Index (EASI) ≥16
  - Investigator's Global Assessment (IGA) ≥3
  - ≥10% body surface area of AD involvement
- Candidate for systemic therapy or with a history of inadequate response or medically inadvisable to topical therapies
- Dupilumab and tralokinumab naïve.

Population and Analysis

Analysis population

- This analysis includes the N=291 patients initially randomized to LEB who were responders at the end of the Induction Period.
- Responders were defined as patients who achieved IGA 0/1 with ≥2-point improvement or EASI 75, with no rescue medication use.
- Analyses were conducted on the pooled modified maintenance primary population (mMPP) from ADvocate1 and ADvocate2.
  - ADvocate2 efficacy analyses were performed on a modified population, excluding 18 patients (from a single study site) whose eligibility could not be confirmed.

Analysis period

- Maintenance Period, Week 16 to Week 52

Efficacy endpoints

- % change from baseline (CFB) in EASI obtained by dividing LS mean CFB by total baseline mean in each clinical sign for each anatomical region.

Statistical model

- The mixed-effects model of repeated measures (MMRM) was used to evaluate CFB at Week 52 in clinical signs of AD by anatomical regions. Data after rescue therapy usage or discontinuation of treatment were considered as missing and were handled using MMRM.

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References

1. Simpson EL et al. J Clin Aesthet Dermatol 2023;16(4 Suppl 1):S5–S31.

Abbreviations: AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; CFB=change from baseline; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; EMA=European Medicines Agency; FDA=US Food and Drug Administration; IGA=Investigator's Global Assessment; IR=inadequate responder; LD=loading dose; LEB=lebrikizumab; LS=least square; LTE=long-term extension; mMPP=modified maintenance primary population; MMRM=mixed-effects model of repeated measures; NRS=Numerical Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation.

Baseline demographics and disease characteristics

	mMPP Population		
	LEB Q4W (N=118)	LEB Q2W (N=113)	LEB Withdrawal (N=60)
Age, years	35.8 (17.3)	36.1 (17.0)	33.8 (16.6)
Adolescent (≥12 to <18 years), n (%)	17 (14.4)	13 (11.5)	8 (13.3)
Adult (≥18 years), n (%)	101 (85.6)	100 (88.5)	52 (86.7)
Female, n (%)	69 (58.5)	53 (46.9)	36 (60.0)
Region, n (%)			
USA	51 (43.2)	44 (38.9)	22 (36.7)
Europe	38 (32.2)	40 (35.4)	18 (30.0)
Rest of the world	29 (24.6)	29 (25.7)	20 (33.3)
Race, n (%)			
White	86 (72.9)	80 (70.8)	33 (55.0)
Asian	17 (14.4)	19 (16.8)	15 (25.0)
Black	12 (10.2)	9 (8.0)	8 (13.3)
BMI, kg/m^2	26.2 (5.9)	26.3 (6.9)	25.3 (4.8)
Prior systemic treatment, n (%)	66 (55.9)	51 (45.1)	30 (50.0)
Disease duration since AD onset, years	22.6 (14.8)	21.7 (14.2)	20.4 (14.9)
IGA, n (%)			
3 (Moderate)	78 (66.1)	70 (61.9)	37 (61.7)
4 (Severe)	40 (33.9)	43 (38.1)	23 (38.3)
EASI	28.8 (12.6)	29.5 (10.8)	28.9 (11.2)
BSA % involvement	43.9 (23.2)	45.3 (20.6)	42.9 (22.4)
Pruritus NRS, median (range)	7.2 (1.0-10.0)	7.3 (2.1-10.0)	7.6 (3.0-10.0)
<4, n (%)	9 (7.8)	3 (2.7)	2 (3.4)
≥4, n (%)	107 (92.2)	108 (97.3)	57 (96.6)
Sleep-Loss Scale (interference of itch on sleep)	2.1 (1.0)	2.3 (0.9)	2.3 (1.1)
DLQI[a]	14.6 (7.5)	14.9 (6.9)	15.2 (7.5)

[a] DLQI was completed only for patients ≥16 years at baseline; patients <16 years used the Children's DLQI.
Note: Data are mean (SD) unless stated otherwise.

Disclosures SK is an employee of Almirall Hermal GmbH **: KE** reports consulting fees/honoraria from Abbvie, Almirall, BMS, Leo, Janssen, Lilly, Sanofi, Boehringer Ingelheim, Galderma, Pfizer, UCB, and Novartis; and contract services from Abbvie, Janssen, UCB, Leo. **MdB-W** has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Amgen, Aslan, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron, and Sanofi-Genzyme. **ELS** reports personal fees from AbbVie, Amgen, Arena Pharmaceuticals, Aslan Pharma, Boston Consulting Group, Collective Acumen, LLC (CA), Dermira, Eli Lilly, Evidera, ExcerptaMedica, Forte Bio RX, Galderma, GlaxoSmithKline, Incyte, Janssen, Kyowa Kirin Pharmaceutical Development, Leo Pharm, Medscape LLC, Merck, Pfizer, Physicians World LLC, Regeneron, Roivant, Sanofi- Genzyme, Trevi therapeutics, Valeant, WebMD. Dr. Simpson reports grants (or serves as Principal investigator role) from AbbVie, Amgen, Arcutis, Aslan, CorEvitas, Dermavant, Dermira, Eli Lilly, Incyte, Kymab, Kyowa Hakko Kirin, Leo Pharmaceuticals, Pfizer, Regeneron, Sanofi, and TARGET-DERM. **JIS** has received grants and/or personal honoraria from AbbVie, AFYX Therapeutics, Arena Pharmaceuticals, Asana BioSciences, Bluefin, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte, Kiniksa, LEO Pharma, Luna Pharma, Menlo Therapeutics, Novartis, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi. **HC-HH** has been a speaker/consultant and/or investigator for Abbvie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Meyes Squibb, Celgene, Dermavant, Eli Lilly, Galderma, Glaxo-Smith-Kline, Incyte, Janssen, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, and UCB. **ARA** is an employee of Eli Lilly and Company. **MF** and **LB** are employees of Almirall S.A. **DS-S** has been an investigator for Abbvie, Almirall, Amgen, Astra-Zeneca, Galderma, Eli Lilly, Leo Pharma, Novartis, and Sanofi-Regeneron; a consultant for Abbvie, Almirall, Astra-Zeneca, Eli Lilly, Leo Pharma, Janssen, Novartis, Sanofi, Pfizer, and UCB; and a speaker for Abbvie, Eli Lilly, Janssen, Novartis, Pfizer, Sanofi, and UCB.