Absolute responses of lebrikizumab at Week 52 in patients with moderate-to-severe atopic dermatitis who did not achieve protocol-defined response after initial 16 weeks of treatment

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BACKGROUND & OBJECTIVE

- Lebrikizumab (LEB) is a monoclonal antibody that binds with high affinity and slow off-rate to interleukin-13, which has previously demonstrated clinical efficacy and safety in adults and adolescents with moderate-to-severe atopic dermatitis (AD) in 3 randomized, placebo-controlled, phase 3 trials.[1-3]
- Efficacy based on absolute values is considered clinically relevant as they show response and remaining disease regardless of baseline severity.
- Here, we present Week 52 absolute responses with LEB in patients who did not achieve protocol-defined criteria for response after initial 16 weeks of treatment in ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) clinical trials (pooled data).

CONCLUSION

- Despite not meeting the Week 16 per-protocol response definition, a high percentage of patients reported meaningful improvements in different dimensions of the disease (skin, itch, quality of life) at Week 16, and continued to improve through Week 52.
- Continuing long-term therapy with LEB beyond 16 weeks can lead to high levels of response up to Week 52, even in cases where short-term treatment outcomes are not optimal.

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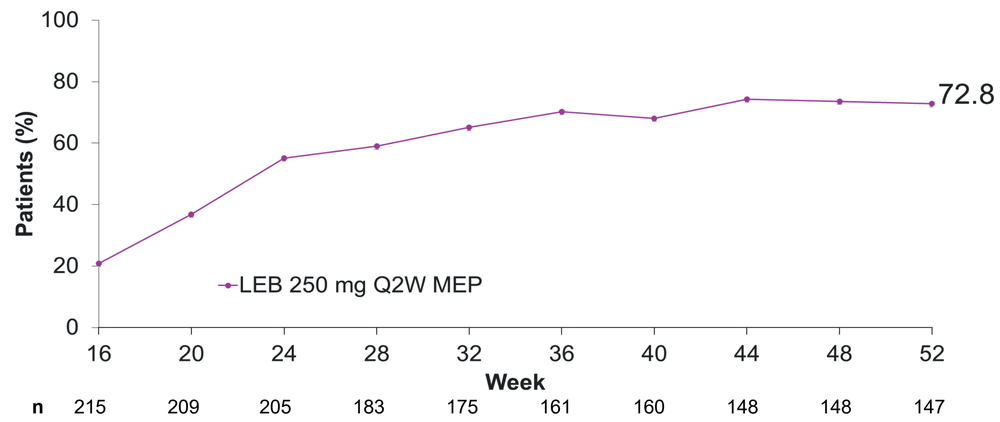
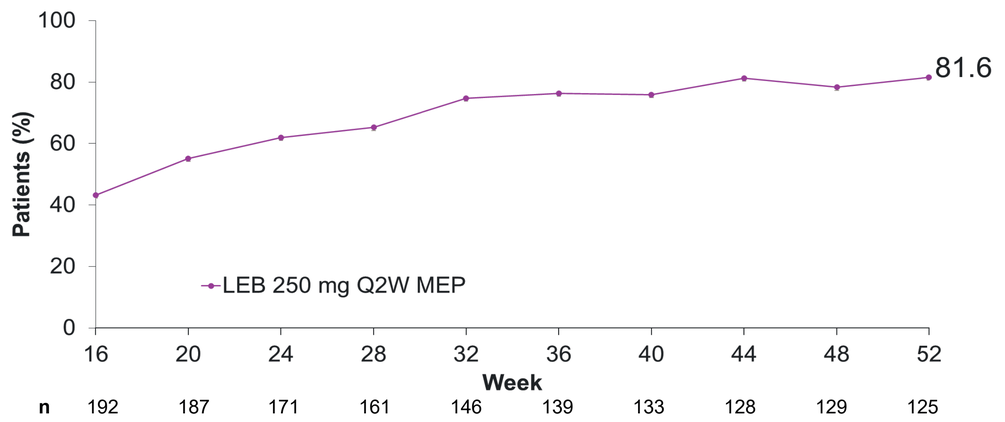
KEY FINDINGS

Signs, symptoms and quality of life in absolute values for LEB Week 16 per-protocol non-responders up to Week 52 (OC)

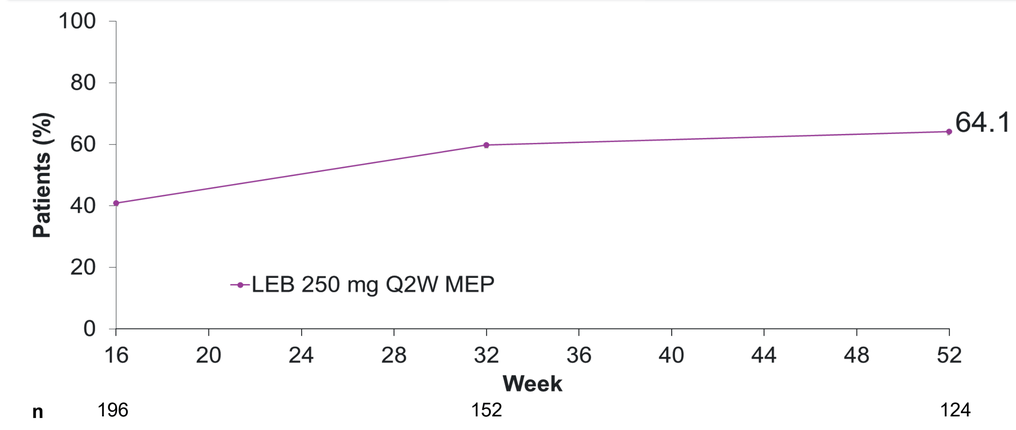
EASI ≤7



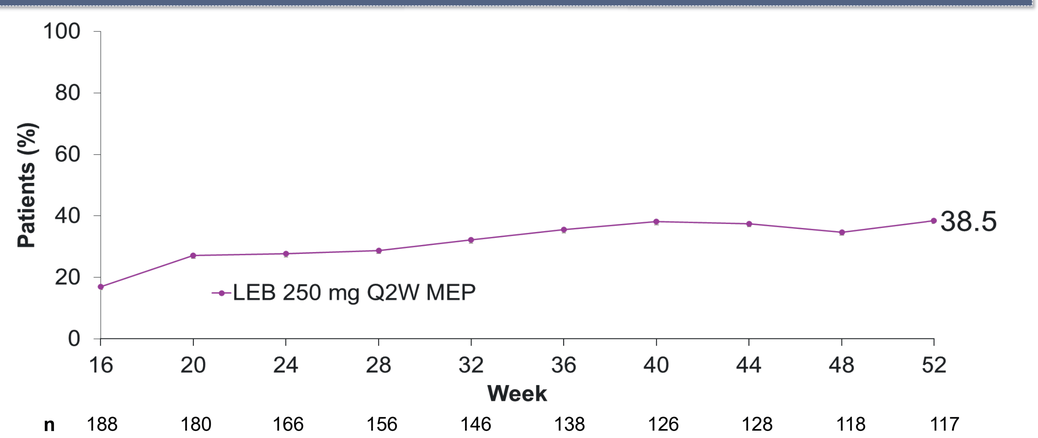
Pruritus NRS ≤4



DLQI ≤5



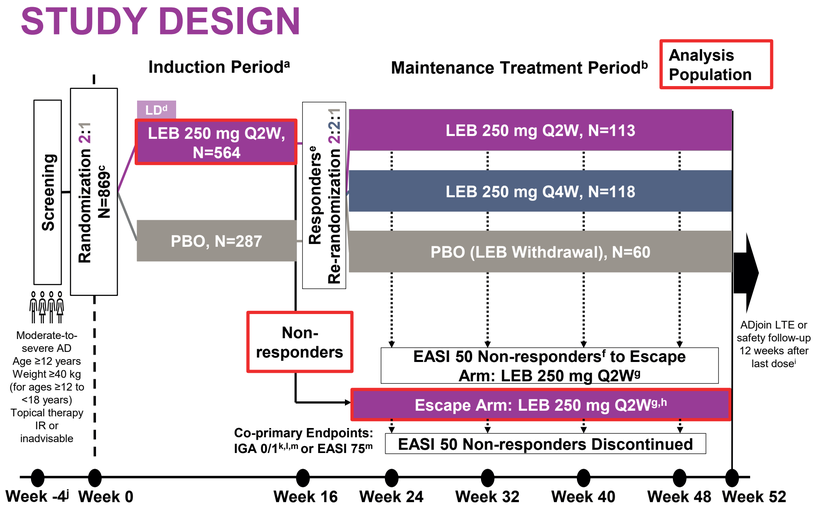
POEM ≤7



- In the pooled population of LEB treated patients who did not achieve the per protocol-defined response criteria at Week 16 (N=215) and continued to receive LEB 250 mg Q2W up to Week 52, 72.8% of patients achieved EASI ≤7, 81.6% achieved Pruritus NRS ≤4, 64.1% achieved DLQI ≤5 and 38.5% achieved POEM ≤7 at Week 52.

Note 1: For Pruritus NRS ≤4 assessment, only patients with Pruritus NRS >4 at baseline were included. For DLQI ≤5 assessment, only patients with DLQI >5 at baseline were included. For POEM ≤7 assessment, only patients with POEM >7 at baseline were included.
Note 2: Response rates at Week 16 does not start from 0, as some patients achieved the efficacy endpoints with use of rescue medication prior to Week 16.

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 weighing ≥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 a subset of patients initially randomized to LEB who were considered per-protocol non-responders at the end of the Induction Period (Week 16) and entered the Maintenance Escape Population (MEP).
- Non-responders were defined as patients who did not achieve IGA 0/1 with ≥2-point improvement or EASI 75, or who received rescue medication prior to Week 16.
- Non-responders to LEB at Week 16 who were assigned to the escape arm (MEP) continued to receive LEB 250 mg Q2W up to Week 52.

Analysis period

- Week 16 to Week 52

Efficacy endpoints

- EASI ≤7
- Pruritus NRS ≤4
- DLQI ≤5
- POEM ≤7

Statistical model

- As observed analysis was the per-protocol analysis for the MEP. Data are presented as observed cases (with no imputation for missing data).

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References

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2. Simpson EL, et al. JAMA Dermatol. 2023;159:182-91.
3. Blauvelt A, et al. Br J Dermatol. 2023;188:740-8.

Abbreviations: AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; IGA=Investigator's Global Assessment; LD=loading dose; LEB=lebrikizumab; MEP=Maintenance Escape Population; NRS=Numerical Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation.

Baseline demographics and disease characteristics

	LEB per-protocol non-responders/ LEB 250 mg Q2W (N=215)
Age, years	36.6 (17.3)
Adolescent (≥12 to <18 years), n (%)	23 (10.7)
Adult (≥18 years), n (%)	192 (89.3)
Female, n (%)	88 (40.9)
Region, n (%)	
USA	81 (37.7)
Europe	59 (27.4)
Rest of the world	75 (34.9)
Race, n (%)	
White	124 (57.7)
Asian	58 (27.0)
Black	23 (10.7)
BMI, kg/m^2	27.0 (6.2)
Prior systemic treatment, n (%)	126 (58.6)
Disease duration since AD onset, years	21.9 (15.3)
IGA, n (%)	
3 (Moderate)	119 (55.3)
4 (Severe)	96 (44.7)
EASI	29.9 (11.4)
BSA % involvement	47.6 (23.3)
Pruritus NRS	
<4, n (%)	12 (5.7)
≥4, n (%)	198 (94.3)
Sleep-Loss Scale (interference of itch on sleep)	2.3 (0.9)
DLQI[a]	16.2 (6.9)

[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 **SW** has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Boehringer, Eli Lilly, Galderma, GSK, Leo Pharma, Pfizer, Regeneron, and Sanofi. **TB** was speaker and/or consultant and/or Investigator for AbbVie, Allmiral, AnaptysBio, Arena, Asana Biosciences, Bayer Health, BioVerSys, Böhringer-Ingelheim, Bristol-Myers Squibb, Celgene, Daichi-Sankyo, Dermavant/Roivant, DermTreat, Domain Therapeutics, DS Pharma, RAPT/FLX Bio, Galapagos/MorphoSys, Galderma, Glenmark, GSK, Incyte, IQVIA, Janssen, Kirin, Kymab, LEO, LG Chem, Lilly, L´Oréal, MenloTx, Novartis, OMPharma/Vifor, Pfizer, Pierre Fabre, Sanofi/Regeneron, UCB. Thomas Bieber is founder of the non-profit biotech company "Davos Biosciences" within the International Kühne-Foundation. **EG-Y** is an employee of Mount Sinai and has received research funds (grants paid to the institution) from Abbvie, Almirall, Amgen, AnaptysBio, Asana Biosciences, AstraZeneca, Boerhinger-Ingelheim, Cara Therapeutics, Celgene, Eli Lilly, Galderma, Glenmark/Ichnos Sciences, Innovaderm, Janssen, KAO, Kiniksa, Kyowa Kirin, Leo Pharma, Novan, Novartis, Pfizer, Ralexar, Regeneron Pharmaceuticals, and UCB; and is a consultant for AbbVie, Almirall, Amgen, Arena, Asana Biosciences, Aslan Pharmaceuticals, AstraZeneca, Boerhinger-ingelheim, Bristol-Meyers Squibb, Cara Therapeutics, Celgene, Connect Pharma, Eli Lilly, EMD Serono, Evidera, Galderma, Ichnos Sciences, Incyte, Janssen Biotech, Kyowa Kirin, Leo Pharma, Pandion Therapeutics, Pfizer, RAPT Therapeutics, Regeneron Pharmaceuticals, Inc., Sanofi, SATO Pharmaceutical, Siolta Therapeutics, Target Pharma Solutions, UCB, and Ventyx Biosciences. **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. These potential conflicts of interest have been reviewed and managed by OHSU. 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. **DR** has received honoraria as a consultant for AbbVie, Celgene, Dermavant, Dermira, Janssen, Lilly, Novartis, Pfizer, and Regeneron Pharmaceuticals Inc.; has received research support from AbbVie, Bristol Meyers Squibb, Celgene, Dermira, Incyte, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals Inc.; and has served as a paid speaker for AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., 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 employee of Eli Lilly and Company. **LB** is an employee of Almirall S.A. **MdB-W** has been a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Arena, Aslan, Eli Lilly, Galderma, Janssen, Leo Pharma, Pfizer, Regeneron, and Sanofi-Genzyme.