Absolute itch and quality of life response with lebrikizumab through 52 weeks

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BACKGROUND & OBJECTIVE

- Lebrikizumab (LEB) is a monoclonal antibody that selectively binds with high affinity to interleukin-13 and inhibits its signal with high potency.[1]
- LEB has demonstrated efficacy and safety in adults and adolescents with moderate-to-severe atopic dermatitis (AD) in 3 randomized, placebo-controlled, phase 3 trials using relative endpoints recommended by Harmonizing Outcome Measures in Eczema (HOME).[2-5]
- Pruritus is the most frequent symptom of AD and may impact on patient's quality of life (QoL).[6]
- The attainment of absolute endpoints is clinically relevant and provides additional information of the remaining amount of disease.
- Here, we report the efficacy of LEB in terms of achieving Pruritus Numeric Rating Scale (NRS) ≤4 (indicative of mild pruritus) and Dermatology Life Quality Index (DLQI) ≤5 (indicative of no or minimal effect on patient's QoL) at Week 52 among Week 16 responders in the ADvocate1 and ADvocate2 trials.

CONCLUSION

- At Week 52, 8 out of 10 Week 16 LEB responders treated with LEB Q2W or Q4W had mild pruritus (Pruritus NRS ≤4) and 7 out of 10 had no or minimal effect on patient's QoL (DLQI ≤5).
- Thus, continued treatment with LEB in Week 16 responders provides sustained clinically meaningful improvements in the long-term in both symptoms and QoL in patients with moderate-to-severe AD.

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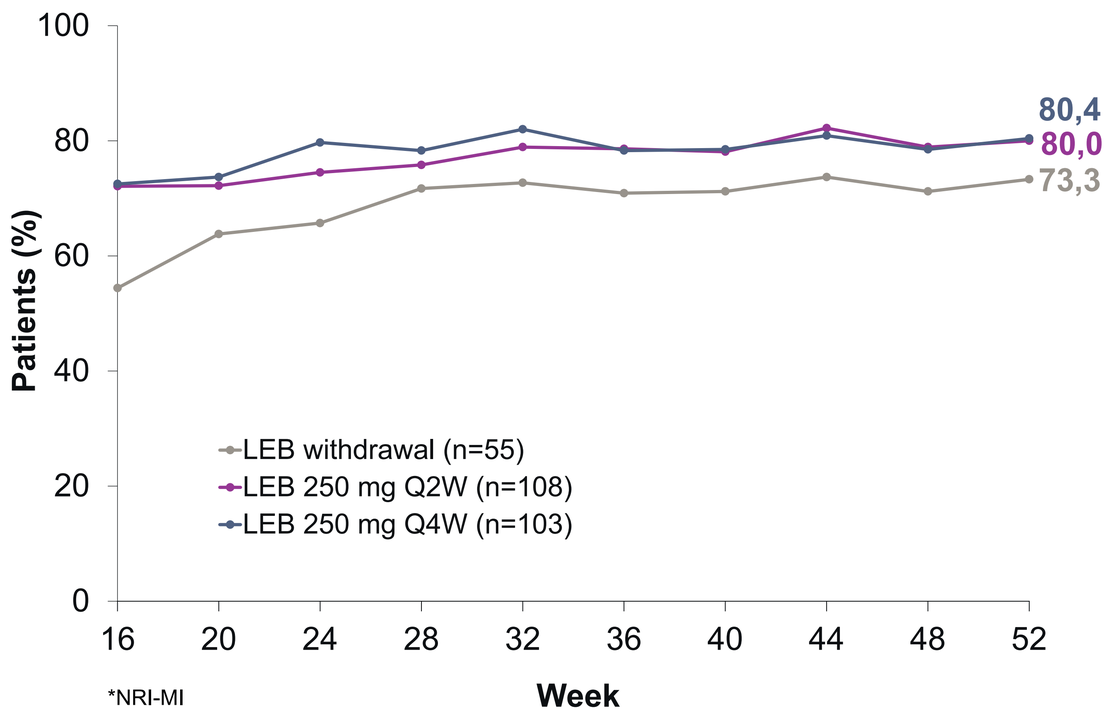
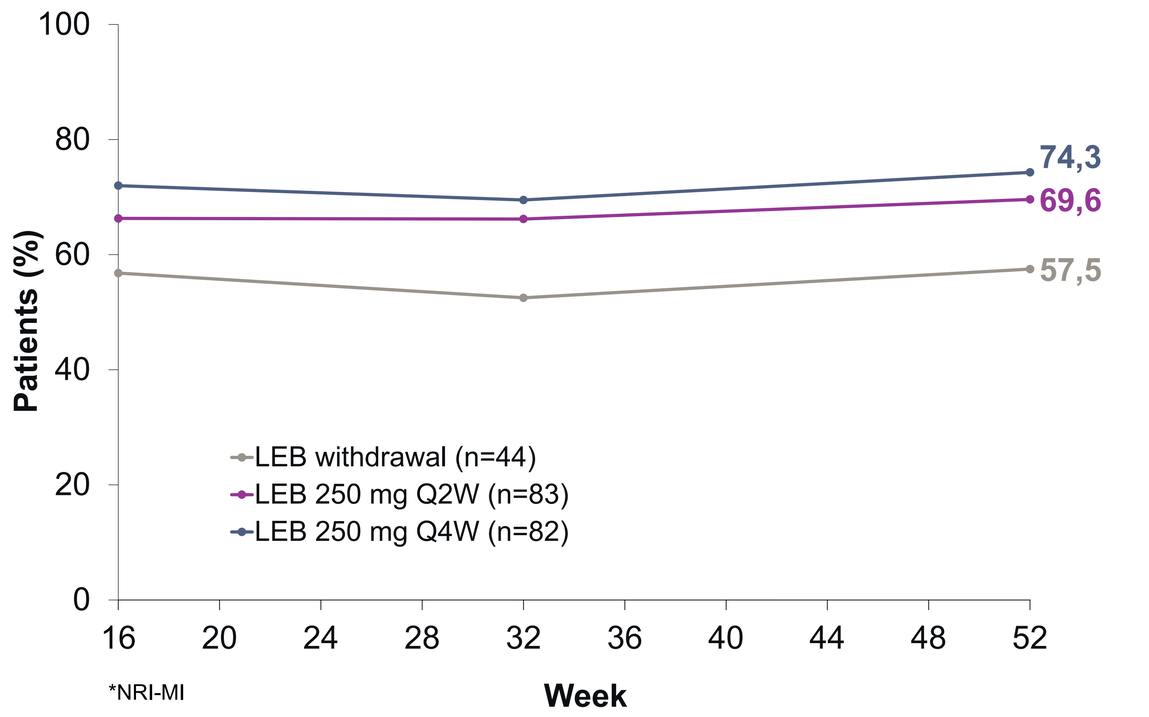
KEY FINDINGS

Absolute itch and quality of life response of Week 16 LEB responders at Week 52

Pruritus NRS ≤4*



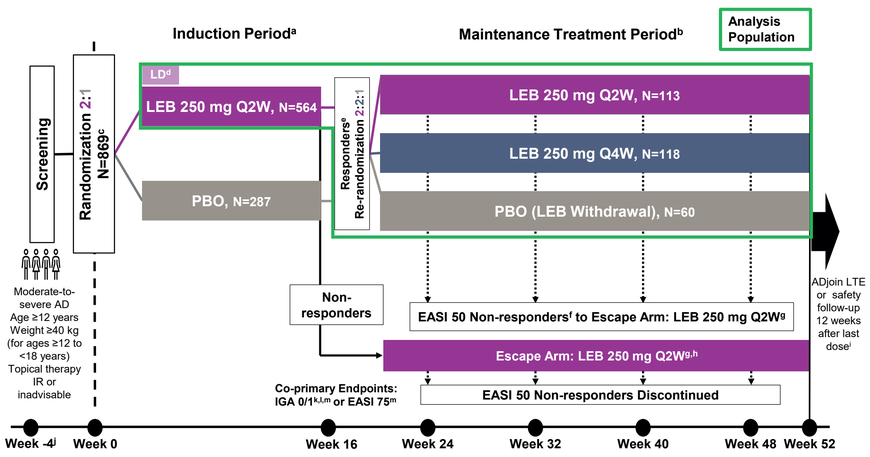
DLQI ≤5*



- Among LEB W16 responders, the proportion of patients reporting Pruritus NRS ≤4 at Week 52 was 80.4% in the LEB Q4W arm, 80.0% in the LEB Q2W arm, and 73.3% in the PBO (LEB withdrawal) arm.
- Among LEB W16 responders, the proportion of patients reporting a DLQI ≤5 response at Week 52 was 74.3% in the LEB Q4W arm, 69.6% in the LEB Q2W arm, and 57.5% in the PBO (LEB withdrawal) arm.

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.
Note 2: DLQI analysis only included adult patients.

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.

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Population and Analysis

Analysis population

- This analysis was done in 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

- Pruritus NRS ≤4, from Week 16 to Week 52
- DLQI ≤5, from Week 16 to Week 52

Statistical model

- Data after systemic rescue medication or discontinuation due to lack of efficacy were imputed with non-responder imputation (NRI); data after topical corticosteroids usage and other discontinuations were imputed with multiple imputation (MI).

References

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Abbreviations: AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; 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; LTE=long-term extension; MI=multiple imputation; mMPP=modified maintenance primary population; NRI=non-responder imputation; 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. **DT** has received honoraria as an advisor, speaker and/or investigator from AbbVie, Amgen, Almirall, Bristol-Myers-Squibb, Biogen Idec, Boehringer Ingelheim, Eli Lilly and Company, Galapagos, Janssen, LEO Pharma, Novartis, Pfzier, Regeneron, Sanofi, Roche-Possay, Samsung, and UCB. **LP** has received research support, honoraria for lecturing, and is on consulting/advisory board agreements with Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius-Kabi, Horizon, J&J Innovative Medicine, Leo-Pharma, Lilly, Novartis, Pfizer, STADA, Sun-Pharma, and UCB. **KP** has received honoraria and/or grants from AbbVie, Acelyrin, Akros, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, Dermavant, Dermira, DiCE Pharmaceuticals, DiCE Therapeutics, Eli Lilly and Company, Evelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte, Janssen, Kymab, Kyowa Hakko Kirin, LEO Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Nimbus Therapeutics, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tarsus Pharmaceuticals, UCB Pharma, and Zai Lab. **LSG** has been an investigator, consultant, and/or lecturer for Lilly, Amgen, Abbvie, Novartis, Pfizer, Arcutis, Dermavant, Galderma, and Incyte. **P F-P** has served on advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squib, Eli Lilly, Janssen, L'Oreal, LEO Pharma, Merck, Merck Sharp & Dohme, Novartis, Pfizer, Sanofi, and UCB; has given educational lectures for AbbVie, Amgen, Bristol Myers Squib, Eli Lilly, Galderma, Janssen, L'Oreal, LEO Pharma, Merck, Merck Sharp & Dohme, Novartis, Pfizer, Sanofi, UCB Pharma and Zuellig Pharma; has conducted clinical trials for AbbVie, Akaal, Akesobio, Amgen, Arena, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, CSL, Eisai, Eli Lilly, Galderma, Incyte, Janssen, Jiangsu Hengrui, KoBioLabs, Kyowa Hakko Kirin, Merck, Merck Sharp & Dohme, miRagen, Moderna, Nektar, Novartis, OncoSec, Pfizer, Regeneron, Sanofi, Sun Pharma, UCB Pharma. **Y-H H** has conducted clinical trials/served as principal investigator for Eli-Lilly, Galderma, Janssen, and Novartis; is an advisory board member for Pfizer, AbbVie, and Celgene; and is a speakers bureau member for AbbVie, Eli-Lilly, and Novartis. **AB** has served as a speaker (received honoraria) for Eli Lilly and Company and UCB, has served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Celldex, CTI BioPharma, Dermavant, EcoR1, Eli Lilly and Company, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, InnoventBio, Janssen, Landos, Leo, Lipidio, Microbion, Merck, Monte Rosa Therapeutics, Nektar, Novartis, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Ventyx, Vibliome, and Xencor, has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Allakos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Concert, Dermavant, DermBiont, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB Pharma, and Ventyx, and owns stock in Lipidio and Oruka. **BS** has received consultant honoraria from AbbVie, Acelyrin, Alamar, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Kangpu Pharmaceuticals, Bristol-Myers-Squibb, Capital One, Celltrion, CorEvitas, Dermavant, Imagenebio, Janssen, Leo, Eli Lilly, Maruho, Okura, Meiji Seika Pharma, Protagonist, Monte Carlo, Takeda, Novartis, Pfizer, UCB Pharma, Rapt, Regeneron, Sanofi-Genzyme, SG Cowen, Union Therapeutics; Stock Options in Connect Biopharma, Mindera Health; Speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Regeneron, Sanofi-Genzyme; Scientific Co-Director (consulting fee) from CorEvitas Psoriasis Registry. Investigator for CorEvitas Psoriasis Registry. Editor-in-Chief (honorarium) of Journal of Psoriasis and Psoriatic Arthritis. **MD** is an employee of Eli Lilly and Company. **MF** and **LB** are employees of Almirall. **CV** has received honoraria and research grants from Leo Pharma, Sanofi, Novartis, AbbVie, Pfizer, andd served as speaker for Leo Pharma, Sanofi, Novartis, AbbVie, Pfizer, Eli lilly, astra Zeneca, and served on advisory borad s for Sanofi, LEO pharma, Pfizer, ELI Lilly, and Abbvie, and been on aftey boards for OM Pharma, and MEDA.