Lebrikizumab Every 8 Weeks as Maintenance Dose Provides Long-lasting Response in Patients with Moderate-to-Severe Atopic Dermatitis

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BACKGROUND AND OBJECTIVE

- Lebrikizumab 250 mg dosed every 4 weeks (LEBQ4W) in the long-term extension ADjoin demonstrated sustained response for up to 3 years in patients with moderate-to-severe AD who achieved clinical response at week 16.[1]
- In the phase 3 ADvocate 1 and ADvocate 2 trials, during the maintenance periods (weeks 16–52), a high proportion of patients in the lebrikizumab withdrawal (placebo) arm exhibited durable efficacy,[2] suggesting that a less frequent dosing regimen could maintain efficacy.
- We report results from the ADjoin addendum, a 32-week extension of ADjoin assessing the efficacy and safety of lebrikizumab 250 mg every 8 weeks (LEBQ8W) as a maintenance dose regimen.

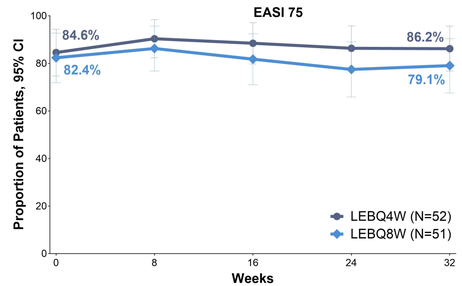
CONCLUSIONS

- Lebrikizumab dosed every 8 or 4 weeks provided long-lasting response in patients with moderate-to-severe AD, supporting its durable and potential disease-modifying effect in AD.
- The safety profile was consistent with other lebrikizumab Phase 3 trials.

Fall Clinical 2025; Las Vegas, USA; 23-26 October 2025

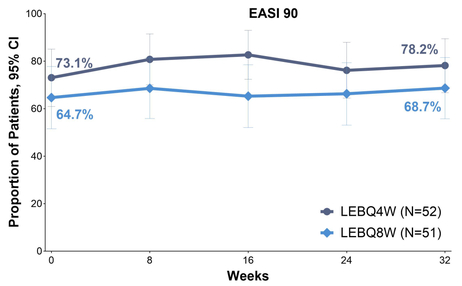
Results

EASI 75[a]
NRI/MI



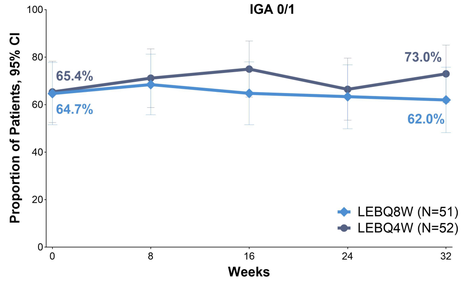
[a]EASI 75 wascalculated from parent study baseline
Note: Week 0 is the Adjoin Addendum baseline

EASI 90[a]
NRI/MI



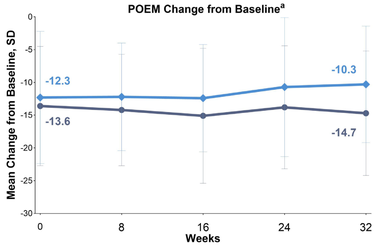
[a]EASI 90 was calculated from parent study baseline
Note: Week 0 is the Adjoin Addendum baseline

IGA 0/1 with ≥2-Point Improvement[a]
NRI/MI



[a]IGA 0/1 was calculated from parent study baseline
Note: Week 0 is the Adjoin Addendum baseline

POEM Mean Change from Baseline and Absolute Scores
As Observed



Absolute POEM Score	LEBQ8W				
	Week 0	Week 8	Week 16	Week 24	Week 32
Mean (SD) [Nx]	8.7 (7.6) [39]	7.3 (6.0) [30]	6.9 (6.0) [29]	8.9 (8.1) [31]	9.2 (7.3) [29]
Absolute POEM Score	**LEBQ4W**				
	Week 0	Week 8	Week 16	Week 24	Week 32
Mean (SD) [Nx]	6.0 (5.4) [41]	5.7 (5.1) [32]	5.0 (5.6) [32]	6.0 (5.1) [30]	5.4 (5.2) [31]

[a]Patients without baseline POEM scores were excluded from the change from baseline calculations; POEM was only collected from patients who came from ADvocate1, ADvocate 2 and ADopt-VA.
Note: Week 0 is the Adjoin Addendum baseline.
The POEM is patient-reported, 7-item scale in which patients respond to questions about the frequency of seven symptoms (itching, sleep disturbance, bleeding, weeping/oozing, cracking, flaking, and dryness/roughness) over the past week. Overall scores range from 0 to 28, with higher total scores indicating greater disease severity[3].

Overview of Treatment-Emergent Adverse Events

	LEBRI 250 mg Q4W (N=52)	LEBRI 250 mg Q8W (N=51)	All LEBRI (N=103)
Any TEAEs, n (%)	16 (30.8)	10 (19.6)	26 (25.2)
Mild, n (%)	9 (17.3)	6 (11.8)	15 (14.6)
Moderate, n (%)	7 (13.5)	4 (7.8)	11 (10.7)
Severe, n (%)	0	0	0
Serious AEs, n (%)	0	0	0
Death, n (%)	0	0	0
AEs leading to treatment discontinuation, n (%)	0	0	0
AEs of special interest, n (%)			
Eosinophilia and eosinophil-related disorders	0	0	0
Herpes infections	0	0	0
Parasitic infections	0	0	0
Conjunctivitis cluster	1 (1.9)	0	1 (1.0)

Immunogenicity

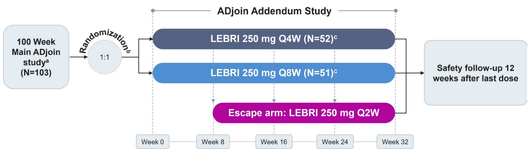
- 81/103 (78.6%) patients were treatment-emergent anti-drug antibody (TE ADA) evaluable[a] during the ADjoin addendum.
- Of the 81 patients, 4 (4.9%) developed TE ADAs[b]:
  - 3 patients on Q4W dosing (3.7% of TE ADA-evaluable, 7.0% of patients on Q4W dosing)
  - 1 patient on Q8W dosing (1.2% of TE ADA-evaluable, 2.6% of patients on Q8W dosing).
- Titers of the 4 patients who became TE ADA-positive were low (1:20–1:40).
- No clinical impact on efficacy or safety was observed in the TE ADA+ patients.
- In summary, no evidence of an increased risk of immunogenicity was observed in association with lebrikizumab Q8W dosing regimen compared with Q2W or Q4W.

[a]Only TE ADA-evaluable participants from the ADjoin main study who had at least 1 sample drawn in the ADjoin addendum were included.

[b]TE ADA included treatment-induced ADA, defined as patients with a titer 2-fold (1 dilution) greater than the minimum required dilution if no ADAs were detected at baseline, or treatment-boosted ADA, defined as patients with a 4-fold (2 dilutions) increase in titer compared with baseline if ADAs were detected at baseline. TE ADA status at the end of ADjoin main study was the last recorded status before the patient enrolled in the ADjoin addendum.

Methods

Study Design



[a]Patients enrolled in the ADjoin addendum originated from the ADvocate 1, ADvocate 2, ADore, and ADopt-VA parent studies at study sites located in the following countries: Australia, Canada, South Korea, Singapore, Taiwan, and the US.
[b]Randomization was stratified by IGA score (0,1 vs. >1) and region (US vs. non-US).
[c]Patients who did not maintain an EASI 50 response from the parent study baseline moved to the LEBQ2W escape arm for the remainder of the ADjoin addendum.

- The ADjoin addendum was a 32-week study involving patients from ADvocate 1 and 2, ADore, and ADopt-VA who completed the ADjoin long-term extension and were rerandomized to open-label LEBQ8W or LEBQ4W for 32-weeks.
- Patients were eligible to enter the study:
  - At week 100 of ADjoin, or
  - After week 100 of ADjoin, provided they had not yet completed the safety follow-up visit for Adjoin.

Outcomes

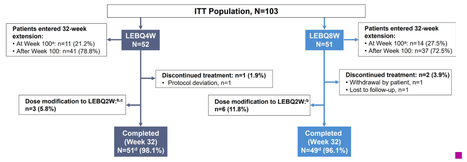
Efficacy analyses for the ADjoin addendum included:

- Primary outcomes:
  - Proportion of patients achieving or maintaining IGA 0/1 at week 32
  - Proportion of patients achieving or maintaining EASI 75 at week 32.
- Key secondary outcomes:
  - Proportion of patients achieving or maintaining EASI 90
  - Change from baseline in the POEM.

Statistical Analysis

- The analysis population included the ITT population enrolled in the ADjoin addendum.
  - For IGA 0/1, EASI 75, and EASI 90, data collected after treatment discontinuation due to lack of efficacy or dose modification to LEBQ2W were imputed as nonresponders, and missing data and data after treatment discontinuation due to any other reasons were imputed by multiple imputation.
  - As observed data were used to analyze the POEM outcomes regardless of treatment discontinuation or dose modifications.
- The study was not powered to detect whether LEBQ8W dosing was comparable to LEBQ4W dosing.
- Safety data were collected throughout the study, and descriptive statistics were used to summarize the safety results.

Patient Disposition



[a]Patients who entered at Week 100 enrolled in the ADjoin addendum on the same day of their ADjoin week 100 visit. [b]From Week 8, patients who did not maintain an EASI 50 response from parent study baseline were moved to LEBQ2W and were considered nonresponders. [c]One patient qualified for dose modification at week 24 but remained on LEBQ4W due to site entry error. [d]Includes patients who had dose modification to LEBQ2W.

- Of the total patients who entered the ADjoin addendum study after completing week 100 of ADjoin (n=78, 75.7%), the mean (SD) duration to enter the addendum was 60 (20.5) days.
- No study treatment was given between the week 100 visit and the ADjoin addendum baseline.

Results

Baseline Demographics

Parent Study Baseline of ADjoin Addendum Population

	LEBRI 250 mg Q4W (N=52)	LEBRI 250 mg Q8W (N=51)	Any LEBRI (N=103)
Age, (years), mean (SD)	26.4 (13.7)	28.8 (15.3)	27.6 (14.5)
Adolescents (≥12 to <18 years), n (%)	22 (42.3)	18 (35.3)	40 (38.8)
Female, n (%)	25 (48.1)	24 (47.1)	49 (47.6)
Race, n (%)			
White	18 (34.6)	20 (39.2)	38 (36.9)
Black or African American	3 (5.8)	3 (5.9)	6 (5.8)
Asian	26 (50.0)	26 (51.0)	52 (50.5)
Region, n (%)			
US	25 (48.1)	24 (47.1)	49 (47.6)
Europe	0	0	0
Rest of world, n (%)			
Australia	4 (7.7)	4 (7.8)	8 (7.8)
Canada	10 (19.2)	8 (15.7)	18 (17.5)
South Korea	7 (13.5)	8 (15.7)	15 (14.6)
Singapore	3 (5.8)	1 (2.0)	4 (3.9)
Taiwan	3 (5.8)	6 (11.8)	9 (8.7)

Disease Characteristics

Parent Study Baseline and ADjoin Addendum Baseline

	Parent Baseline			Adjoin Addendum Baseline		
	LEBRI 250 mg Q4W (N=52)	LEBRI 250 mg Q8W (N=51)	Any LEBRI (N=103)	LEBRI 250 mg Q4W (N=52)	LEBRI 250 mg Q8W (N=51)	Any LEBRI (N=103)
IGA, n (%)						
0*	-	-	-	17 (32.7)	15 (29.4)	32 (31.1)
1*	-	-	-	17 (32.7)	18 (35.3)	35 (34.0)
2*	-	-	-	13 (25.0)	15 (29.4)	28 (27.2)
3	37 (71.2)	29 (56.9)	66 (64.1)	5 (9.6)	3 (5.9)	8 (7.8)
4	15 (28.8)	22 (43.1)	37 (35.9)	0	0	0
EASI, mean (SD)	26.6 (12.0)	31.0 (14.3)	28.8 (13.3)	2.4 (3.6)	3.0 (4.3)	2.7 (3.9)
EASI 75, n (%)	-	-	-	44 (84.6)	42 (82.4)	86 (83.5)
BSA %, mean (SD)	39.3 (21.2)	48.3 (23.1)	43.8 (22.5)	5.2 (7.6)	5.2 (6.2)	5.2 (6.9)
POEM, mean (SD) [N]	19.8 (6.9) [37]	20.9 (5.7) [39]	20.4 (6.3) [76]	6.0 (5.4) [41]	8.7 (7.6) [39]	7.3 (6.7) [80]

Abbreviations: AD=atopic dermatitis; AE=adverse event; BSA=body surface area; EASI 50=achieving ≥50% improvement in the Eczema Area and Severity Index; EASI 75=achieving ≥75% improvement in the Eczema Area and Severity Index; EASI 90=achieving ≥90% improvement in the Eczema Area and Severity Index; IGA=Investigator's Global Assessment; ITT=intention-to-treat; LEBQ2W=lebrikizumab 250 mg every 2 weeks; LEBQ4W=lebrikizumab 250 mg every 4 weeks; LEBQ8W=lebrikizumab 250 mg every 8 weeks; N=number of patients in the analysis set; POEM=Patient-Oriented Eczema Measure; SD= standard deviation; TE ADA=treatment-emergent antidrug antibody; TEAE=treatment-emergent adverse event.

References

1. Simpson E, et al. JAAD. 2025;93(3):Suppl AB280.
2. Blauvelt A, et al. Br J Dermatol. 2023;188(6):740–8.
3. Charman CR, et al. Arch Dermatol. 2004;140(12):1513–9.

Disclosures: Jonathan I. Silverberg Jonathan I. Silverberg has received grants and/or personal fees from AbbVie, AFYX Therapeutics, Arena Pharmaceuticals, Asana BioSciences, Bluefin Biomedicine, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Kiniksa, LEO Pharma, Luna Pharma, Menlo Therapeutics, Novartis, Pfizer, Rapt Therapeutics, Regeneron, and Sanofi. **Vivian Laquer** conducts research for Abbvie, Acelyrin, Acrotech, Amgen, Argenx, Arcutis, Aslan, Biofrontera, Bristol Meyers Squibb, Cara, Dermavant, Eli Lilly and Company, Galderma, Horizon Therapeutics, Incyte, Janssen, Leo, Novartis, Padagis, Pfizer, Q32, Rapt, Sun, UCB, and Ventyx. **Peter Lio** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from AbbVie, AcBiome, Arcutis, Aveeno, Burt's Bees, Dermavant, Dermira, Eli Lilly and Company, Exeltis, Franklin Bioscience/Altus Labs, Incyte, IntraDerm, Johnson & Johnson, Kiniksa, La Roche-Posay/L'Oréal, LEO Pharma, Menlo Therapeutics, The National Eczema Association, Pfizer, Pierre Fabre, Realm Therapeutics, Sanofi, Therapiex, TopMD, UCB, Unilever, and Verrica Pharmaceuticals. **Kim Papp** has served as a consultant/speaker/scientific officer/has attended advisory boards/steering committees for, or received grants or honoraria from AbbVie, Acelyrin, Akros, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite Biopharma, Celltrion, Concert Pharmaceuticals, CorEvitas, Dermavant, Dice Pharmaceuticals, Dice Therapeutics, Eli Lilly and Company, Evelo Biosciences, Forbion, Galderma, Horizon Therapeutics, Incyte, Janssen, Kymab, Kyowa Hakko Kirin, Leo, Meiji Seika Pharma, Mitsubishi Pharma, Navigator Medicines, Nimbus Therapeutics, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, Takeda, Tarsus Pharmaceuticals, Inc., UCB, and Zai Lab Co., Ltd. **Alan D. Irvine** has served as a speaker and/or consultant for AbbVie, Alexion, Almirall, Apoilo, Arena, Dermavant, Galderma, Janssen, LEO Pharma, Eli Lilly and Company, Novartis, Pfizer, Regeneron, Sanofi, Stiryx, and UCB. **Andrew Blauvelt** has served as a speaker for and received honoraria from Eli Lilly and Company and UCB; has served as a scientific adviser to and received honoraria from AbbVie, Abeona, Aclaris, Affibody, Algos, 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, Highlightll Pharma, Incyte, InnoventBio, Janssen, Landos, LEO Pharma, Lipidio, Merck Microbion, Monte Rosa Therapeutics, Nektar, Novartis, Oruka Therapeutics, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Sphera Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Ventyx, Viboleme, and Xencor; has acted as a clinical study investigator for AbbVie, Acelyrin, Aclaris, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Concert, Dermavant, DermTech, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB Pharma, and Ventyx (for which his institution has received clinical study funds); and owns stock in Lipidio and Oruka. **Hany Elmaraghy, Louise DeLuca-Carter, Heidi Crane, Gaia Gallo, Evangeline Pierce**, and **Yuxin Ding** are employees and stockholders of Eli Lilly and Company. **Amy S. Paller** is an investigator for AbbVie, Biomendics, Dermavant, Eli Lilly, Incyte, Johnson & Johnson Innovative Medicine, Regeneron, TWI, UCB; a consultant for Abeona, Arcutis, BioCryst, Boehringer-Ingelheim, Castle Creek, Chieu, Dermavant, Johnson & Johnson Innovative Medicine, Krystal, LEO, Lilly, L'Oreal, MoonLake Immunotherapeutics, Pethecs, Quoin, Regeneron, and Sanofi and has served on the data safety monitoring board for AbbVie, Abeona, Biocryst, Daiichi Sankyo, and Galderma.

Medical writing assistance was provided by Kathy Oneacre, MA, CMPP, of Syneos Health and was funded by Eli Lilly and Company.

Funding: These studie, were funded by Dermira, a wholly owned subsidiary of Eli Lilly and Company. Almirall, S.A. has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including atopic dermatitis, in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world.

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