Long-Term Efficacy and Safety of Lebrikizumab Is Maintained in Patients With Moderate-to-Severe Atopic Dermatitis: Results Up to 3 Years From ADjoin

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OBJECTIVE

- To evaluate the long-term efficacy and safety of 3 years of continuous treatment of lebrikizumab, with or without TCS, in responders[a] from ADvocate1&2 (NCT04146363; NCT04178967)[1] and ADhere (NCT04250337)[2] enrolled into the extension study ADjoin (NCT04392154)[3]

[a]Responders in ADvocate1&2 and ADhere were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

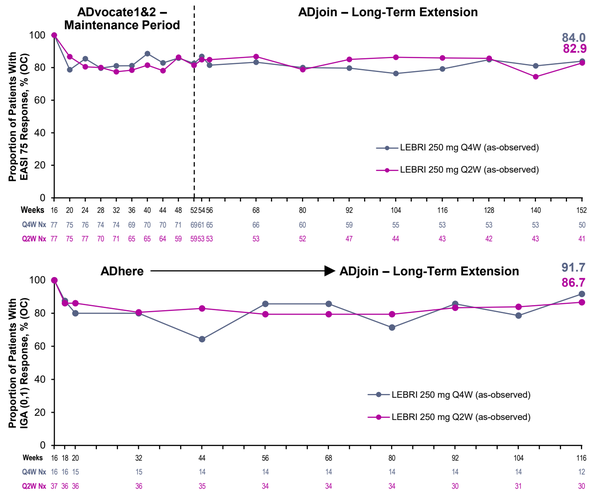
CONCLUSIONS

- Efficacy outcomes were maintained through 3 years of continuous lebrikizumab treatment, with or without TCS, in Week 16 responders in both the lebrikizumab 250 mg Q4W and Q2W dose regimens, with most patients maintaining clear or almost clear skin as assessed by IGA (0,1)
  - Additionally, most patients maintained EASI 75 and EASI 90 through 3 years of continuous lebrikizumab for both dose regimens
- Most patients did not require rescue therapy with continuous lebrikizumab treatment
- The safety profile of lebrikizumab in ADjoin was consistent with that observed in ADvocate1&2, ADhere, and other lebrikizumab studies in patients with moderate-to-severe AD
  - Rates of adverse events did not increase over time
- These long-term 3-year data demonstrate that lebrikizumab provides disease control over time, and helps inform clinical practice in a chronic and relapsing disease

Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

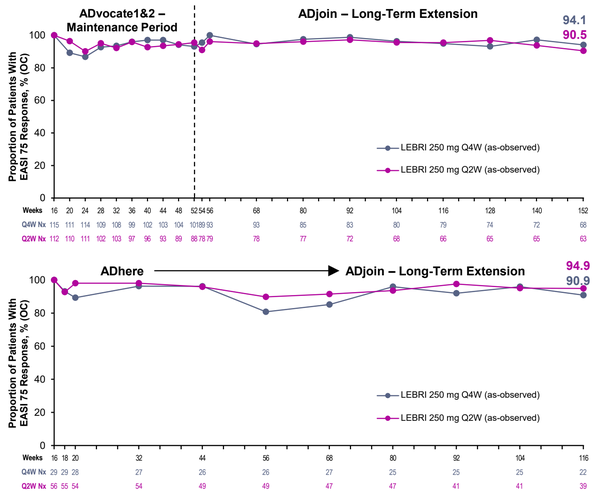
KEY RESULTS

IGA (0,1) Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



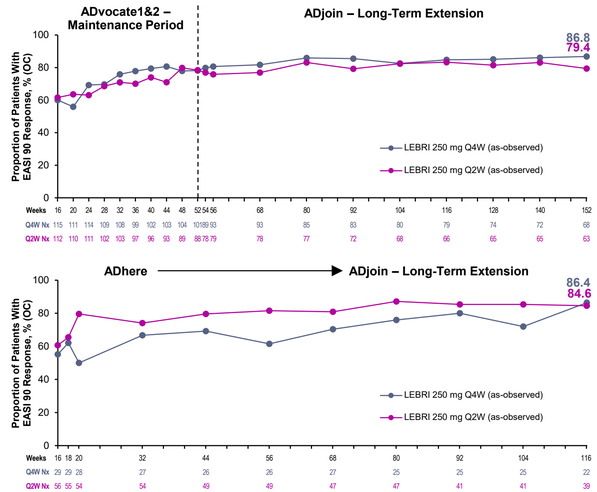
[a]Data from W16 responders achieving IGA (0,1) at W16 of parent study.

EASI 75 Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



[a]Data from W16 responders achieving EASI 75 at W16 of parent study.

EASI 90 Response Rates[a] Were Maintained and Improved in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



[a]Data from W16 responders achieving EASI 75 at W16 of parent study.

Methods

Outcomes

- Maintenance of response for:
  - IGA (0,1) (in Week 16 responders achieving IGA [0,1] at Week 16 of parent study)
  - EASI 75 (in Week 16 responders achieving EASI 75 at Week 16 of parent study)
  - EASI 90 (in Week 16 responders achieving EASI 75 at Week 16 of parent study

Note: Responders in ADvocate1&2 and ADhere were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

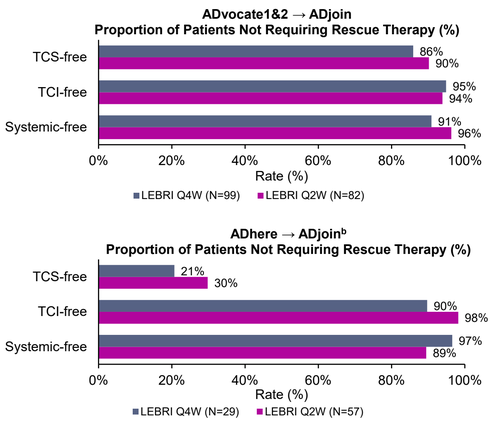
Statistical Analyses and Assessment

- Analysis population
  - *Modified intent-to-treat population*[a]: ADvocate1&2 → ADjoin: Lebrikizumab responders[b] who were randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W at Week 16, and enrolled into ADjoin with the same dose regimen at Week 52
  - *Modified intent-to-treat population*[a]: ADhere → ADjoin: Lebrikizumab responders[b] in ADhere who were randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W and enrolled into ADjoin at Week 16
- Efficacy analysis
  - As-observed (OC) analyses used all collected data regardless of rescue medication use
  - In addition to as-observed analyses, the non-responder imputation-multiple imputation[c] method was implemented to handle missing data. For each imputation process, 25 datasets with imputations were calculated using SAS® software version 9.4
  - ADvocate1&2 → ADjoin: Efficacy outcomes were assessed during the maintenance period of ADvocate1&2 (Weeks 16-52) and then for 100 weeks in ADjoin (Weeks 52-152)
  - ADhere → ADjoin: Efficacy outcomes were assessed up to 100 weeks in ADjoin (Weeks 16-116)
- Safety data were reported from ADjoin enrollment up to the data cut-off April 24, 2024

[a]Patients from one site participating in ADvocate2 and ADhere not included in the modified intent-to-treat population due to site audit findings; [b]Responders in ADvocate1&2 and ADhere were defined as those who achieved either EASI 75 or IGA (0,1) following 16 weeks of lebrikizumab 250 mg Q2W treatment without use of rescue therapy; [c]Patients who discontinued treatment due to lack of efficacy had values set to their parent study baseline value subsequent to this time. Observations after discontinuing treatment due to other reasons are set as missing and handled with multiple imputation.

Results

Most Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks Did Not Require Rescue Therapy[a]



[a]Rescue therapy included any topical or systemic therapy during the treatment period; [b]Patients enrolling into ADjoin from ADhere, continued or stopped TCS use, as needed.
Notes: Topical rescue therapy included TCS and TCI; systemic rescue therapy included systemic corticosteroids, immunosuppressants, biologics, phototherapy, and photochemotherapy. Majority of systemic rescue was used to treat TEAEs.

Safety Summary for Patients Entering ADjoin From ADvocate1&2 and ADhere

	ADvocate1&2 → ADjoin[a]		ADhere → ADjoin[a]	
	LEBRI 250 mg Q4W (N=99)	LEBRI 250 mg Q2W (N=82)	LEBRI 250 mg Q4W (N=29)	LEBRI 250 mg Q2W (N=57)
Patients with ≥1 TEAE	67 (67.7)	59 (72.0)	17 (58.6)	35 (61.4)
Mild	25 (25.3)	28 (34.1)	12 (41.4)	13 (22.8)
Moderate	36 (36.4)	28 (34.1)	4 (13.8)	21 (36.8)
Severe	6 (6.1)	3 (3.7)	1 (3.4)	1 (1.8)
Serious AE	3 (3.0)	3 (3.7)	2 (6.9)	3 (5.3)
Death	0	0	0	1 (1.8)[b]
Discontinuation from study treatment due to AE	3 (3.0)	2 (2.4)	0	2 (3.5)
TEAEs of Special Interest				
Conjunctivitis cluster[c]	5 (5.1)	3 (3.7)	3 (10.3)	8 (14.0)
Keratitis cluster[d]	1 (1.0)	0	0	0
Infections[e]	45 (45.5)	38 (46.3)	11 (37.9)	24 (42.1)
Potential opportunistic infections[f]	1 (1.0)	4 (4.9)	1 (3.4)	0
Skin infections	3 (3.0)	1 (1.2)	1 (3.4)	2 (3.5)
Herpes infections	3 (3.0)	6 (7.3)	1 (3.4)	2 (3.5)
Parasitic infections	0	0	1 (3.4)	0
Injection site reactions[g]	0	1 (1.2)	1 (3.4)	1 (1.8)
Malignancies[h]	0	0	0	1 (1.8)[i]
Hypersensitivity	1 (1.0)	2 (2.4)	1 (3.4)	1 (1.8)
Eosinophilia[j]	1 (1.0)	1 (1.2)	0	0

[a]Modified safety population from Week 0 of ADjoin through to data cut-off of April 24, 2024; [b]As reported by the investigator, a 55-year-old male patient died of natural causes on Study Day 462 and the event was assessed to be unrelated to study treatment; the patient had a medical history of hypertension, cardiac ablation, AD, insomnia, and gastroesophageal reflux; [c]Conjunctivitis cluster includes MedDRA preferred terms of conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, giant papillary conjunctivitis; [d]Keratitis cluster includes MedDRA preferred terms of keratitis, atopic keratoconjunctivitis, allergic keratitis, ulcerative keratitis, and vernal keratoconjunctivitis; [e]Infections are defined using the MedDRA preferred terms from the Infections and Infestations System Organ Class; [f]All potential opportunistic infections were assessed as not opportunistic based on the Winthrop criteria; [g]Injection site reactions are defined using MedDRA High Level Term of injection site reactions, excluding joint-related preferred terms; [h]Includes both NMSC and malignancies excluding NMSC; [i]The patient was diagnosed with basal cell carcinoma; [j]Eosinophilia is defined as 2 preferred terms of eosinophilia and allergic eosinophilia and the following preferred terms under the high-level term of white blood cell analysis: eosinophil count abnormal eosinophil count increased, and eosinophil percentage increased. No eosinophilic-related disorders were reported.

Notes: Data are presented as n (%). A TEAE is defined as an event that first occurred or worsened in severity after baseline and on or prior to the date of the last visit within the specified treatment period. Patients with multiple occurrences of these categories are counted once for each category. Patients may be counted in >1 category. Deaths are also included as serious AEs and discontinuations due to AEs. MedDRA Version 27.0.

References: 1. Blauvelt A, et al. *Br J Dermatol.* 2023;188:740-748.
2. Simpson E, et al. *JAMA Dermatol.* 2023;159:182-191.
3. Guttman-Yassky E, et al. Poster presented at: *Fall CDC 2023.* Abstract 494.

Abbreviations: *AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 75=at least 75% improvement from baseline in EASI; EASI 90=at least 90% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; LEBRI=lebrikizumab; NMSC=non-melanoma skin cancer; NRS=Numeric Rating Scale; Nx=number of patients with non-missing values; OC=observed case; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization; SAE=serious adverse event; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TEAE=treatment-emergent AE; W=Week.*

Disclosures: E. Guttman-Yassky is an employee of: Mount Sinai; and has received research funds (grants paid to institution) from and/or been a consultant for: AbbVie, Almirall, Amgen, AnaptysBio, Asana BioSciences, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Connect Biopharma, Eli Lilly and Company, EMD Serono, Evidera, Galderma, Incyte Corporation, Innovaderm Research, Janssen, Kiniksa, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, Sato Pharmaceutical, TARGET PharmaSolutions, UCB Pharma, and Ventyx Biosciences; **A. Irvine** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Connect BioPharma, Eli Lilly and Company, LEO Pharma, OM Pharma, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi; **E. Simpson** has received grants (or serves as principal investigator role) for: AbbVie, Acrotech, Amgen, Arcutis, ASLAN Pharmaceuticals, Castle Biosciences, CorEvitas, Dermavant, Dermira, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Kirin, LEO Pharma, National Jewish Health, Pfizer, Regeneron, Sanofi, TARGET PharmaSolutions, VeriSkin; and personal fees from: AbbVie, Amgen, Arcutis, Areteia Therapeutics, Bristol Myers Squibb, CorEvitas, Corvus Pharmaceuticals, Dermira, Eli Lilly and Company, Evelo Biosciences, FIDE, Forte Biosciences, Galderma, GlaxoSmithKline, Gilead Sciences, Impetus Healthcare, Incyte Corporation, Innovaderm Reche, Janssen, Johnson & Johnson, Kyowa Kirin Pharmaceutical Development, LEO Pharma, Merck, NUMAB Therapeutics AG, Pfizer, Physicians World LLC, PRIME, Recludix Pharma, Regeneron, Roivant Sciences, Sanofi Genzyme, Sitryx Therapeutics, Trevi Therapeutics, and Valeant Pharmaceuticals; **M. Gooderham** has been an investigator, speaker, and/or advisor for: AbbVie, Akros Pharma, Alumis, Amgen, Arcutis, Aristea Therapeutics, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Merck, MoonLake Immunotherapeutics, Nimbus Therapeutics, Novartis, Pfizer, Regeneron, Reistone Biopharma, Roche, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Vyne Therapeutics; **S. Weidinger** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Eli Lilly and Company, Kymab, LEO Pharma, Novartis, Pfizer, Regeneron, and Sanofi; and has received research grants from: La Roche-Posay, Pfizer, and Sanofi; **L. Spelman** has been a consultant, and/or scientific advisor, and/or investigator, and/or scientific officer, and/or speaker for: AbbVie, Akesio Biopharma, Alphyn Biologics, Amgen, Anacor, Ascend, ASLAN Pharmaceuticals, Astellas, AstraZeneca, Blaze Bioscience, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Connect Biopharmaceuticals Australia, Dermira, Eli Lilly and Company, Evelo Biosciences, Galderma, Genentech, GlaxoSmithKline, Hexima, Immunic Therapeutics, Invion, Janssen, Kiniksa Pharmaceuticals, Kobiolab, LEO Pharma, Lipidio Pharma, Mayne Pharma, MedImmune, Merck Sharp & Dohme, Merck Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Reistone Biopharma, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma ANZ, Trius, UCB Pharma, Vyne Therapeutics, and Zai Lab; **J. 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; **H. Crane, D. Elmaraghy, L. DeLuca-Carter, M. L. Buziqui Piruzeli, C. Hu,** and **E. Pierce** are employees and stockholders of: Eli Lilly and Company; **H. Agell** is an employee of: Almirall; **D. Thaçi** has received personal fees from: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Janssen Cilag, Kyowa Kirin, LEO Pharma, NewBridge Pharmaceuticals, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, and UCB Pharma; and has received grants from: AbbVie, LEO Pharma, and Novartis. Medical writing assistance was provided by Thai Cao, MS, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

These studies 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 outside of Europe.

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