# Efficacy and Safety of Lebrikizumab Is Maintained to Two Years in Patients With Moderate-to-Severe Atopic Dermatitis


**Emma Guttman-Yassky[1], Stephan Weidinger[2], Eric Simpson[3], Melinda Gooderham[4], Alan Irvine[5], Lynda Spelman[6], Jonathan Silverberg[7], Hany Elmaraghy[8], Louise DeLuca-Carter[8], Maria Lucia Buziqui Piruzeli[8], Chaoran Hu[8], Fan Emily Yang[8], Evangeline Pierce[8], Laia Bardolet[9], Diamant Thaci[10]**

[1]Icahn School of Medicine at Mount Sinai, New York, USA; [2]University Hospital Schleswig-Holstein, Kiel, Germany; [3]Oregon Health & Science University, Portland, USA; [4]SKiN for Dermatology, Probity Medical Research and Queen's University, Peterborough, Canada; [5]Children's Health Ireland, Dublin, Ireland; [6]Veracity Clinical Research, Brisbane, Australia, and Probity Medical Research, Woolloongabba, Queensland, Australia; [7]George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [8]Eli Lilly and Company, Indianapolis, USA; [9]Almirall S.A, Barcelona, Spain; [10]Institute and Comprehensive Center for Inflammatory Medicine at the University of Lübeck, Lübeck, Germany


## BACKGROUND

- Lebrikizumab is a novel monoclonal antibody that binds with high affinity and slow off-rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[1]
- The efficacy and safety of lebrikizumab have been investigated in a number of Phase 3 trials including: ADvocate1 (NCT04146363), ADvocate2 (NCT04178967), ADhere (NCT04250337), and ADjoin (NCT04392154)[2-4]
- Lebrikizumab (with or without TCS) was efficacious in providing clinically meaningful improvements in the signs and symptoms of AD through Week 52 in adult and adolescent patients with moderate-to-severe AD[2-4]

## OBJECTIVE

- To evaluate the efficacy and safety of lebrikizumab through 2 years in the long-term extension study ADjoin in responders[a] enrolled from the parent studies ADvocate1&2 and ADhere

[a] Responders in ADvocate 1&2 and ADhere were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250mg Q2W treatment without use of rescue therapy
Note: Statistical results of the primary and major secondary endpoints for ADvocate1&2 and ADhere were confirmed through replicate statistical programming, validation, and quality reviews[2-4]

## SUMMARY OF KEY FINDINGS

**Efficacy Outcomes Were Maintained Through 2 Years of Treatment With Lebrikizumab**

| Outcome, % | ADvocate 1&2 → ADjoin | ADhere → ADjoin |
|---|---|---|
| | LEBRI 250 mg Q4W (N=99) | LEBRI 250 mg Q4W (N=29) |
| IGA (0,1) | 76.4 | 78.6 |
| EASI 75 | 96.3 | 96.0 |
| EASI 90 | 82.5 | 72.0 |
| Pruritus NRS ≥4-point improvement | 89.7 | 90.0[a] |

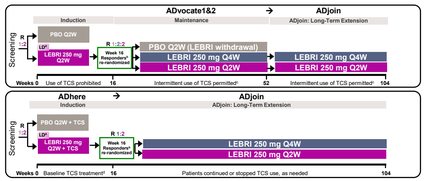
[a] All outcomes shown through 104 weeks apart from Pruritus NRS ≥4-point improvement for ADhere → ADjoin study (68 weeks)

## CONCLUSIONS

- Lebrikizumab provided durable efficacy in skin and itch outcomes through 2 years of treatment with both monthly and 2-week dosing
- The lebrikizumab safety data in ADjoin is consistent with previous lebrikizumab studies in patients with moderate-to-severe AD, and no new safety signals were noted

## METHODS

### Study Design




[a] LEBRI-treated patients received a 500-mg LD at Weeks 0 and 2; [b] Responders in ADvocate 1&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; [c] Patients who required short-term systemic treatment for AD in the Maintenance Period were assessed on a case-by-case basis; [d] TCS treatment was initiated at baseline in all patients and was tapered or stopped, as needed, based on treatment response

### Key Eligibility Criteria

#### Parent Study (ADvocate 1&2 or ADhere)

- Adults (≥18 years) and adolescents (≥12 to <18 years; weight ≥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 all the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - BSA involvement ≥10%

### ADjoin

- Patients could be included if they completed the study treatments and the last patient visit of the parent trial
- Patients were excluded if in the parent trial they:
  - Developed an SAE related to lebrikizumab, or an AE related to lebrikizumab that led to treatment discontinuation, which indicated that continued treatment with lebrikizumab could present an unreasonable risk for the patient
- Conditions in the previous parent study were consistent with protocol-defined criteria for permanent study drug discontinuation, if deemed related to lebrikizumab or led to investigator- or sponsor-initiated withdrawal of patient from the study

### 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)
  - Pruritus NRS ≥4-point improvement (in Week 16 responders achieving Pruritus NRS ≥4-point improvement at Week 16 of parent study and with Pruritus NRS ≥4 at parent study baseline)

Note: Responders in ADvocate 1&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

- Analysis population
  - ADvocate 1&2 → ADjoin: Lebrikizumab responders[a] were randomized to LEBRI 250 mg Q2W or LEBRI 250 mg Q4W at Week 16, and enrolled into ADjoin with the same dose regimen at Week 52
  - ADhere → ADjoin: Lebrikizumab responders[a] in ADhere were randomized to LEBRI 250 mg Q2W or LEBRI 250 mg Q4W and enrolled into ADjoin at Week 16
- Efficacy analysis
  - As observed analyses used all collected data regardless of rescue medication use; response rates were reported as descriptive
  - ADvocate 1&2 → ADjoin: Efficacy outcomes were assessed during the Maintenance Period of ADvocate 1&2 (Week 16-52) and then for 52 weeks in ADjoin (Week 52-104)
  - ADhere → ADjoin: Efficacy outcomes were assessed up to 88 weeks in ADjoin (Week 16-104)
- Safety data were reported from ADjoin enrollment up to the data cut-off April 14, 2023

[a] Responders in ADvocate 1&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

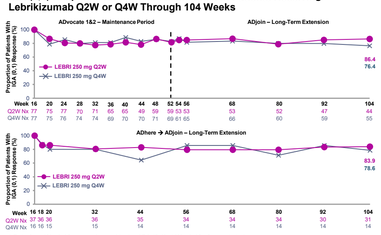
## RESULTS

**Baseline Demographics and Disease Characteristics for Parent Studies**

| | ADvocate 1&2 → ADjoin | | ADhere → ADjoin | |
|---|---|---|---|---|
| | LEBRI 250 mg Q4W (N=99) | LEBRI 250 mg Q2W (N=82) | LEBRI 250 mg Q4W (N=29) | LEBRI 250 mg Q2W (N=57) |
| Age, years | 35.8 (17.2) | 35.5 (16.2) | 29.8 (15.9) | 37.0 (19.9) |
| Adolescent (≥12 to <18), n (%) | 14(14.1) | 11 (13.4) | 10 (34.5) | 15 (26.3) |
| Adult (≥18), n (%) | 85 (85.9) | 71 (86.6) | 19 (65.5) | 42 (73.7) |
| Female, n (%) | 60 (60.6) | 42 (51.2) | 15 (51.7) | 27 (47.4) |
| Region, n (%) | | | | |
| USA | 41 (41.4) | 32 (39.0) | 22 (75.9) | 38 (66.7) |
| Europe | 33 (33.3) | 32 (39.0) | 6 (20.7) | 13 (22.8) |
| Rest of the world | 25 (25.3) | 18 (22.0) | 1 (3.4) | 6 (10.5) |
| BMI, kg/m² | 26.4 (6.3) | 26.4 (6.2) | 25.2 (6.9) | 26.3 (6.6) |
| Disease duration since AD onset, years | 22.4 (14.2) | 23.6 (14.7) | 21.7 (14.1) | 21.6 (18.2) |
| IGA, n (%) | | | | |
| 3 (Moderate) | 63 (63.6) | 50 (61.0) | 20 (69.0) | 39 (68.4) |
| 4 (Severe) | 36 (36.4) | 32 (39.0) | 9 (31.0) | 18 (31.6) |
| EASI | 28.9 (12.2) | 29.2 (11.2) | 26.2 (7.8) | 28.2 (11.1) |
| Pruritus NRS | | | | |
| <4, n (%) | 9 (9.2) | 3 (3.7) | 2 (7.4) | 3 (5.5) |
| ≥4, n (%) | 89 (90.8) | 79 (96.3) | 25 (92.6) | 52 (94.5) |

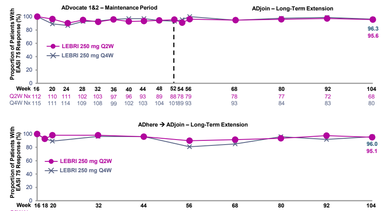
Note: Data are mean (SD) unless stated

**IGA (0,1) Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q2W or Q4W Through 104 Weeks**



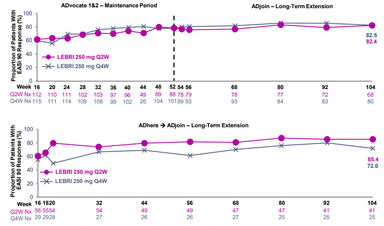

[a] Data from Week 16 responders achieving IGA (0,1) at Week 16 of parent study

**EASI 75 Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q2W or Q4W Through 104 Weeks**



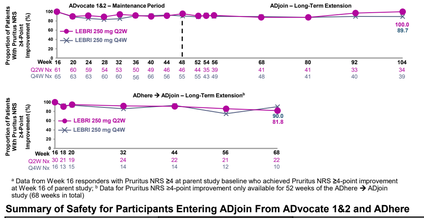

[a] Data from Week 16 responders achieving EASI 75 at Week 16 of parent study

**EASI 90 Response Rates[a] Were Improved and Maintained in Patients Receiving Lebrikizumab Q2W or Q4W Through 104 Weeks**




[a] Data from Week 16 responders achieving EASI 75 at Week 16 of parent study

**Pruritus NRS ≥4-Point Improvement[a] Rates Were Maintained in Patients Receiving Long-Term Treatment With Lebrikizumab Q2W or Q4W**




[a] Data from Week 16 responders with Pruritus NRS ≥4 at parent study baseline who achieved Pruritus NRS ≥4-point improvement at Week 16 of parent study; [b] Data for Pruritus NRS ≥4-point improvement only available for 52 weeks of the ADhere → ADjoin study (68 weeks in total)

**Summary of Safety for Participants Entering ADjoin From ADvocate 1&2 and ADhere**

| | ADvocate 1&2 → ADjoin | | ADhere → Adjoin | |
|---|---|---|---|---|
| | 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 | 58 (58.6) | 56 (68.3) | 17 (58.6) | 35 (61.4) |
| Mild | 26 (26.3) | 31 (37.8) | 12 (41.4) | 15 (26.3) |
| Moderate | 27 (27.3) | 22 (26.8) | 4 (13.8) | 19 (33.3) |
| Severe | 5 (5.1) | 3 (3.7) | 1 (3.4) | 1 (1.8) |
| Serious AE | 3 (3.0) | 2 (2.4) | 2 (6.9) | 3 (5.3) |
| Death | 0 | 0 | 0 | 1 (1.8)[a] |
| Discontinuation from study treatment due to AE | 2 (2.0) | 2 (2.4) | 0 | 2 (3.5) |
| Conjunctivitis cluster[b] | 4 (4.0) | 2 (2.4) | 3 (10.3) | 7 (12.3) |
| Keratitis cluster[c] | 0 | 0 | 0 | 0 |
| Infections | 38 (38.4) | 34 (41.5) | 11 (37.9) | 24 (42.1) |
| Potential opportunistic infections[d] | 1 (1.0) | 2 (2.4) | 1 (3.4) | 0 |
| Herpes infections | 3 (3.0) | 5 (6.1) | 1 (3.4) | 2 (3.5) |
| Parasitic infections | 0 | 0 | 1 (3.4) | 0 |
| Injection-site reactions | 0 | 1 (1.2) | 1 (3.4) | 1 (1.8) |
| Malignancies[e] | 0 | 0 | 0 | 0 |
| Anaphylactic reactions | 0 | 0 | 0 | 0 |
| Eosinophilia[f] | 0 | 1 (1.2) | 0 | 0 |

[a] As reported by the investigator, a 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; [b] The preferred terms of conjunctivitis, conjunctivitis allergic and conjunctivitis viral, were reported under the conjunctivitis cluster; [c] Includes preferred terms of keratitis, atopic keratoconjunctivitis, allergic keratitis, ulcerative keratitis, and vernal keratoconjunctivitis; [d] All potential opportunistic infections were assessed as not opportunistic based on the Winthrop criteria; [e] Includes both NMSC and malignancies excluding NMSC; [f] Eosinophilia reported as a TEAE
Note: Data are n (%)


**REFERENCES**

1. Okragly AJ, et al. *Dermatol Ther (Heidelb).* 2023;13:1535-1547. 2. Silverberg JI, et al. *N Engl J Med.* 2023;388:1080-1091. 3. Simpson E, et al. *JAMA Dermatol.* 2023;159:182-191. 4. Blauvelt A, et al. *Br J Dermatol.* 2023;188:740-748.


**ABBREVIATIONS**

*AD=atopic dermatitis; AE=adverse event; 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; IL=interleukin; LD=loading dose; LEBRI=lebrikizumab; NMSC=non-melanoma skin cancer; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation; TCS=topical corticosteroids; TEAE=treatment-emergent adverse event*


**DISCLOSURES**

**E. Guttman-Yassky** is a consultant for: AbbVie, Almirall, Amgen, Asana BioSciences, Boehringer Ingelheim, Cara Therapeutics, Celgene, Concert Pharmaceuticals, DBV Technologies, Dermira, DS Biopharma, Eli Lilly and Company, EMD Serono, Escalier Biosciences, Galderma, Glenmark Pharmaceuticals, Kyowa Kirin, LEO Pharma, Mitsubishi Tanabe, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, Sienna Biopharmaceuticals, and UNION Therapeutics; and reports institute grants for research from: AbbVie, Almirall, Amgen, AnaptysBio, Asana BioSciences, Boehringer Ingelheim, Celgene, Dermavant, DS Biopharma, Eli Lilly and Company, Galderma, Glenmark Pharmaceuticals, Innovaderm Research, Janssen, Kiniska Pharmaceuticals, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar Therapeutics, Regeneron, Sienna Biopharmaceuticals, UCB Pharma, and UNION Therapeutics; **S. Weidinger** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Eli Lilly and Company, Galderma, Kymab, LEO Pharma, Pfizer, Regeneron, and Sanofi; and has received research grants from: LEO Pharma, Pfizer, and Sanofi; **E. Simpson** reports personal fees from: AbbVie, Amgen, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Boston Consulting Group, Collective Acumen, Dermira, Eli Lilly and Company, Evidera, Excerpta Medica, Forte Biosciences, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, Kyowa Kirin, LEO Pharma, Medscape, Merck, Pfizer, Physicians World, Regeneron, Roivant Sciences, Sanofi Genzyme, Trevi Therapeutics, Valeant Pharmaceuticals, and WebMD; and reports grants from or serves in a Principal Investigator role for: AbbVie, Amgen, Arcutis, ASLAN Pharmaceuticals, CorEvitas, Dermavant, Dermira, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Hakko Kirin, LEO Pharma, Pfizer, Regeneron, Sanofi, and TARGET; **M. Gooderham** has been an investigator, speaker, consultant, or advisory board member for: AbbVie, Akros Pharma, Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Merck, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Valeant Pharmaceuticals/Bausch Health; **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; **L. Spelman** has been a consultant, and/or scientific adviser, and/or investigator, and/or scientific officer, and/or speaker for: AbbVie, Akesobio, Alphyn Biologics, Amgen, Anacor, Ascend, Aslan, Astellas, AstraZeneca, Blaze Bioscience, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Connect Biopharmaceuticals Australia, Dermira, Eli Lilly and Company, Evelo Biosciences, Galderma, Genentech, GSK, Hexima, Immunic Therapeutics, Invion, Janssen, Kiniksa Pharmaceuticals, Kobiolab, LEO Pharma, Lipidio, Mayne, Medimmune, Merck (MSD), Merck Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Reistone, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma ANZ, Trius, UCB Pharma, Vyne Therapeutics and Zai Lab; **J. I. Silverberg** has received grants and/or personal fees from: AbbVie, AFYX Therapeutics, Almirall, Arena Pharmaceuticals, Asana BioSciences, Bluefin Biomedicine, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Kiniksa Pharmaceuticals, LEO Pharma, Luna Pharma, Menlo Therapeutics, Novartis, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi; **H. Elmaraghy**, **L. DeLuca-Carter**, **C. R. Natalie**, **M.L. Buziqui Piruzeli**, **C. Hu**, **F.E. Yang**, and **E. Pierce** are employees and stockholders of: Eli Lilly and Company; **L. Bardolet** is an employee of Almirall; **D. Thaci** has received personal fees from: AbbVie, Almirall, Amgen, Asana BioSciences, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, Janssen Cilag, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, and UCB Pharma; and has received grants from: AbbVie, LEO Pharma, and Novartis

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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.