Lebrikizumab Confirms a Consistent Safety Profile in Adults and Adolescents With Moderate-to-Severe Atopic Dermatitis: Data From 11 Trials With Over 3000 Patient-Years of Exposure

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OBJECTIVE

- To provide updated long-term safety data for lebrikizumab treatment in adults and adolescents with moderate-to-severe AD, using data from 11 Phase 2/3 clinical trials

CONCLUSIONS

- This study confirms a safety profile for lebrikizumab that is consistent with previously reported data from the lebrikizumab clinical trial program in adolescents and adults with AD[1]
- Overall, TEAEs did not increase with longer duration of exposure to lebrikizumab
- No new safety signals were detected

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KEY RESULTS

Most TEAEs Were Mild or Moderate in Severity and Did Not Lead to Treatment Discontinuations

	PBO (N=719) PYE=205.9	LEBRI 250 mg Q2W (N=1251) PYE=375.8	ALL LEBRI (N=2415) PYE=3167.8
	n (adj%) [adj IR]	n (adj%) [adj IR]	n (adj%) [adj IR]
Patients with ≥1 TEAE	368 (51.9) [284.2]	661 (52.7) [276.4]	1681 (69.6) [133.2]
Mild	198 (27.6)	366 (29.3)	778 (32.2)
Moderate	144 (20.7)	268 (21.3)	784 (32.5)
Severe	26 (3.6)	27 (2.2)	119 (4.9)
Death[a]	1 (0.1)	0	4 (0.2)
Serious AE	12 (1.7) [5.9]	15 (1.2) [3.9]	90 (3.7) [2.9]
AE leading to treatment discontinuation	12 (1.5) [5.4]	25 (2.0) [6.8]	100 (4.1) [3.2]

[a]1 death due to myocardial infarction in a 56-year-old male in the PBO group during the 16-week induction of ADvocate2 and 4 deaths in participants treated with LEBRI 250 mg Q2W (a 74-year-old male due to pancreatic cancer, a 64-year-old male due to metastatic pancreatic cancer, a 56-year-old male due to natural causes, and a 13-year-old male due to cardiac arrest). No deaths were considered related to study drug by investigators.

- In the PBO-Controlled dataset, the frequency of TEAEs was similar between treatment groups
- Frequency of serious AEs were low in the PBO-Controlled dataset and IR decreased with longer lebrikizumab exposure

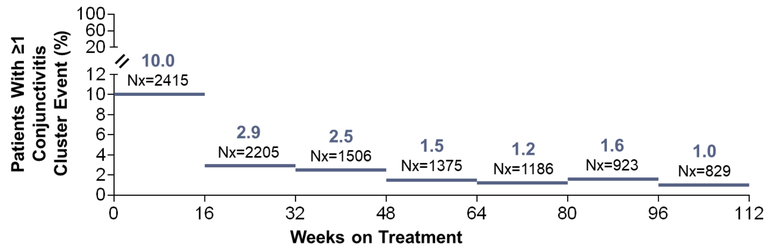
AEs of Special Interest Did Not Increase With Longer Duration of Exposure

	PBO (N=719) PYE=205.9	LEBRI 250 mg Q2W (N=1251) PYE=375.8	ALL LEBRI (N=2415) PYE=3167.8
	n (adj%) [adj IR]	n (adj%) [adj IR]	n (adj%) [adj IR]
Conjunctivitis cluster[a]	21 (3.0) [10.7]	148 (11.7) [43.1]	345 (14.3) [12.3]
Mild	15 (2.1)	81 (6.4)	187 (7.7)
Moderate	6 (0.9)	67 (5.3)	151 (6.3)
Severe	0	0	7 (0.3)
Injection site reactions[b]	12 (1.6) [5.7]	35 (2.9) [9.7]	87 (3.6) [2.8]
Herpes zoster	1 (0.1) [0.4]	5 (0.4) [1.3]	25 (1.0) [0.8]

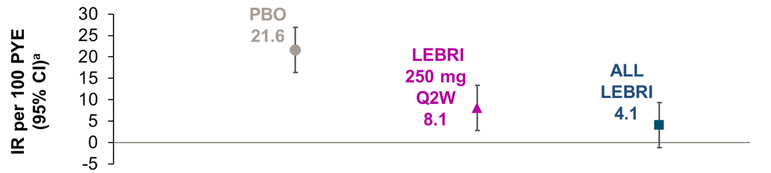
[a]Conjunctivitis cluster was defined by MedDRA preferred terms of conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, and giant papillary conjunctivitis; Conjunctivitis (single MedDRA preferred term of conjunctivitis) leading to treatment discontinuation was reported by 1 patient in the PBO group (adj IR=0.5), 3 patients in the LEBRI 250 mg Q2W group (adj IR=0.8), and 13 patients in the ALL LEBRI dataset (IR=0.4); [b]Injection site reactions were defined using MedDRA high-level term of injection site reactions excluding joint-related preferred terms.

- None of the herpes zoster events were severe and none led to discontinuation.
- No eosinophilic-related disorders were reported

Conjunctivitis Cluster: Frequency Decreased With Longer Duration of Lebrikizumab Exposure



Skin Infections: IR Was Lower in the Lebrikizumab Q2W Group Than in the Placebo Group and Decreased With Longer Duration of Lebrikizumab Exposure (ALL LEBRI Dataset)

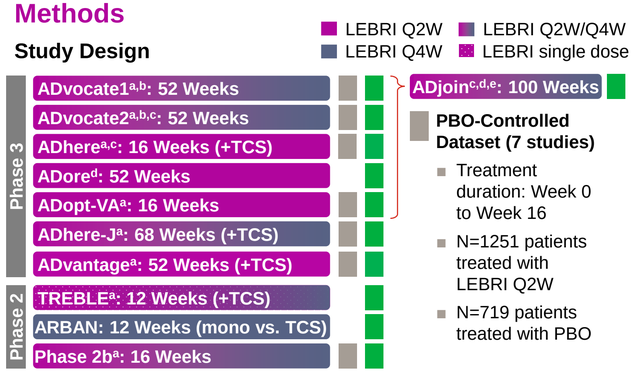


	PBO (N=719; PYE=205.9)	LEBRI 250 mg Q2W (N=1251; PYE=375.8)	Any LEBRI (N=2415; PYE=3167.8)
Patients with ≥1 event, n (%)	43 (6.0)	30 (2.4)	124 (5.1)
PYR	199.1	370.0	3051.1

[a]IR and 95% CI (not adjusted by study size).
Note: Skin infections were defined using the MedDRA high-level term of "skin structures and soft tissue infections" and included the following preferred terms: cellulitis, eczema impetiginous, folliculitis, staphylococcal skin infection, cellulitis staphylococcal, furuncle, erysipelas, and fungal skin infection; IR was defined as the number of patients experiencing the adverse event divided by the event-specific exposure to treatment (exposure time up to the event for patients with the event and exposure time up to the end of the period for patients without the event) multiplied by 100, in years.

Methods

Study Design



[a]PBO-Controlled; [b]TCS/TCI use was permitted during the Maintenance Period of ADvocate1 and 2; [c]Modified safety population, defined as patients who received ≥1 dose of study treatment, excluding 45 patients from 2 study sites (17 patients in ADhere who continued in ADjoin [site 1], 18 patients in ADvocate2 who continued in ADjoin [site 1], 3 patients in ADjoin [site 1], 7 patients in ADopt-VA [2 patients from site 1 and 5 patients from site 2]), as the patient eligibility criteria could not be confirmed; [d]TCS/TCI use was permitted; [e]This study has direct entry patients too.
Note: Database lock date was 31 October 2023.

ALL LEBRI Dataset (11 studies)

- Treatment duration: Any time from any of the 11 studies
- N=2415 patients who received ≥1 dose of LEBRI (any LEBRI dose)

Assessments and Statistical Analyses

- Integrated data from 11 Phase 2/3 clinical trials are presented
- The safety assessment for lebrikizumab treatment in adults and adolescents with moderate-to-severe AD was based on patients who received ≥1 dose of study treatment, excluding 45 patients from 2 study sites,[a] as the patient eligibility criteria could not be confirmed
- Percentage and exposure adjusted IR[b] are provided for the PBO-Controlled and ALL LEBRI datasets, with study-size adjusted values provided for the PBO-Controlled dataset, as studies had different randomization ratios

[a]17 patients in ADhere who continued in ADjoin (site 1), 18 patients in ADvocate2 who continued in ADjoin (site 1), 3 patients in ADjoin (site 1), and 7 patients in ADopt-VA (2 patients from site 1 and 5 patients from site 2); [b]IR is defined as the number of patients experiencing the adverse event divided by the event-specific exposure to treatment (exposure time up to the event for patients with the event and exposure time up to the end of the period for patients without the event) multiplied by 100, in years.

Results

- This analysis provides data for a total of 2415 patients and 3168 patient-years in the ALL LEBRI dataset
  - Median exposure: 391.0 days
  - Maximum exposure: 1138 days (3.12 years)
- Compared with the previous integrated data analysis[1] that reported data from 10 trials[a], this analysis includes data from:
  - 1 additional study: ADvantage[b]
  - Approximately 1 additional year from ADjoin
  - Additional data from the now-completed ADhere-J and ADopt-VA

[a]ADvocate1, ADvocate2, ADhere, ADore, ADopt-VA, ADhere-J, ADjoin, TREBLE, ARBAN, and Phase 2b; [b]European study.

Disclosures: L. Stein Gold is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma; **E. Simpson** reports personal fees from: AbbVie, Advances in Cosmetic Medical Dermatology Hawaii, Amgen, AOBiome, Arcutis, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Bristol Myers Squibb, CorEvitas, Dermira, Eli Lilly and Company, Evelo Biosciences, Excerpta Medica, FIDE, Forte Biosciences, Galderma, GlaxoSmithKline, Impetus Healthcare, Incyte Corporation, Innovaderm Research, Janssen, Johnson & Johnson, Kyowa Kirin, LEO Pharma, Maui Derm, Medscape, Merck, MJH Holding, MLG Operating, Pfizer, Physicians World, PRIME, Recludix Pharma, Regeneron, Revolutionizing Atopic Dermatitis, Roivant Sciences, Sanofi, Trevi Therapeutics, Valeant Pharmaceuticals, Vindico Medical Education, and WebMD; and has received grants or serves as principal investigator for: AbbVie, Acrotech, Amgen, Arcutis, ASLAN Pharmaceuticals, Castle, CorEvitas, Dermira, Dermavant, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Kirin, National Jewish Health, LEO Pharma, Pfizer, Regeneron, Sanofi, Target, and VeriSkin. These potential conflicts of interest have been reviewed and managed by Oregon Health & Science University; **D. Thaci** has received personal fees from: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celtrion, Eli Lilly and Company, Janssen Cilag, Kyowa Kirin, LEO Pharma, NewBridge Pharmaceuticals, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, and UCB Pharma; and has received grants from: AbbVie, LEO Pharma, and Novartis; **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; **M. de Bruin-Weller** has served as a consultant, speaker, advisor, and/or advisory board member for: AbbVie, Almirall, Amgen, ASLAN Pharmaceuticals, Eli Lilly and Company, Galderma, LEO Pharma, Pfizer, Regeneron, and Sanofi; **M. L. Buziqui Piruzeli**, **H. Elmraghy**, **S. Montmayeur**, and **G. Gallo** are employees and shareholders of: Eli Lilly and Company; **J. Zhong** is an employee of: IQVIA; **R. Coll** is an employee of: Almirall; **M. G. Lebwohl** is an employee of: Mount Sinai and receives research funds from: AbbVie, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Clexio Biosciences, Dermavant Sciences, Eli Lilly and Company, Incyte Corporation, Inozyme, Janssen, Pfizer, Sanofi Regeneron, and UCB Pharma; and is a consultant for Almirall, AltruBio, Apogee, Arcutis, AstraZeneca, Atomwise, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celtrion, CorEvitas, Dermavant, Dermsquared, Evommune, FIDE, Forte Biosciences, Galderma, Genentech, Incyte Corporation, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi Regeneron, Seanergy, STRATA Skin Sciences, Takeda, Trevi Therapeutics, and Verrica Pharmaceuticals

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Reference: 1. Stein Gold L, et al. Poster presented at *AAD 2024*. Presentation 52041.

Abbreviations: *AD=atopic dermatitis; adj %=study size-adjusted percentage; adj IR=study size-adjusted IR; AE=adverse event; CI=confidence interval; IR=incidence rate; LEBRI=lebrikizumab; MedDRA=Medical Dictionary for Regulatory Activities; mono=monotherapy; N=number of patients in the analysis set; Nx=number of patients at risk in the specified category; PBO=placebo; PYE=patient-years at risk; Q2W=every 2 weeks; Q4W=every 4 weeks; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TEAE=treatment-emergent AE*

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