Conjunctivitis Does Not Increase With Longer Duration of Lebrikizumab Exposure in Patients With Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

- AD is a chronic skin disease that can be a serious burden, affecting sleep, daily activities, and social relationships[1]
- Lebrikizumab is a 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[2]
- Integrated safety data for lebrikizumab treatment in moderate-to-severe AD has been previously published in Phase 2 and 3 clinical trials[3-6]
- Conjunctivitis and keratitis are events of special interest in moderate-to-severe AD and are reported more frequently in lebrikizumab-treated patients[7]

OBJECTIVE

- To further characterize patient-reported conjunctivitis and keratitis AEs in patients with moderate-to-severe AD participating in lebrikizumab clinical trials for AD

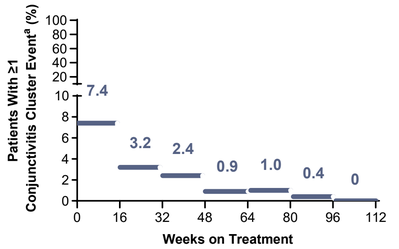
KEY RESULTS

Incidence Rate of Conjunctivitis and Keratitis Clusters Did Not Increase With Longer Duration of Exposure

Patients With ≥1 Event	PBO-Controlled, Weeks 0-16		All LEBRI
	PBO (N=404) PYE=113.8 n (%)[a]	LEBRI 250 mg Q2W (N=783) PYE=233.3 n (%)[a]	Any LEBRI Dose (N=1720) PYE=1637.0 n (%)
Conjunctivitis cluster, [IR][a]	**10 (2.5[b]) [8.9]**	**67 (8.5[b]) [30.6]**	**183 (10.6) [12.2]**
Conjunctivitis	7 (1.8)	51 (6.5)	112 (6.5)
Conjunctivitis allergic	3 (0.7)	14 (1.8)	70 (4.1)
Conjunctivitis bacterial	0	3 (0.4)	11 (0.6)
Keratitis cluster, [IR][a]	**1 (0.3[c]) [0.9]**	**5 (0.6[c]) [2.2]**	**9 (0.5) [0.6]**
Keratitis	1 (0.3)	1 (0.1)	3 (0.2)
Vernal keratoconjunctivitis	0	2 (0.2)	3 (0.2)
Atopic keratoconjunctivitis	0	2 (0.3)	3 (0.2)

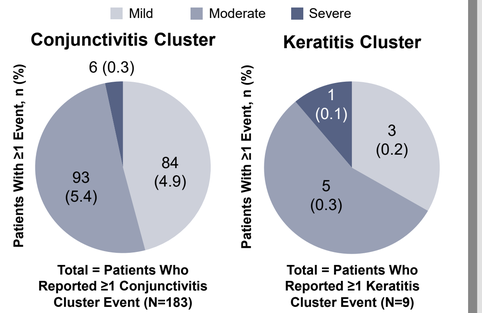
[a] For PBO-controlled group, adj % and adj IRs were used; [b] For PBO-controlled group, non-adj % were: PBO=2.5%, LEBRI 250 mg Q2W=8.6%; [c] For the PBO-controlled group, non-adjusted % were: PBO=0.2%, LEBRI 250 mg Q2W=0.6%

In All LEBRI Dataset, Most Patients Who Reported ≥1 Conjunctivitis Cluster Event Did So During the First 16 Weeks of Lebrikizumab Treatment



[a] Patients could be in multiple time frames due to exposure duration, a total of 10.6% of patients reported conjunctivitis cluster

In All LEBRI Dataset, Most Conjunctivitis or Keratitis Cluster Events That Were Reported Were Mild or Moderate in Severity

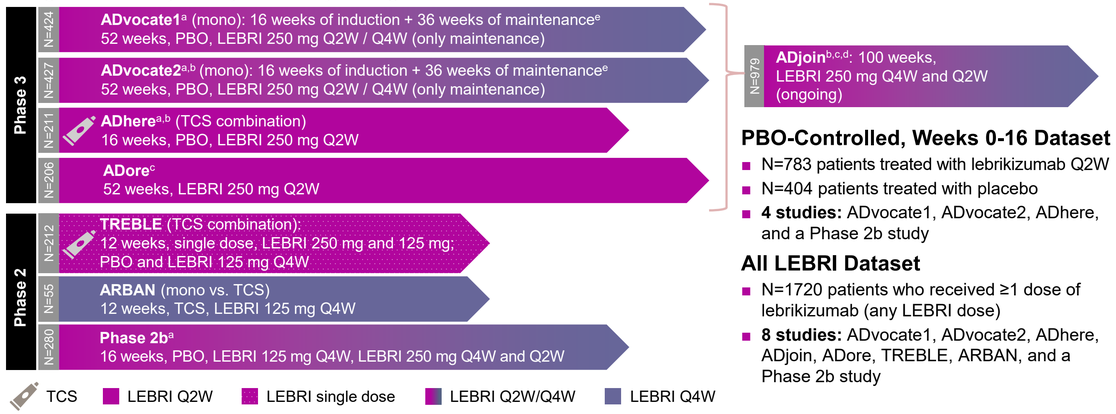


CONCLUSIONS

- The majority of conjunctivitis and keratitis cluster events reported by lebrikizumab-treated patients were mild or moderate in severity, did not lead to treatment discontinuation, and were resolved or resolving at the time of the database lock
- The majority of conjunctivitis cluster events were reported during the first 16 weeks of treatment
- Incidence rate of conjunctivitis and keratitis cluster events did not increase with longer duration of exposure
- Patients with medical history of conjunctivitis may have higher risk of developing treatment-emergent conjunctivitis or keratitis

METHODS

Integrated Safety Analysis Study Design[7]



[a] PBO-controlled; [b] Modified safety population; [c] TCS/TCI use was permitted; [d] Data cut-off was June 6, 2022; [e] TCS/TCI use was permitted during the Maintenance Period of ADvocate1 and ADvocate2

PBO-Controlled, Weeks 0-16 Dataset

- N=783 patients treated with lebrikizumab Q2W
- N=404 patients treated with placebo
- **4 studies:** ADvocate1, ADvocate2, ADhere, and a Phase 2b study

All LEBRI Dataset

- N=1720 patients who received ≥1 dose of lebrikizumab (any LEBRI dose)
- **8 studies:** ADvocate1, ADvocate2, ADhere, ADjoin, ADore, TREBLE, ARBAN, and a Phase 2b study

Assessments and Statistical Analyses

- Patient-reported conjunctivitis[a] and keratitis[b] cluster AEs were assessed in adults and adolescents with moderate-to-severe AD based on patients who received ≥1 dose of study treatment, excluding 38 patients from one study site as the patient eligibility criteria could not be confirmed
- For PBO-controlled group, adj % and adj IRs were used to report AEs
- For All LEBRI group, crude % and IRs were reported
- Exposure-adjusted IRs were calculated as the number of patients reporting an event per 100 PYs at risk
- Event rate over time was calculated as the number of patients with events divided by the number of patients who were at risk during the specified time interval

[a] Conjunctivitis cluster was defined by MedDRA preferred terms of conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, and viral conjunctivitis; [b] Keratitis cluster was defined by MedDRA preferred terms of keratitis, atopic keratoconjunctivitis, and vernal keratoconjunctivitis

RESULTS

Most Patients Who Reported ≥1 Conjunctivitis or Keratitis Event Did Not Discontinue Treatment

Patients With ≥1 AE Leading to Treatment Discontinuation, n (%)	PBO-Controlled, Weeks 0-16		All LEBRI
	PBO (N=404)	LEBRI 250 mg Q2W (N=783)	Any LEBRI Dose (N=1720)
Conjunctivitis cluster	**1 (0.2)**	**3 (0.4)**	**17 (1.0)**
Conjunctivitis	1 (0.2)	2 (0.3)	11 (0.6)
Allergic conjunctivitis	0	0	5 (0.3)
Bacterial conjunctivitis	0	1 (0.1)	1 (0.1)
Keratitis cluster	**0**	**2 (0.3)**	**3 (0.2)**
Keratitis	0	1 (0.1)	1 (0.1)
Vernal keratoconjunctivitis	0	0	1 (0.1)
Atopic keratoconjunctivitis	0	1 (0.1)	1 (0.1)

Similar Proportions of Adult and Adolescent Patients Reported Conjunctivitis and Keratitis Events

	All LEBRI (N=1720)	
	Adolescent ≥12 to <18 years (N=372)	Adults ≥18 years (N=1348)
Conjunctivitis cluster	31 (8.3)	152 (11.3)
Keratitis cluster	1 (0.3)	8 (0.6)

In All LEBRI Dataset, the Majority of Conjunctivitis and Keratitis Events Were Recovered or Resolved

Baseline Patient Demographics

	PBO-Controlled, Weeks 0-16		All LEBRI
	PBO (N=404)	LEBRI 250 mg Q2W (N=783)	Any LEBRI Dose (N=1720)
Age, years, mean (SD)	36.1 (17.3)	36.8 (17.8)	34.0 (17.8)
Adolescent ≥12 to <18	48 (11.9)	99 (12.6)	372 (21.6)
Adult ≥18	356 (88.1)	684 (87.4)	1348 (78.4)
Female	204 (50.5)	396 (50.6)	877 (51.0)
Region			
USA	222 (55.0)	413 (52.7)	945 (54.9)
Europe	94 (23.3)	196 (25.0)	428 (24.9)
Rest of the world	88 (21.8)	174 (22.2)	347 (20.2)
Race			
White	244 (60.4)	493 (63.0)	1079 (62.7)
Asian	93 (23.0)	141 (18.0)	311 (18.1)
Black	51 (12.6)	100 (12.8)	232 (13.5)
BMI, kg/m², mean (SD)	27.5 (7.1)	26.8 (6.4)	26.8 (6.6)
Prior treatments			
TCS/TCI	395 (97.8)	768 (98.1)	1494 (97.3)
Systemic treatment	188 (46.5)	351 (44.8)	674 (43.9)
IGA			
3 (Moderate)	258 (63.9)	495 (63.2)	1123 (65.3)
4 (Severe)	146 (36.1)	288 (36.8)	597 (34.7)
EASI, mean (SD)	29.5 (11.7)	28.6 (11.5)	32.5 (21.3)
Medical history of conjunctivitis	68 (19.3)	152 (21.5)	291 (22.2)[a]
Medical history of facial dermatitis	267 (75.9)	513 (72.5)	942 (72.0)

[a] In All LEBRI patients who reported conjunctivitis or keratitis AEs, 40% had medical history of conjunctivitis.
Note: Data are n (%) unless stated otherwise

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ABBREVIATIONS

AD=atopic dermatitis; adj %=study size-adjusted; AE=adverse event; BMI=body mass index; EASI=Eczema Area and Severity Index; IGA=investigator's Global Assessment; IL=interleukin; IR=incidence rate; LEBRI=lebrikizumab; MedDRA=Medical Dictionary for Regulatory Activities; PBO=placebo; PY=patient-years; PYE=patient-years of exposure; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroids

DISCLOSURES

A. Armstrong has served as a consultant, speaker, and/or investigator for: AbbVie, Almirall, Arcutis, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, EPI Health, Incyte Corporation, Janssen, LEO Pharma, Modernizing Medicine, Nimbus Therapeutics, Novartis, Ortho Dermatologics, PAREXEL, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma; **A. Wollenberg** has served as an advisor and/or paid speaker for and/or participated in clinical trials sponsored by: AbbVie, Aileens Pharma, Almirall, Amgen, Beiersdorf, Bioderma, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai Pharmaceutical, Eli Lilly and Company, Galapagos NV, Galderma, GlaxoSmithKline, Janssen, LEO Pharma, L'Oréal, Novartis, Pfizer, Pierre Fabre, Regeneron, and Sanofi; **M. de Bruin-Weller** has served as a consultant, speaker, advisor, and/or advisory board member for: AbbVie, Almirall, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme; **P. A. Lio** reports research grants and/or funding from: AbbVie, ACBiome, Eczema Foundation; has been on speaker's bureaus for: AbbVie, Eli Lilly and Company, Galderma, Hyphens Pharma, Incyte Corporation, La Roche-Posay/L'Oréal, MyOR Diagnostics, ParentMD, Pfizer, Pierre Fabre, Regeneron/Sanofi Genzyme; has received consulting fees from and/or been on advisory boards for: AbbVie, Almirall, Amyris, Arbonne, Arcutis, ASLAN Pharmaceuticals, Bodewell, Boston Skin Science, Bristol Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosciences, Dermavant, Dermira, Dermveda, Eli Lilly and Company, Galderma, IntraDerm, Janssen, Johnson & Johnson, Kaleido Biosciences, Kimberly-Clark, L'Oréal, LEO Pharma, Lipidor, Menlo Therapeutics, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Sibel Health, Skinfix, Sonica, Theraplex, UCB Pharma, Unilever, Verrica Pharmaceuticals, and Yobee Care; has stock options with: LearnSkin/Learn Health, Medable, Micreos, Modernizing Medicine, and Yobee Care; has a patent pending for: Theraplex product with royalties paid; and is a board member and scientific advisory committee member of: the National Eczema Association; **C. R. Natalie**, **F. Zhao**, and **A. R. Atwater** are employees and shareholders of: Eli Lilly and Company; **G. Jimenez** is an employee of: Almirall; **C.-Y. Chu** is an investigator, consultant, speaker, and/or advisory board member for: AbbVie, Dermira, Eli Lilly and Company, Janssen, Mylan, Novartis, Oneness Biotech, Pfizer, Regeneron, Roche, Sanofi, United BioPharma, and Viatris; **C. Vestergaard** has served as an advisor and/or speaker and/or has received fees or grant and/or research support for and/or has participated in clinical trials sponsored by: AbbVie, Almirall, AstraZeneca, Eli Lilly and Company, Galderma, LEO Pharma, Novartis, OM Pharma, Pfizer, Pierre Fabre, and Sanofi Genzyme

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