Efficacy of Lebrikizumab in Moderate-to-Severe Atopic Dermatitis Based on Australian Reimbursement Criteria for Severe Atopic Dermatitis

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BACKGROUND

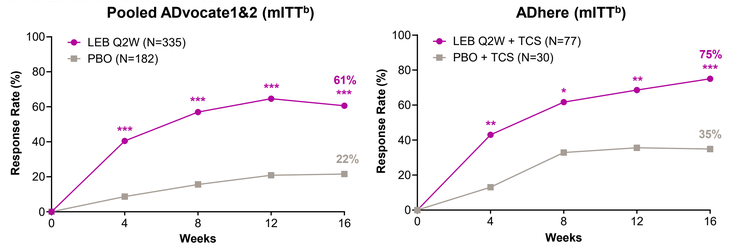
- Atopic dermatitis (AD) is a chronic inflammatory skin disease that can be a serious burden, affecting sleep, daily activities, and social relationships[1]
- Lebrikizumab is a monoclonal antibody that binds with high affinity and slow off-rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[2,3]
- Lebrikizumab has demonstrated efficacy with a positive benefit-risk profile:
  - As monotherapy in patients with moderate-to-severe AD at the primary endpoints of the 2 Phase 3, randomized, double-blind, placebo-controlled, 52-week ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) trials[4]
  - In combination with TCS, in patients with moderate-to-severe AD at the 16-week primary endpoint in the Phase 3, randomized, double-blind, placebo-controlled ADhere study (NCT04250337)[5]

OBJECTIVE

- To evaluate the 16-week efficacy of lebrikizumab treatment, based on the Australian reimbursement criteria used for currently approved systemic agents in the treatment of chronic severe AD, in the ADvocate1, ADvocate2, and ADhere clinical trials

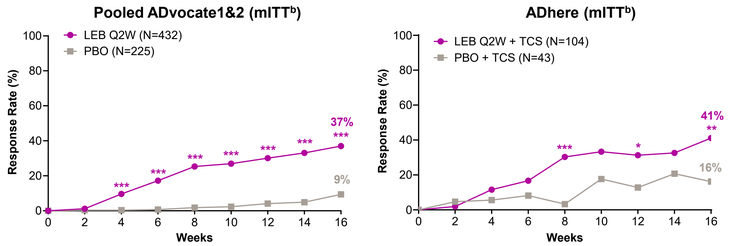
SUMMARY OF KEY FINDINGS

61-75% of Lebrikizumab-Treated Patients Achieved DLQI ≥4-Point Improvement[a] and EASI 50 at Week 16



* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] In patients ≥16 years with baseline DLQI ≥4
[b] Analysis population includes mITT patients with baseline EASI ≥20 and prior use of TCS/TCI who had anatomical area affected by AD

37-41% of Lebrikizumab-Treated Patients Achieved IGA (0,1)[a] at Week 16



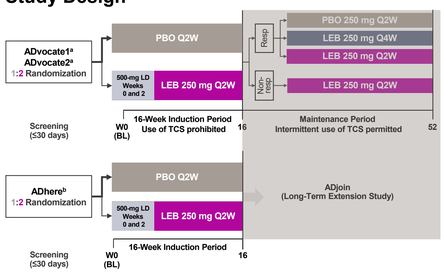
* p<0.05; ** p<0.01; *** p<0.001 vs. PBO
[a] With ≥2-point improvement from baseline
[b] Analysis population includes mITT patients with baseline EASI ≥20 and prior use of TCS/TCI who had anatomical area affected by AD who met Australian Reimbursement Criteria

CONCLUSIONS

- Lebrikizumab demonstrated statistically significant improvements when used as monotherapy and in combination with TCS, according to the Australian reimbursement criteria for currently approved systemic agents in the treatment of chronic severe AD
- The difference in rate of achievement of DLQI ≥4-point improvement between the lebrikizumab- and placebo-treated groups was not significant in the TCS combination study ADhere
  - Post hoc analysis, smaller sample size, or concomitant use of TCS may have contributed to this effect

METHODS

Study Design



[a] Full study designs of the ADvocate1 and ADvocate2 trials are not shown; only the 16-week Induction Period is included in this analysis; [b] In the ADhere trial, study treatment was given in combination with low- and mid-potency TCS. Use of TCS was required and TCS were provided within the trial; use could be tapered and stopped and then resumed as needed at the patient's discretion

Key Eligibility Criteria: ADvocate1&2 and Adhere

- Adults or 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%
- Candidate for systemic therapy

Australian Reimbursement Criteria

- Adults or adolescents (≥12 years)
- Baseline EASI of ≥20, despite prior use of topical therapy
- Anatomical area affected by AD regardless of body region at baseline
- Age-appropriate DLQI baseline score (of any value), measured following treatment with daily topical therapy (TCS or TCI) for ≥28 days
- Severe AD diagnosis:
  - ≥6 months before the date of assessment per reimbursement criteria
  - ≥12 months per study enrollment criteria
- Responders must have achieved EASI 50 and DLQI ≥4-point improvement[a] within the first 16 weeks of treatment, and maintain this response at biannual evaluations thereafter

[a] In patients ≥16 years with baseline DLQI ≥4; patients <16 years used cDLQI

Outcomes

- Composite endpoint: DLQI ≥4-point improvement[a] and EASI 50
- IGA (0,1) with ≥2-point improvement from baseline, indicating clear or almost clear skin
- Measures of clinical burden according to the validated EASI scoring system:
  - EASI 50
  - EASI 75
  - EASI 90
- DLQI ≥4-point improvement[a]

[a] In patients ≥16 years with baseline DLQI ≥4

Statistical Analyses

- This analysis includes a subset of patients who met the baseline requirements for Australian reimbursement criteria; pooled data for ADvocate1&2 are presented; ADhere data were analyzed separately
- Efficacy analyses were performed on a modified population (mITT):
  - ADvocate2 and ADhere efficacy analyses excluded 18 and 17 patients, respectively (from a single study site), whose eligibility could not be confirmed
- Treatment discontinuation due to lack of efficacy or data after rescue medication usage were imputed with NRI; data after treatment discontinuation due to other reasons were set to missing; other missing data were imputed with MI
  - ADvocate1&2 were lebrikizumab monotherapy trials and any TCS use during the first 16 weeks was considered rescue medication; in ADhere, low/moderate potency TCS use was permitted
- Proportion of responders in comparing lebrikizumab vs. placebo used the Cochran-Mantel-Haenszel test

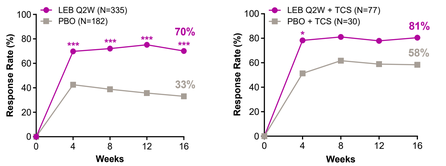
RESULTS:

Baseline Demographics and Patient Characteristics

	Australian Reimbursement Criteria			
	Pooled ADvocate1&2 (mITT)		ADhere (mITT)	
	PBO (N=225)	LEB 250 mg Q2W (N=432)	PBO + TCS (N=43)	LEB 250 mg Q2W + TCS (N=104)
Adolescents (12 to <18 years), n (%)	26 (11.6)	52 (12.0)	10 (23.3)	24 (23.1)
Adults (≥18 years), n (%)	199 (88.4)	380 (88.0)	33 (76.7)	80 (76.9)
Region, n (%)				
USA	82 (36.4)	151 (35.0)	29 (67.4)	71 (68.3)
Europe	76 (33.8)	148 (34.3)	7 (16.3)	22 (21.2)
Rest of world	67 (29.8)	133 (30.8)	7 (16.3)	11 (10.6)
IGA, n (%)				
3 (Moderate)	122 (54.2)	228 (52.8)	26 (60.5)	62 (59.6)
4 (Severe)	103 (45.8)	204 (47.2)	17 (39.5)	42 (40.4)
EASI	33.3 (11.2)	32.7 (11.2)	31.3 (10.2)	31.6 (10.9)
DLQI[a]	16.5 (7.3)[b]	16.0 (7.1)[c]	15.1 (8.2)[d]	15.8 (7.0)[e]

[a] In patients ≥16 years; [b] N=187; [c] N=345; [d] N=32; [e] N=78
Data are mean (SD) unless stated otherwise

70-81% of Lebrikizumab-Treated Patients Achieved DLQI ≥4-Point Improvement[a] at Week 16



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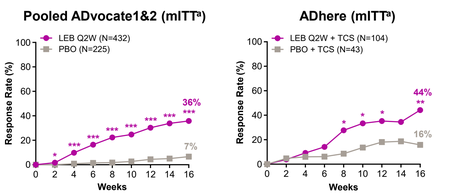
[a] In patients ≥16 years with baseline DLQI ≥4
[b] Analysis population includes mITT patients with baseline EASI ≥20 and prior use of TCS/TCI who had anatomical area affected by AD

36-44% of Lebrikizumab-Treated Patients Achieved EASI 90 at Week 16



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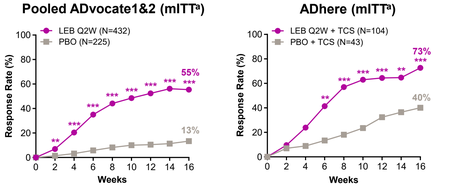
55-73% of Lebrikizumab-Treated Patients Achieved EASI 75 at Week 16



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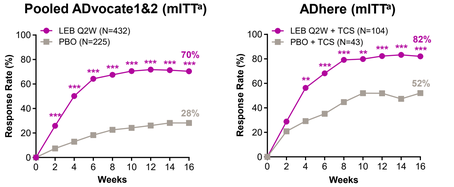
70-82% of Lebrikizumab-Treated Patients Achieved EASI 50 at Week 16



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1. Grant L, et al. *Dermatitis*. 2019;30:247-254.
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ABBREVIATIONS

AD=atopic dermatitis; BL=baseline; BMI=body mass index; BSA=body surface area; cDLQI=children's DLQI; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; EASI 50/75/90=at least 50%/75%/90% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IL=interleukin; LD=loading dose; LEB=lebrikizumab; MI=multiple imputation; mITT=modified Intent-to-Treat; Non-resp=non-responder; NRI=non-responder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization; Resp=responder; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroids; W=Week

DISCLOSURES

P. Fernández-Peñas has served on advisory boards for: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, LEO Pharma, Eli Lilly and Company, Merck, Merck Sharp & Dohme, Novartis, Roche, Sanofi, and Sun Pharma; has given educational lectures for: AbbVie, Amgen, Avene, Eli Lilly and Company, Galderma, Janssen, La Roche-Posay, LEO Pharma, Merck, Novartis, Pfizer, Roche, Sanofi, Schering Plough, Sun Pharma, and UCB Pharma; has conducted clinical trials for AbbVie, Amgen, Arena, AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, CSL, Dermira, Eisai, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, Jiangsu Hengrui, Kyowa Hakko Kirin, LEO Pharma, miRagen, Novartis, OncoSec, Pfizer, Regeneron, Roche, Sun Pharma, UCB Pharma, and Xoma; **D. Rubel** has served as advisor, investigator, and/or received travel honoraria from: AbbVie, Amgen, 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.

This study was funded by Dermira, a wholly owned subsidiary of Eli Lilly and Company.

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