Lebrikizumab in Combination With Topical Corticosteroids Improves Quality of Life in Patients With Moderate-to-Severe Atopic Dermatitis: Results From a Phase 3, Randomized, Double-Blinded, Placebo-Controlled Trial (ADhere)

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BACKGROUND

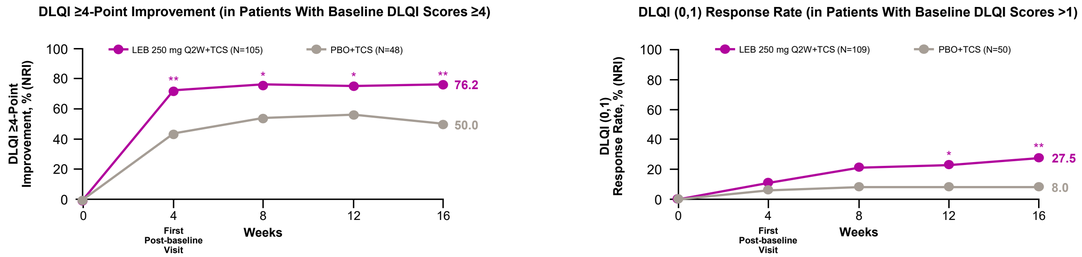
- Atopic dermatitis (AD) is a chronic, relapsing, heterogeneous skin disease characterized by intense itching, erythema, and dry, scaly, often lichenified papules/plaques associated with unpredictable flares[1]
- AD can be a serious burden for adolescents and adults, affecting sleep, daily activities, and social relationships; therefore, AD can significantly impair patient quality of life (QoL)[2]
- Lebrikizumab is a novel, high-affinity immunoglobulin G4 monoclonal antibody targeting interleukin (IL)-13 that selectively prevents the formation of the IL-13Rα1/IL-4Rα heterodimer receptor signaling complex[3]
- Lebrikizumab monotherapy demonstrated efficacy and a favorable safety profile in patients with moderate-to-severe AD at the 16-week primary endpoint of the 2 ongoing, 52-week, randomized, double-blind, placebo-controlled Phase 3 trials, ADvocate1 and ADvocate2[4]
- Lebrikizumab combination therapy also demonstrated efficacy in the 16-week randomized, double-blind, placebo-controlled Phase 3 trial, ADhere[5]

OBJECTIVE

To report the 16-week QoL outcomes of lebrikizumab in combination with topical corticosteroids (TCS) vs. placebo in combination with TCS in the treatment of AD from the ADhere trial

KEY RESULTS

Figure 1. DLQI Response Rates



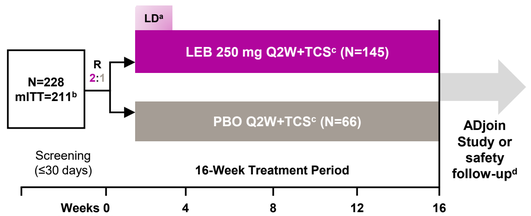
* p<0.05; ** p<0.01 vs. PBO using the Cochran-Mantel-Haenszel test adjusted by geographic region, age group, and baseline IGA score

CONCLUSIONS

- Lebrikizumab 250 mg every 2 weeks in combination with TCS for 16 weeks provided significant improvements in QoL for patients with moderate-to-severe AD
- Statistically significant increases in DLQI change from baseline and in the response rate for DLQI ≥4-point improvement were seen for lebrikizumab vs. placebo at the first post-baseline assessment at Week 4 and were sustained through Week 16

METHODS

Study Design, ADhere



[a] 500-mg LD at Weeks 0 and 2; [b] Efficacy analyses used the mITT population; 17 patients from 1 site were excluded from the ITT population because some or all of the study participants did not meet the eligibility criteria for moderate-to-severe AD; [c] 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; [d] Patients completing the study could enter the ADjoin Extension Study or complete a safety follow-up 12 weeks after their last dose

Key Eligibility Criteria

- Adult or adolescent (≥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 of the following at the baseline visit:
  - Eczema Area and Severity Index score ≥16
  - Investigator's Global Assessment score ≥3
  - Percent of body surface area involvement ≥10%
- Candidate for systemic therapy

Outcomes

- Dermatology Life Quality Index (DLQI)[6] at baseline and at Weeks 4, 8, 12, and 16[a]
  - Ranges from 0-30, with higher scores indicating greater impairment of QoL
- EQ-5D-5L US Health State Index[7] at baseline and at Week 16
  - Ranges from 0-1, with higher scores indicating better health
- EQ-5D visual analog scale[7] at baseline and at Week 16
  - Ranges from 0-100, with higher scores indicating better health

[a] DLQI was completed only for patients ≥16 years of age at baseline; patients <16 years of age completed the Children's DLQI

Statistical Analyses

Measure	Analyses	Analysis Population[a]
DLQI change from baseline	MMRM[b]	mITT
Percent of patients achieving ≥4-point improvement in DLQI	NRI[b]	mITT patients with baseline DLQI score ≥4
Percent of patients achieving DLQI (0,1)	NRI[c]	mITT patients with baseline DLQI score >1
EQ-5D-5L US Health State Index change from baseline	ANCOVA with LOCF[b]	mITT
EQ-5D VAS change from baseline	ANCOVA with LOCF[b]	mITT

[a] Efficacy analyses used the mITT population; 17 patients from 1 site were excluded from the ITT population because some or all of the study participants did not meet the eligibility criteria for moderate-to-severe AD; [b] Patients who received high-potency topical or systemic rescue medication or discontinued treatment for any reason were thereafter set to missing (change from baseline analyses) or non-response (responder analyses) through Week 16; [c] Patients who received high-potency topical or systemic rescue medication or discontinued treatment due to lack of efficacy were thereafter set to non-response through Week 16

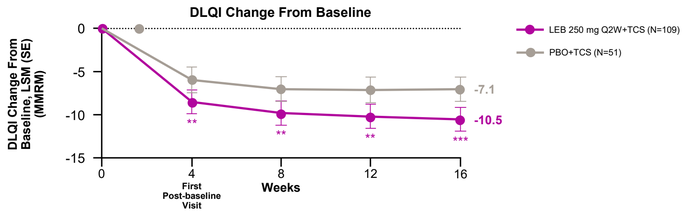
RESULTS

Table 1. Demographics and Baseline Characteristics

	PBO Q2W+TCS (N=66)	LEB 250 mg Q2W+TCS (N=145)
Age, years	36.7 (17.9)	37.5 (19.9)
Adolescent (12 to <18 years), n (%)	14 (21.2)	32 (22.1)
Adult (≥18 years), n (%)	52 (78.8)	113 (77.9)
Female, n (%)	33 (50.0)	70 (48.3)
Region, n (%)		
US	48 (72.7)	103 (71.0)
Europe	10 (15.2)	28 (19.3)
Rest of world	8 (12.1)	14 (9.7)
Race, n (%)		
White	40 (60.6)	90 (62.1)
Asian	13 (19.7)	18 (12.4)
Black/African American	9 (13.6)	19 (13.1)
BMI, kg/m^2	27.9 (7.5)	26.5 (7.2)
IGA, n (%)		
3 (moderate)	48 (72.7)	98 (67.6)
4 (severe)	18 (27.3)	47 (32.4)
EASI	26.4 (10.6)	27.7 (11.1)
BSA % involvement	38.2 (20.8)	40.4 (21.9)
EQ-5D-5L US Health State Index	0.8 (0.2)[a]	0.8 (0.2)[b]
EQ-5D VAS	72.8 (22.3)[a]	72.7 (18.9)[b]
DLQI[c]	13.5 (7.5)[d]	14.9 (7.2)[e]

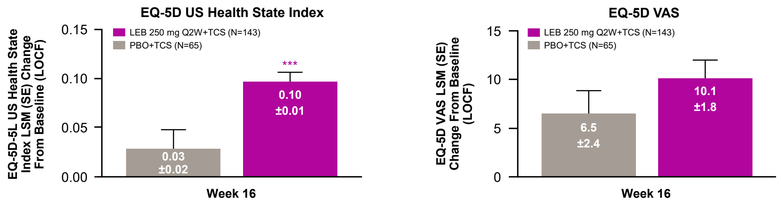
Data presented as mean (standard deviation) unless otherwise specified
[a] n=65; [b] n=143; [c] DLQI was completed only for patients ≥16 years of age at baseline; [d] n=51; [e] n=109

Figure 2. DLQI Total Score Change From Baseline



** p<0.01; *** p<0.001 vs. PBO using an MMRM model, including treatment, baseline value, visit, baseline value-by-visit interaction, treatment-by-visit interaction, geographic region, age group, and baseline IGA score

Figure 3. Improvements in EQ-5D



*** p<0.001 vs. PBO using an ANCOVA model with treatment, baseline value, geographic region, age group, and baseline IGA score as fixed factors

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ABBREVIATIONS

AD=atopic dermatitis; ANCOVA=analysis of covariance; BMI=body mass index; BSA=body surface area; DLQI=Dermatology Life Quality Index; DLQI (0,1)=DLQI response of clear or almost clear; EASI=Eczema Area and Severity Index; IGA=Investigator's Global Assessment; ITT=Intent-to-Treat; LD=loading dose; LEB=lebrikizumab; LOCF=last observation carried forward; LSM=least squares mean; mITT=modified ITT; MMRM=mixed model repeated measures; NRI=non-responder imputation; PBO=placebo; Q2W=every 2 weeks; R=randomization; SE=standard error; TCS=topical corticosteroids; VAS=visual analog scale

DISCLOSURES

- **S. Forman** has served as a consultant, advisory board member, speaker, and/or investigator for: AbbVie, Aclaris, Asana BioSciences, AstraZeneca, Athenex, Celgene, Cutanea, Eli Lilly and Company, Incyte Corporation, Innovaderm Research, Novartis, Pfizer, Promius Pharma, Regeneron, UCB Pharma, Valeant Pharmaceuticals, and XBiotech; **J. Gutermuth** has served as a speaker for: AbbVie, Almirall, Celgene, Eli Lilly and Company, Eucerin, Janssen, La Roche-Posay, LEO Pharma, Nestlé, Pierre Fabre, Regeneron/Sanofi, and Thermo Fisher Scientific; and has served as a consultant for: AbbVie, ALK-Abelló, Almirall, Ariez International, Celgene, Eli Lilly and Company, Janssen, LEO Pharma, Pfizer, and Regeneron/Sanofi; **M. de Bruin-Weller** has served as a consultant, advisory board member, and/or speaker for: AbbVie, Almirall, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme; **A. Moore** has served as a consultant, advisory board member, speaker, and/or investigator for: AbbVie, Almirall, Arcutis, Biofrontera, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, DS Biopharma, Eli Lilly and Company, EPI Health, Evolus, Galderma, Incyte Corporation, Janssen, LEO Pharma, Mayne Pharma, Nimbus Therapeutics, Novartis, PAREXEL, Pfizer, UCB Pharma, Verrica Pharmaceuticals, and Vyne Therapeutics; **S. Guenthner** has served on advisory boards and received grants/research funding and honoraria from: AbbVie, Amgen, Dermira, Eli Lilly and Company, Genentech, Janssen, LEO Pharma, Pfizer, Sun Pharma, UCB Pharma, and Vanda Pharmaceuticals; **E. Wolf**, **E. Pierce**, and **M. M. Witte** are employees and shareholders of: Eli Lilly and Company; **J. Zhong** is an employee of: IQVIA; **A. Wollenberg** has served as an advisor, speaker, and/or investigator for: AbbVie, Almirall, Amgen, Beiersdorf, Bioderma, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Chugai Pharmaceutical, Eli Lilly and Company, Galapagos NV, Galderma, Janssen Cilag, LEO Pharma, L'Oréal, Novartis, Pfizer, Pierre Fabre, Regeneron, and Sanofi
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