Lebrikizumab Treatment Improves Quality of Life in Patients With Moderate-to-Severe Atopic Dermatitis: Results From Two Phase 3, Randomized, Double-Blinded, Placebo-Controlled Trials (ADvocate1 and ADvocate2)

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BACKGROUND

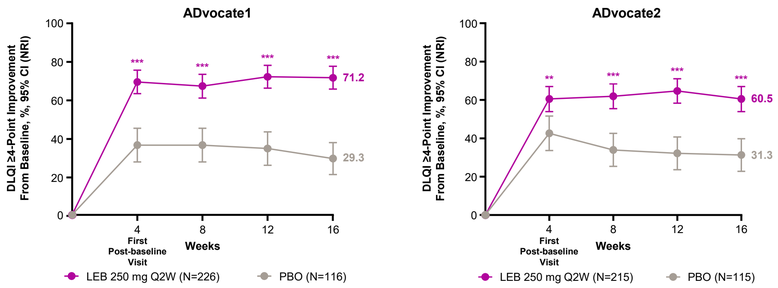
- Atopic dermatitis (AD) is a chronic, relapsing, heterogenous skin disorder that affects children and adults[1]
- Moderate-to-severe AD causes intense itching, negatively impacting sleep and patient quality of life (QoL)[2]
- Lebrikizumab is a novel, high-affinity immunoglobulin G4 monoclonal antibody 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 monotherapy in patients with moderate-to-severe AD from the ADvocate1 and ADvocate2 trials

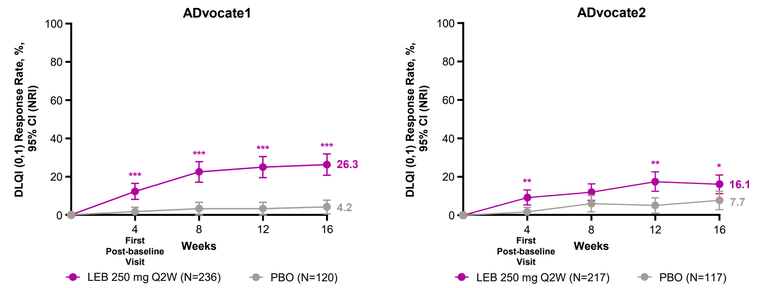
KEY RESULTS

Figure 1. DLQI ≥4-Point Improvement (in Patients With Baseline DLQI Scores ≥4)



** p<0.01; *** p<0.001 vs. PBO using the Cochran-Mantel-Haenszel test adjusted by geographic region, age group, and baseline IGA score

Figure 2. DLQI (0,1) Response Rate (in Patients With Baseline DLQI Scores >1)



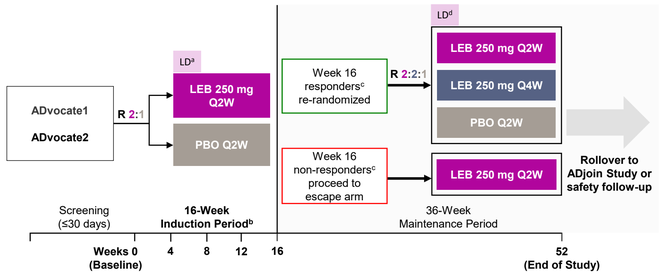
* p<0.05; ** p<0.01; *** p<0.001 vs. PBO using the Cochran-Mantel-Haenszel test adjusted by geographic region, age group, and baseline IGA score

CONCLUSIONS

- Lebrikizumab 250 mg every 2 weeks for 16 weeks resulted in clinically significant improvements in QoL, as assessed by the DLQI and EQ-5D, for patients with moderate-to-severe AD
- Improvements were seen as early as Week 4 (first post-baseline assessment) and continued through Week 16

METHODS

Study Design, ADvocate1 and ADvocate2



Note: Only data from the 16-week Induction Period are presented; the Maintenance Period is ongoing
[a] LEB-treated patients received a 500-mg LD at Weeks 0 and 2; [b] Patients who used rescue therapy (including topical) during the Induction Period were considered to be non-responders; [c] Responders were patients who achieved an IGA response of 0,1 or EASI75 at Week 16; [d] Responders who received PBO and were re-randomized to LEB received an LD of LEB 500 mg at Week 16 or at Weeks 16 and 18, based on the active treatment group assigned in the Maintenance Period

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

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

- Data are from the 16-week primary outcome database lock with data cut-offs on June 21, 2021 (ADvocate1) and July 12, 2021 (ADvocate2)

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

[a] Patients who received topical or systemic rescue medication or discontinued treatment for any reason were thereafter set to missing (change from baseline analyses) or non-responders (responder analyses) through Week 16; [b] Efficacy analyses in ADvocate1 used the ITT population (all randomized patients); [c] In ADvocate2, 18 patients from 1 site were excluded from the ITT population because some or all the study participants did not meet the eligibility criteria of having moderate-to-severe AD; thus, efficacy analyses in ADvocate2 used the mITT population; [d] Patients who received topical or systemic rescue medication or discontinued treatment due to lack of efficacy were thereafter set to non-response through Week 16

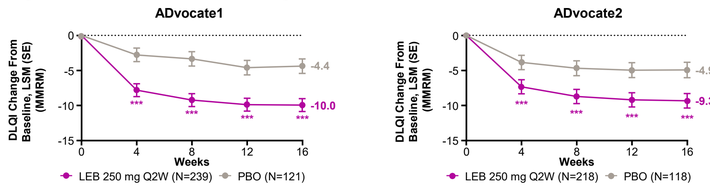
RESULTS

Table 1. Demographics and Baseline Characteristics

	ADvocate1		ADvocate2	
	PBO (N=141)	LEB 250 mg Q2W (N=283)	PBO (N=146)	LEB 250 mg Q2W (N=281)
Age, years	34.2 (16.4)	36.1 (17.8)	35.3 (17.2)	36.6 (16.8)
Adolescent (12 to <18 years), n (%)	18 (12.8)	37 (13.1)	17 (11.6)	30 (10.7)
Adult (≥18 years), n (%)	123 (87.2)	246 (86.9)	129 (88.4)	251 (89.3)
Female, n (%)	73 (51.8)	141 (49.8)	75 (51.4)	136 (48.4)
Region, n (%)				
US	62 (44.0)	128 (45.2)	60 (41.1)	107 (38.1)
Europe	46 (32.6)	92 (32.5)	38 (26.0)	76 (27.0)
Rest of world	33 (23.4)	63 (22.3)	48 (32.9)	98 (34.9)
Race, n (%)				
White	93 (66.0)	196 (69.3)	85 (58.2)	168 (59.8)
Asian	31 (22.0)	39 (13.8)	44 (30.1)	78 (27.8)
Black/African American	16 (11.3)	33 (11.7)	10 (6.8)	25 (8.9)
BMI, kg/m^2	27.8 (7.2)	26.5 (5.8)	26.2 (6.2)	26.6 (6.6)
Asthma, n (%)	50 (35.5)	93 (32.9)	35 (24.0)	78 (27.8)
Allergic rhinitis, n (%)	76 (53.9)	146 (51.6)	69 (47.3)	130 (46.3)
IGA, n (%)				
3 (moderate)	83 (58.9)	170 (60.1)	95 (65.1)	175 (62.3)
4 (severe)	58 (41.1)	113 (39.9)	51 (34.9)	106 (37.7)
EASI	31.0 (12.9)	28.8 (11.3)	29.6 (10.8)	29.7 (12.0)
BSA % involvement	47.8 (23.9)	45.3 (22.5)	46.0 (21.1)	46.1 (22.6)
EQ-5D-5L US Health State Index	0.7 (0.17)	0.7 (0.17)[a]	0.7 (0.18)[b]	0.8 (0.16)[c]
EQ-5D VAS	67.0 (22.2)	68.2 (22.0)[a]	68.6 (21.6)[b]	66.7 (20.7)[c]
DLQI[d]	15.7 (7.2)[e]	15.3 (7.4)[f]	15.9 (7.6)[g]	15.4 (7.0)[h]

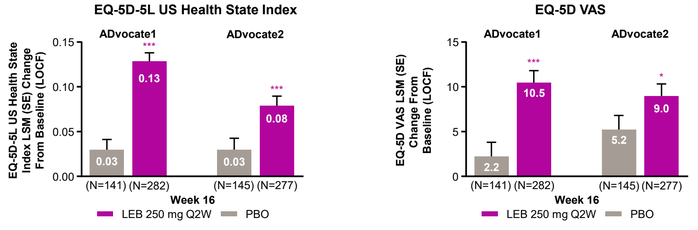
Data presented as mean (standard deviation) unless otherwise specified
[a] n=282; [b] n=145; [c] n=277; [d] DLQI was completed only for patients ≥16 years of age at baseline; [e] n=141; [f] n=239; [g] n=118; [h] n=218

Figure 3. DLQI Total Score Change From Baseline



*** 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 4. Improvements in EQ-5D



* p<0.05; *** p<0.001 vs. PBO using an ANCOVA model with treatment, geographic region, age group, and baseline IGA score as fixed factors and baseline value as covariate

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ABBREVIATIONS

AD=atopic dermatitis; ANCOVA=analysis of covariance; BMI=body mass index; BSA=body surface area; CI=confidence interval; DLQI=Dermatology Life Quality Index; DLQI (0,1)=DLQI response of clear or almost clear; EASI=Eczema Area and Severity Index; EASI75=75% reduction from baseline in EASI score; 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; Q4W=every 4 weeks; R=randomization; SE=standard error; VAS=visual analog scale

DISCLOSURES

- **P. A. Lio** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from: AbbVie, AOBiome, Arbonne, Burt's Bees, Dermavant, Dermira, Eli Lilly and Company, Exeltis, Franklin Bioscience/Altus Labs, Incyte Corporation, IntraDerm, Johnson & Johnson, Kiniksa, La Roche-Posay/L'Oréal, LEO Pharma, Menlo Therapeutics, the National Eczema Association, Pfizer, Pierre Fabre, Realm Therapeutics, Regeneron/Sanofi Genzyme, Theraplex, TopMD, UCB Pharma, Unilever, and Verrica Pharmaceuticals; **A. W. 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; **J. Gutermuth** has served as a speaker for: AbbVie, Almirall, Celgene, Eli Lilly and Company, Eucerin, Janssen, La Roche-Posay, LEO Pharma, Nestlé, Pfizer, 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; **A. Nosbaum** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from: AbbVie, Celgene, Eli Lilly and Company, Incyte Corporation, Janssen, LEO Pharma, Medac, Novartis, Pfizer, Pierre Fabre, and Sanofi Regeneron; **H. Sofen** is a consultant for: Amgen, Celgene, Eli Lilly and Company, Janssen, Novartis, and Pfizer; **M. Casillas**, **E. Pierce**, and **H. Elmaraghy** are employees and shareholders of: Eli Lilly and Company; **S. Chen** is an employee of: Tigermed; **J. P. Thyssen** has been an advisory board member for, received speaker honoraria from, and/or participated in clinical studies for: AbbVie, Eli Lilly and Company, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme
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