Lebrikizumab Demonstrates Consistent Efficacy at 16 Weeks in Patients With Moderate-to-Severe Atopic Dermatitis Regardless of Baseline Disease Severity

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BACKGROUND

- Lebrikizumab is a monoclonal antibody that binds with high affinity and slow dissociation rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[1]
- Lebrikizumab has demonstrated clinical benefit in patients with moderate-to-severe AD in the randomized, placebo-controlled, Phase 3 ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) trials[2,3]

OBJECTIVE

- To assess efficacy of lebrikizumab in the ADvocate1 and ADvocate2 trials within subgroups of patients with moderate (IGA=3) vs. severe (IGA=4) AD at baseline

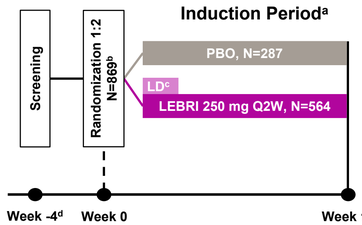
Statistical results of the primary and major secondary endpoints for ADvocate1 and ADvocate2 were confirmed through replicate statistical programming, validation, and quality reviews[2,3]

CONCLUSION

- Regardless of baseline disease severity, lebrikizumab 250 mg Q2W demonstrated consistent and robust efficacy on skin and itch in patients with moderate or severe AD at Week 16

METHODS

Study Design: ADvocate1 and ADvocate2

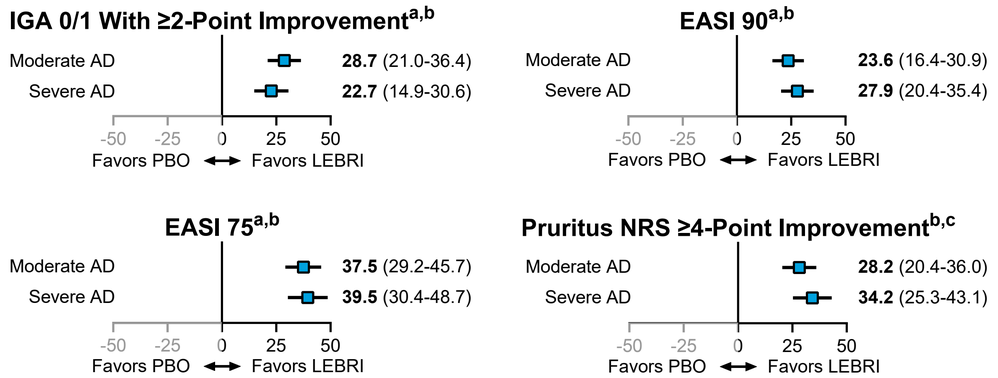


[a] Use of topical/systemic treatments for AD prohibited; [b] 424 patients (ADvocate1) and 445 patients (ADvocate2) with moderate-to-severe AD; [c] 500 mg LD at W0 and W2; [d] ≤30-day screening period; [e] IGA (0,1) with ≥2-point improvement from baseline; [f] FDA primary endpoint; [g] EMA co-primary endpoint

KEY RESULTS

At Week 16, the treatment effect of lebrikizumab was consistent regardless of baseline disease severity

Treatment Difference Between LEBRI 250 mg Q2W and PBO



[a] Pooled modified ITT; [b] Patients who received topical or systemic rescue medication, or discontinued treatment due to lack of efficacy, were imputed as non-responders. Other missing data were imputed with MI; [c] Pooled modified ITT with baseline Pruritus NRS ≥4
Note: Data are risk difference with 95% CI; logistic regression analysis was used to examine the interaction effects of treatment by disease severity subgroup (tested at the 10% significance level)

Key Eligibility Criteria

- Adults (≥18 years of age) and adolescents (12 to <18 years of age, weighing ≥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

Outcome

- Treatment difference for lebrikizumab vs. placebo between the baseline AD subgroups, moderate AD (IGA=3) vs. severe AD (IGA=4), was calculated at Week 16 for:
  - IGA 0/1 with ≥2-point improvement
  - EASI 75
  - EASI 90
  - Pruritus NRS[a] ≥4-point improvement from baseline[b]

[a] The Pruritus NRS is a patient-reported, single-item, 11-point scale that is used daily by participants to rate their worst itch severity over the past 24 hours (0 indicating "no itch"; 10 indicating "worst itch imaginable"†); [b] Based on patients with baseline Pruritus NRS ≥4

ABBREVIATIONS

AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; CI=confidence interval; CMH=Cochran-Mantel-Haenszel; 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; EMA=European Medicines Agency; FDA=US Food and Drug Administration; IGA=Investigator's Global Assessment; IGA 0/1=IGA response of clear or almost clear; IL=interleukin; ITT=Intent-to-Treat; LD=loading dose; LEBRI=lebrikizumab; MI=multiple imputation; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; SD=standard deviation

Statistical Analyses

- Analyses were performed on the pooled modified ITT population[a] of ADvocate1 and ADvocate2
- Data collected after any rescue medication use, or patient discontinued due to lack of efficacy, were imputed as non-responders; data collected after discontinuation due to other reasons were set as missing. Missing data were imputed using multiple imputation
- Lebrikizumab vs. placebo treatment differences were evaluated in patients with baseline moderate (IGA=3) and severe (IGA=4) AD
  - Logistic regression analysis was used to test the interaction of treatment by baseline severity subgroup (p>0.1 indicates consistent treatment effect across 2 subgroups)
  - The CMH test was applied to test the treatment group difference within each subgroup

[a] The pooled modified ITT population excluded 18 patients in the ADvocate2 study (from a single study site), whose eligibility could not be confirmed

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; **K. Eyerich** has received speaker's fees from and/or has been a member of advisory boards for: AbbVie, Almirall, Bristol Myers Squibb, Eli Lilly and Company, Hexal, Janssen, LEO Pharma, Novartis, Sanofi, and UCB Pharma; **H. Sofen** is a consultant for: Amgen, Celgene, Eli Lilly and Company, Janssen, Novartis, and Pfizer; **L. Kircik** has served as an investigator, consultant, and/or speaker, and/or has served on an advisory board for: AbbVie, Acambis, Amgen, Anacor Pharmaceuticals, AnaptysBio, Arcutis, Arena Pharmaceuticals, Assos Pharmaceuticals, Astellas, Asubio Pharma, Dermavant, Dermira, Dow Pharmaceutical Sciences, Eli Lilly and Company, Ferndale Pharma Group, Galderma, Genentech, HealthPoint, Incyte Corporation, INNOCUTIS, INNOVAIL, Kyowa Kirin, LEO Pharma, L'Oréal, Nano Bio, Novartis, NUCRYST Pharmaceuticals, Onset, Ortho Neutrogena, Ortho Dermatologics, Pediapharm, Pfizer, Pharmaderm, Promius Pharma, PuraCap Pharmaceuticals, Quinnova Pharmaceuticals, Regeneron, Sanofi, SkinMedica, Stiefel, Sun Pharma, Taro Pharmaceutical Industries, Triax Technologies, and Valeant Pharmaceuticals; **T. Bewley** has received honoraria and/or consulting fees from: AbbVie, Almirall, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Sanofi, and UCB Pharma; **P. Herranz** is/has been an investigator, lecturer, and/or consultant for: AbbVie, Almirall, Eli Lilly and Company, Galderma, Kymab, LEO Pharma, Novartis, Pfizer, Sanofi/Regeneron, and UCB Pharma; **E. Wolf**, **G. Gallo**, **Y. Ding**, and **F. E. Yang** are employees and shareholders of: Eli Lilly and Company; **I. Pau-Charles** is an employee of: Almirall; **M. Gooderham** has been an investigator, speaker, and/or advisor for: AbbVie, Akros Pharma, Amgen, Arcutis, Aristea Therapeutics, Bausch Health, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Merck, MoonLake Immunotherapeutics, Nimbus Therapeutics, Novartis, Pfizer, Regeneron, Reistone Biopharma, Roche, Sanofi Genzyme, Sun Pharma, and UCB Pharma

RESULTS

Baseline Demographics

	Overall[a]		Moderate AD (Baseline IGA=3)		Severe AD (Baseline IGA=4)	
	PBO (N=287)	LEBRI 250 mg Q2W (N=564)	PBO (N=178)	LEBRI 250 mg Q2W (N=345)	PBO (N=109)	LEBRI 250 mg Q2W (N=219)
Age, years	34.8 (16.8)	36.4 (17.3)	34.7 (16.5)	36.5 (17.4)	34.9 (17.3)	36.2 (17.2)
Age category, n (%)						
Adolescents (12 to <18)	35 (12.2)	67 (11.9)	24 (13.5)	41 (11.9)	11 (10.1)	26 (11.9)
Adults (≥18)	252 (87.8)	497 (88.1)	154 (86.5)	304 (88.1)	98 (89.9)	193 (88.1)
Female, n (%)	148 (51.6)	277 (49.1)	97 (54.5)	180 (52.2)	51 (46.8)	97 (44.3)
Race, n (%)						
White	178 (62.0)	364 (64.5)	120 (67.4)	232 (67.2)	58 (53.2)	132 (60.3)
Asian	75 (26.1)	117 (20.7)	38 (21.3)	59 (17.1)	37 (33.9)	58 (26.5)
Black	26 (9.1)	58 (10.3)	15 (8.4)	41 (11.9)	11 (10.1)	17 (7.8)
Other[b]	8 (2.8)	25 (4.4)	5 (2.8)	13 (3.8)	3 (2.8)	12 (5.5)
BMI	27.1 (6.8)	26.6 (6.2)	26.8 (6.2)	26.8 (6.3)	27.4 (7.8)	26.4 (6.1)

[a] Pooled modified ITT; [b] Includes multiple, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, other, and not reported
Note: Data are mean (SD) unless stated otherwise

Baseline Disease Characteristics

	Overall[a]		Moderate AD (Baseline IGA=3)		Severe AD (Baseline IGA=4)	
	PBO (N=287)	LEBRI 250 mg Q2W (N=564)	PBO (N=178)	LEBRI 250 mg Q2W (N=345)	PBO (N=109)	LEBRI 250 mg Q2W (N=219)
Disease duration since AD diagnosis, years	21.9 (14.9)	21.4 (15.0)	20.8 (14.0)	19.8 (14.3)	23.6 (16.1)	23.9 (15.8)
IGA, n (%)						
3 (Moderate)	178 (62.0)	345 (61.2)	178 (100)	345 (100)	0	0
4 (Severe)	109 (38.0)	219 (38.8)	0	0	109 (100)	219 (100)
EASI	30.3 (11.9)	29.3 (11.6)	25.3 (8.0)	24.4 (7.3)	38.5 (12.6)	36.9 (13.1)
Pruritus NRS	7.2 (1.8)	7.2 (1.9)	7.0 (1.8)	6.8 (1.9)	7.6 (1.7)	7.7 (1.8)
BSA, % involvement	46.9 (22.5)	45.7 (22.5)	38.8 (18.4)	39.3 (19.2)	60.1 (22.3)	55.7 (23.8)
DLQI[b]	15.8 (7.4)	15.3 (7.2)	14.7 (7.1)	13.9 (7.1)	17.7 (7.5)	17.6 (6.8)
Prior systemic therapy, n (%)	166 (57.8)	300 (53.2)	89 (50.0)	161 (46.7)	77 (70.6)	139 (63.5)

[a] Pooled modified ITT; [b] Patients ≤16 years old were not included in the DLQI analysis
Note: Data are mean (SD) unless stated otherwise

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