Patient-Level, Visit-by-Visit Data Highlight the Extent of Skin and Itch Improvement in Atopic Dermatitis With Lebrikizumab

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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 report individual patients' level, visit-by-visit, of response using EASI and Pruritus NRS evaluations over 52 weeks of treatment

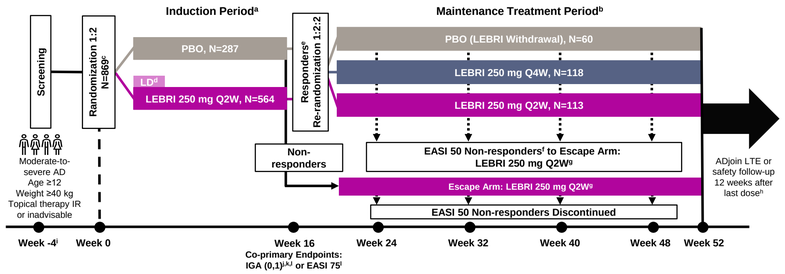
Statistical results of the primary and major secondary endpoints for ADvocate1 and ADvocate2 were confirmed through replicate statistical programming, validation, and quality reviews[2,3]

CONCLUSIONS

- Based on individual patient data, lebrikizumab is an efficacious treatment for AD and shows stable improvements in skin and itch measures through 1 year
- Some patients had deep improvements (eg, EASI 100, Pruritus NRS 0) during the Induction Period; many patients also maintained or improved their skin or itch outcomes with some achieving levels of deep improvement through 1 year

METHODS

Study Design: ADvocate1 and ADvocate2



[a] Use of topical/systemic treatments for AD prohibited; [b] Use of intermittent topical rescue medications for AD permitted. Responders who received PBO during induction and who were re-randomized to LEBRI received an LD of either 500 mg given at W16 or 500 mg given at W16 and W18; [c] 424 patients (ADvocate1) and 445 patients (ADvocate2) with moderate-to-severe AD. The pooled analysis excluded 18 patients (from a single study site) whose eligibility could not be confirmed in ADvocate2; [d] 500 mg LD at W0 and W2; [e] Responders achieved EASI 75 or IGA (0,1) with ≥2-point improvement at W16 without rescue medication use; [f] Patients who did not maintain ≥EASI 50 were assigned to the Escape Arm; [g] Maintenance of response assessed by EASI 50 at W24, W32, W40, and W48, respectively; [h] Patients completing ADvocate1/2 were offered open-label treatment in ADjoin, otherwise patients participated in a safety follow-up 12 weeks after their last dose; [i] ≤30-day screening period; [j] IGA (0,1) with ≥2-point improvement from baseline; [k] FDA primary endpoint; [l] EMA co-primary endpoint

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

Outcomes

- Patient's skin response was evaluated according to the EASI percent change from baseline:
  - 100% (EASI 100), 90% to <100% (EASI 90 to 100), 75% to <90% (EASI 75 to 90), 50% to <75% (EASI 50 to 75), and <50% (< EASI 50)
- Patient's itch response was evaluated using Pruritus NRS:
  - The Pruritus NRS is a patient-reported, single-item, 11-point scale, which 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"[4])
  - Itch response[a] by visit was evaluated for Pruritus NRS 0 (no itch), 1-3 (mild), 4-6 (moderate), 7-8 (severe), and 9-10 (very severe)

[a] Baseline weekly Pruritus NRS was calculated by averaging the daily scores up to 7 days before the first injection with ≥4 non-missing values. Post-baseline weekly Pruritus NRS was calculated by averaging the daily scores from the previous 7 days with ≥1 non-missing values

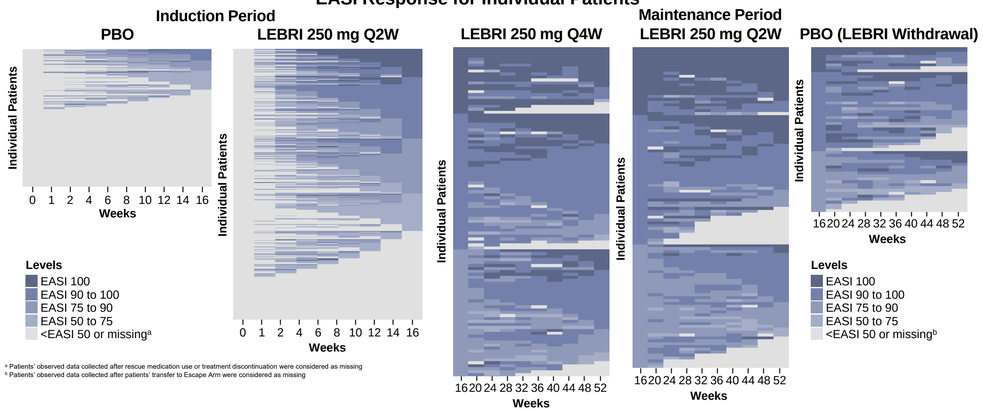
Statistical Analyses

- Skin and itch measures were reported for individual patients in pooled ADvocate1 and 2
  - For Induction Period (Weeks 0-16), the modified Intent-to-Treat population[a] were analyzed. Heatmap presented the observed data for individual visits, with data collected after rescue medication use or treatment discontinuation set as missing
  - For Maintenance Period (Weeks 16-52), the lebrikizumab Week 16 responders[b] were analyzed. Heatmap showed all observed data collected in the Maintenance Period. Patients' observed data collected after patients' transfer to Escape Arm were considered as missing

[a] The pooled analysis excluded 18 patients (from a single study site) whose eligibility could not be confirmed in ADvocate2; [b] Responders were defined in the protocol as those with an IGA (0,1) with ≥2-point improvement or who achieved EASI 75 from baseline to Week 16 without use of rescue therapy

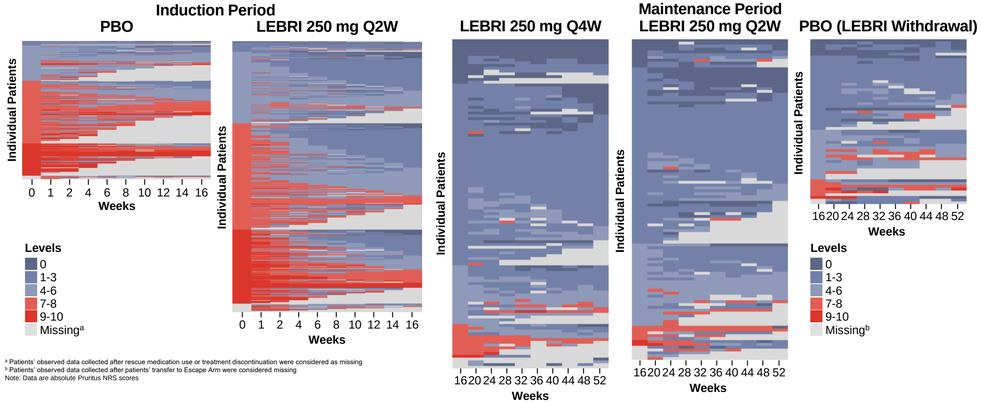
RESULTS

EASI Response for Individual Patients



[a] Patients' observed data collected after rescue medication use or treatment discontinuation were considered as missing
[b] Patients' observed data collected after patients' transfer to Escape Arm were considered as missing

Pruritus NRS Response for Individual Patients



[a] Patients' observed data collected after rescue medication use or treatment discontinuation were considered as missing
[b] Patients' observed data collected after patients' transfer to Escape Arm were considered missing
Note: Data are absolute Pruritus NRS scores

Baseline Demographics and Disease Characteristics

Pooled ADvocate1&2	Induction Period (W0-W16)[a]		Maintenance Period (W16-W52)[b]		
	PBO (N=287)	LEBRI 250 mg Q2W (N=564)	LEBRI 250 mg Q4W (N=118)	LEBRI 250 mg Q2W (N=113)	PBO (LEBRI Withdrawal) (N=60)
Age, years	34.8 (16.8)	36.4 (17.3)	35.8 (17.3)	36.1 (17.0)	33.8 (16.6)
Age category, n (%)					
Adolescents (12 to <18)	35 (12.2)	67 (11.9)	17 (14.4)	13 (11.5)	8 (13.3)
Adults (≥18)	252 (87.8)	497 (88.1)	101 (85.6)	100 (88.5)	52 (86.7)
Female, n (%)	148 (51.6)	277 (49.1)	69 (58.5)	53 (46.9)	36 (60.0)
Race, n (%)					
White	178 (62.0)	364 (64.5)	86 (72.9)	80 (70.8)	33 (55.0)
Asian	75 (26.1)	117 (20.7)	17 (14.4)	19 (16.8)	15 (25.0)
Black	26 (9.1)	58 (10.3)	12 (10.2)	9 (8.0)	8 (13.3)
Other[c]	8 (2.8)	25 (4.4)	3 (2.5)	5 (4.4)	4 (6.7)
BMI	27.1 (6.8)	26.6 (6.2)	26.2 (5.9)	26.3 (6.9)	25.3 (4.8)
Disease duration since AD diagnosis, years	21.9 (14.9)	21.4 (15.0)	22.6 (14.8)	21.7 (14.2)	20.4 (14.9)
IGA, n (%)					
3 (Moderate)	178 (62.0)	345 (61.2)	78 (66.1)	70 (61.9)	37 (61.7)
4 (Severe)	109 (38.0)	219 (38.8)	40 (33.9)	43 (38.1)	23 (38.3)
EASI	30.3 (11.9)	29.3 (11.6)	28.8 (12.6)	29.5 (10.8)	28.9 (11.2)
Pruritus NRS	7.2 (1.8)	7.2 (1.9)	7.0 (2.1)	7.2 (1.7)	7.5 (1.8)
BSA, % involvement	46.9 (22.5)	45.7 (22.5)	43.9 (23.2)	45.3 (20.6)	42.9 (22.4)

[a] Pooled modified ITT population; [b] LEBRI Week 16 responders, defined as those with an IGA (0,1) with ≥2-point improvement or who achieved EASI 75 from baseline to Week 16 without use of rescue therapy; [c] 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

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ABBREVIATIONS

AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 100=100% improvement from baseline in EASI; EASI 90/75/50=at least 90/75/50% 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; IR=inadequate responder; ITT=Intent-to-Treat; LD=loading dose; LEBRI=lebrikizumab; LTE=long-term extension; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation; W=week

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