Eblasakimab Improves Itch and Sleep Loss in Adult Patients with Moderate-to-severe Atopic Dermatitis in a Randomized, Double-blinded, Placebo-controlled, Phase 1 Study

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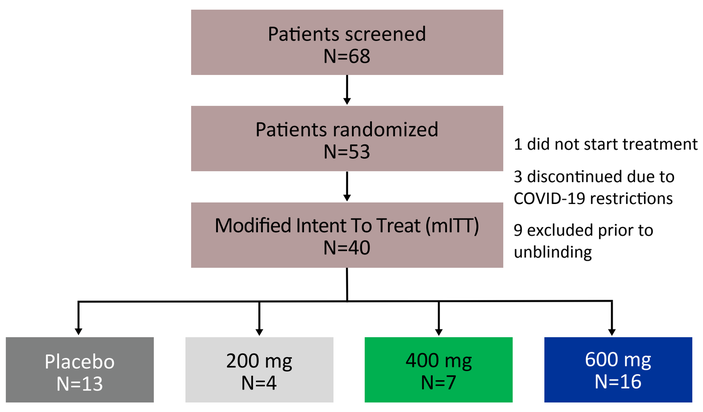
Background

- Interleukin-4 (IL-4) and IL-13 are key drivers of atopic dermatitis (AD). Both signal through a shared type-2 receptor, a heterodimer comprised of IL-4Rα and IL-13Rα1.
- Eblasakimab (ASLAN004), a first-in-class, fully human monoclonal antibody binds IL-13Rα1 with high affinity and blocks the signaling of IL-4 and IL-13 through the type-2 receptor.
- A randomized, double-blind, placebo-controlled, Phase 1b multiple ascending dose monotherapy study [NCT04090229] evaluated the safety, tolerability, and clinical properties for eblasakimab vs. placebo in adult patients with moderate-to-severe AD. Key efficacy results and observations on pharmacodynamic (PD) markers are reported separately .
- The objective of this study was to evaluate the effects of eblasakimab on itch and sleep scores in AD.

Methods

- Three patient cohorts were randomized to receive either 200, 400 or 600 mg eblasakimab or placebo subcutaneously once weekly for 8 weeks in a multiple ascending dose study design (Blauvelt 2022, AAD).
- Adult patients were included with chronic AD present for ≥3 years before screening, and the following AD parameters at screening and baseline: eczema area and severity index (EASI) ≥16, Investigator's Global Assessment (IGA) score ≥3 (scale of 0 to 4), and ≥10% body surface area (BSA) of AD involvement. Rescue medication (moisturizer with active ingredient, topical corticosteroids, topical calcineurin inhibitors) was not allowed; LOCF was used for participants who used rescue medication.
- Patient reported outcomes were measured, including pruritus numeric rating scale (P-NRS) for both worst and average itch and Patient-Oriented Eczema Measure (POEM), which includes a single item sleep loss component.
- Inferential statistical analysis was performed for 600 mg vs. placebo groups at week 8 only; results for 200 and 400 mg groups were descriptively described due to small sample size.

Analysis



- Efficacy analysis in the Phase 1b study used a modified Intent to Treat (mITT) population in which 3 patients discontinued due to COVID-19 restrictions and 9 patients from one site were excluded from the analysis prior to unblinding as the participants did not have disease characteristics consistent with moderate-to-severe AD.

Results

- Baseline demographics and disease characteristics were balanced across treatment groups. (**Tables of Baseline data**).
- Improvements in percent change from baseline (CFBL) in P-NRS for median worst itch were apparent over time and at week 8 (**Figure 1a,b**) and also for median average itch (**Figure 2a,b**) with eblasakimab treatment compared with placebo (worst itch: -48% vs. -13%; average itch: -49% vs. -6%, eblasakimab 600 mg vs. placebo, respectively).
- Improvements in POEM score were apparent over time with eblasakimab treatment compared with placebo, with the 400 and 600 mg doses producing a greater magnitude of response than the 200 mg dose (**Figure 3**). At week 8, median POEM CFBL for 400 mg and 600 mg eblasakimab was -12 and -9 respectively, vs. -1 for placebo.
- A 4-point improvement in POEM score was observed at week 8 for eblasakimab 600 mg vs. placebo.
- There was a greater improvement in POEM sleep scores with eblasakimab vs. placebo (**Figure 4**). A 2-point improvement (mean) in sleep loss (POEM item) was observed at week 8 for 400 mg and 600 mg eblasakimab (43% and 56% vs. 15% for placebo), for patients with sleep scores of 3 or 4 at baseline. The majority of patients (75% [12/16]) in the 600 mg treatment group reported >5 nights of sleep disturbance at baseline vs. placebo (54% [7/13]). More (63% [10/16]) of eblasakimab-treated patients reported 'no days' or '1–2 days' of sleep disturbance at week 8 vs. placebo (38% [5/13]).
- Rescue medication use was low, but higher in the placebo group (data not shown).

Figure 1. Improvements in (median) worst itch: a) over time; b) at week 8.

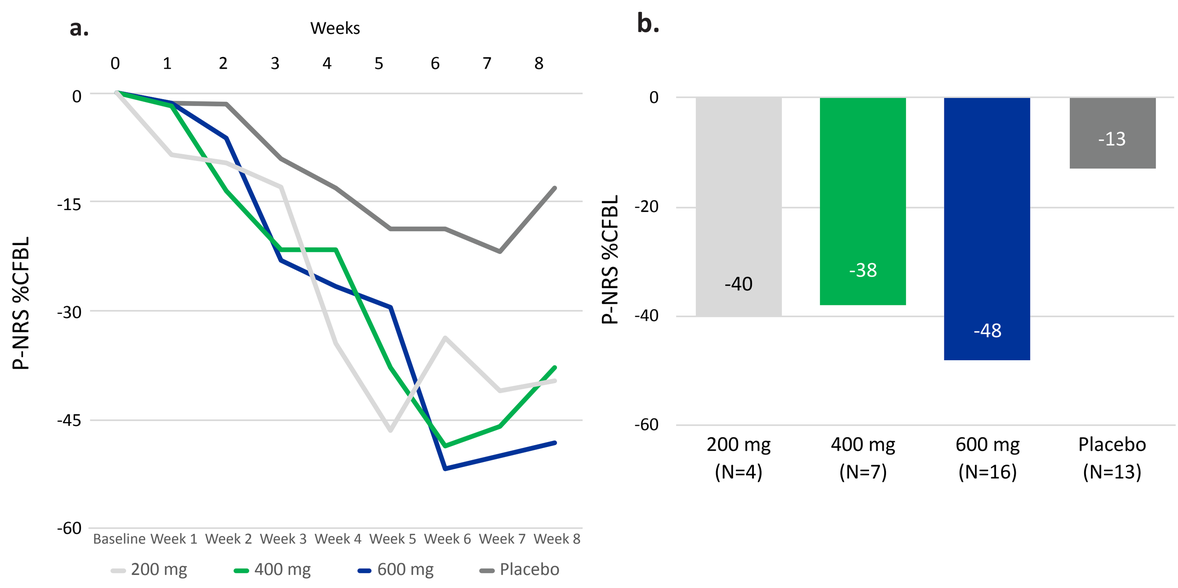


Figure 2. Improvements in (median) average itch: a) over time; b) at week 8.

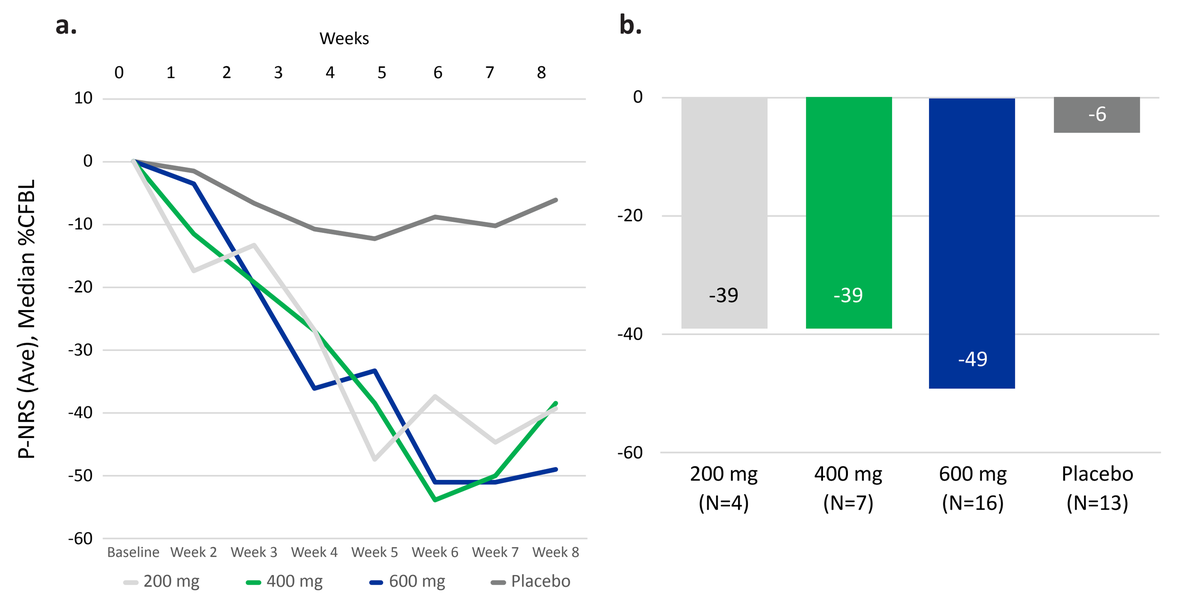


Figure 3. Improvements in POEM CFBL over time

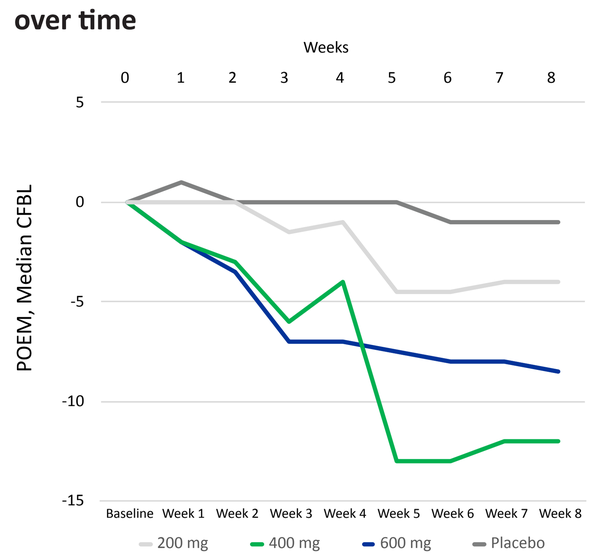
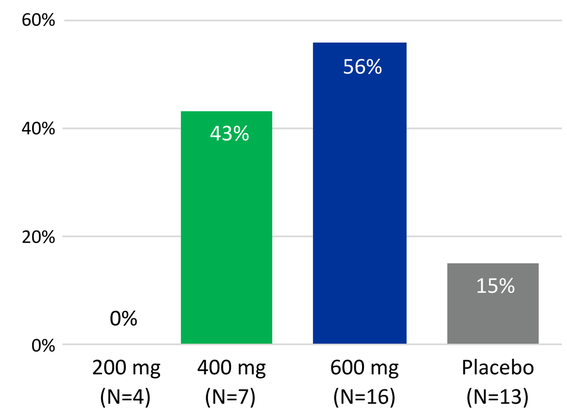


Figure 4. 2-point improvement in sleep loss (POEM), week 8



- Rates of moderate-to-severe AEs were comparable between 600 mg and placebo. AEs related to treatment were similar between groups. AEs leading to treatment discontinuation were higher in the placebo group. 1 SAE reported in the study (mild abdominal pain, 400 mg); considered unrelated to treatment. No deaths reported.
- These PRO findings accompany reductions in disease severity and activity evidenced by changes in efficacy measures and reductions in PD markers of AD (TARC/CCL17, total IgE and LDH) (data presented separately, poster WCD).

Baseline demographics & disease characteristics

Select baseline demographics	Statistic	No. (%)			
		Eblasakimab 200 mg (N=4)	Eblasakimab 400 mg (N=7)	Eblasakimab 600 mg (N=16)	Placebo (N=13)
Age, Mean (SD)	Mean (SD)	32.5 (5.3)	29.4 (4.9)	34.0 (14.4)	34.2 (11.3)
Male, n (%)		3 (75.0%)	5 (71.4%)	12 (75.0%)	10 (76.9%)
Age of onset (yrs)	Mean (SD)				
Race/ethnicity	Asian	4 (100%)	7 (100%)	7 (43.8%)	8 (61.5%)
	Black	0	0	1 (6.2%)	0
	White	0	0	8 (50.0%)	3 (23.1%)
	Other	0	0	0	2 (15.4%)
Weight (kg)	Mean (SD)	75.3 (13.2)	72.2 (14.2)	74.7 (20.7)	75.2 (12.7)

Disease Characteristics	Statistic	No. (%)			
		Eblasakimab 200 mg (N=4)	Eblasakimab 400 mg (N=7)	Eblasakimab 600 mg (N=16)	Placebo (N=13)
EASI	Mean (SD) Median	32.9 (14.3) 30.4	31.3 (12.3) 33.3	30.5 (14.2) 25.1	31.5 (10.1) 33.0
IGA	3, Moderate 4, Severe	2 (50.0) 2 (50.0)	5 (71.4) 2 (28.6)	10 (62.5) 6 (37.5)	7 (53.8) 6 (46.2)
BSA involvement	Mean (SD) Median	55.5 (34.6) 54.5	62.3 (28.5) 74.0	45.82 (24.4) 37.5	50.1 (28.6) 43.0
Pruritus NRS score (Worst)	Mean (SD) Median	7.4 (2.2) 7.7	7.7 (1.6) 7.7	7.5 (1.3) 6.9[a]	7.7 (2.0) 8.0
TARC/CCL17 (pg/mL)	Mean (SD) Median	6,097 (6,247) 5,556	18,310 (40,556) 2,262	4,223 (5,186) 2,128	5,056 (6,842) 2,398
Total IgE (kU/L)	Mean (SD) Median	15,891 (14,993) 12,278	23,297 (28,508) 10,660	8,660 (7,718) 6,468	8,706 (8,175) 7,7173

Medical history/comorbidities	Statistic	No. (%)			
		Eblasakimab 200 mg (N=4)	Eblasakimab 400 mg (N=7)	Eblasakimab 600 mg (N=16)	Placebo (N=13)
Any		1 (25.0)	6 (85.7)	16 (100.0)	11 (84.6)
General	Diabetes Anxiety/depression	0 0	0 0	0 3 (18.8)	0 1 (7.7)
Atopy-associated	Asthma	0	3 (42.9)	8 (50.0)	6 (46.2)
	Allergy (dust, pet, seasonal, etc)	0	1 (14.3)	9 (56.3)	4 (30.8)
	Allergic rhinitis	1 (25.0)	1 (14.3)	5 (31.3)	1 (7.7)
	Allergic conjunctivitis/dry eye	0	2 (28.6)	0	0
	Drug hypersensitivity	0	1 (14.3)	4 (25.0)	3 (23.1)
	Psoriasiform dermatitis	0	0	1 (6.3)	1 (7.7)
	Eczema herpeticum	0	0	0	1 (7.7)
Other		0	3 (42.9)	12 (75.0)	6 (46.2)
None documented		3 (75.0)	1 (14.3)	0	2 (15.4)

Adverse events

	All treated patients minus excluded site (N=43)			
	200 mg (N=5)	400 mg (N=8)	600 mg (N=16)	PBO (N=14)
Any	5 (100%)	8 (100%)	9 (56%)	8 (57%)
Related	5 (100%)	6 (75%)	6 (38%)	7 (50%)
Moderate/ severe	2 (40%)	3 (38%)	4 (25%)	5 (36%)
Serious adverse event (SAE)	0 (0%)	1 (13%)	0 (0%)	0 (0%)
Leading to discontinuation	0 (0%)	1 (13%)	2 (13%)	3 (21%)
Drug-related AEs of interest:				
• Injection site reaction	4 (80%)	3 (38%)	3 (19%)	2 (14%)
• Allergic conjunctivitis	0 (0%)	1 (13%)	2 (13%)	0 (0%)

Conclusion

- Eblasakimab was well tolerated with significant improvements vs. placebo in patient reported outcomes in a Phase 1b study in adults with moderate-to-severe AD.
- Robustness of the data from the small study was supported by sensitivity analyses on the primary analysis set.
- That these significant improvements were seen within the 8-week study period offers the potential for a greater magnitude of effect with prolonged treatment. Further data will be available following the completion of a Phase 2b study (NCT05158023).

Abbreviations: BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment (5-point scale); IgE, immunoglobulin E; NRS, numeric rating scale; TARC/CCL17, thymus- and activation-regulated chemokine/CCL17.
[a]Sample size is (N=13)

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