P0342

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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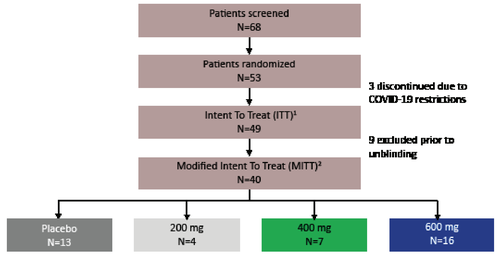
Background

- 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 [Veverka *et al.* EADV **Poster P0343**; Cevikbas *et al.* EADV **Poster 243**].
- 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 9 study patients from one site were excluded from the ITT analysis prior to unblinding as the participants did not have disease characteristics consistent with moderate to severe AD.

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Results

- The Excluded site* set was markedly different from the mITT set at baseline with substantially lower serum TARC/CCL17 (7,350 pg/mL and 461 pg/mL, respectively), serum IgE (12,225 kU/l vs 527 kU/l), and EASI scores (mean 31.2 vs 19.3) showing lower extent and severity of disease. Other notable differences included older age, and lower IGA, BSA and POEM scores. Participants in this site had no atopic disease history but reported other comorbidities including diabetes and hypertension (**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) in the mITT analysis set.

  Participants receiving eblasakimab 600 mg in the Excluded site* exhibited improvement in average itch but not worst itch vs. placebo.
- Improvements in POEM score were apparent over time with eblasakimab treatment compared with placebo in the mITT set, 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 in the mITT set. No improvement vs. placebo was observed in the Excluded site*.
- A 4-point improvement in POEM score was observed at week 8 for eblasakimab 600 mg vs. placebo in the mITT but not the Excluded site* analysis sets (81% vs. 23%; 50% vs. 100%, respectively).
- 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) in the mITT analysis set, and 600 mg eblasakimab in the Excluded site* (33% vs. 0% for placebo). Importantly, these are improvements 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]).

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

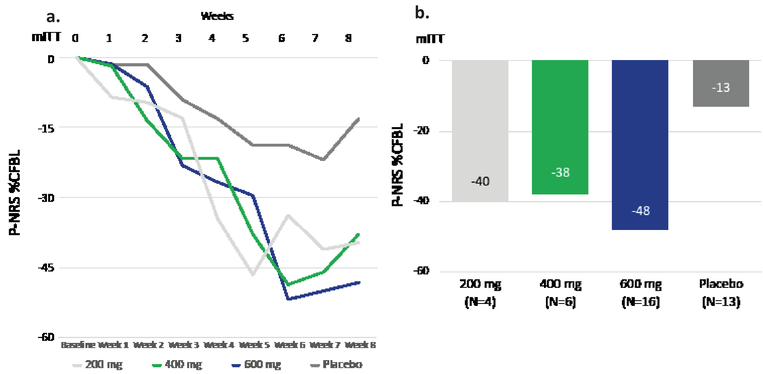


Figure 2. Improvements in (median) average itch: a) over time; b) at week 8.

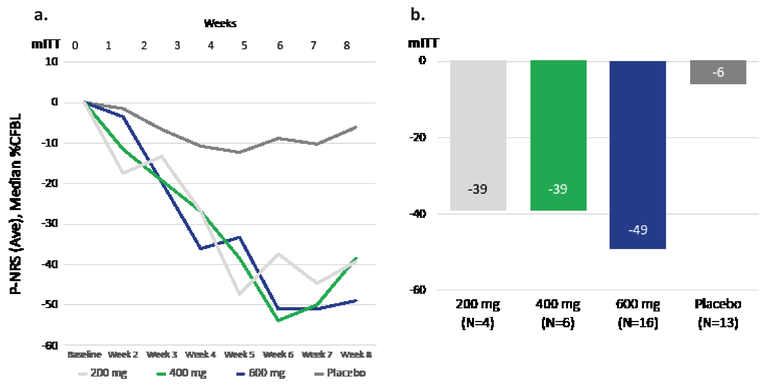


Figure 3. Improvements in POEM CFBL over time

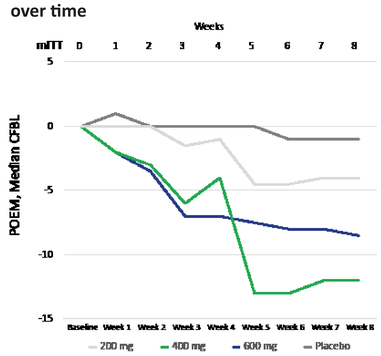
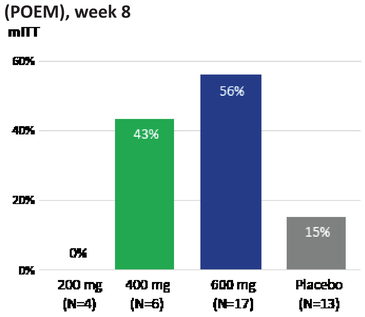


Figure 4. 2-point improvement in sleep loss (POEM), week 8



- Rescue medication use was low, but higher in the placebo group (data not shown).
- 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 (**Poster P0343**) and reductions in PD markers of AD (TARC/CCL17, total IgE and LDH) (**Poster P0243**).

Baseline demographics & disease characteristics

Select baseline demographics	Statistic	ITT (N=49)	mITT (N=40)	Excluded site* (N=9)
Age (yrs)	Mean (SD)	37.6 (15.77)	33.1 (11.30)	57.4 (18.06)
	Min, Max	18, 83	18, 68	21, 83
Sex	Male	32 (65.3%)	30 (65.3%)	2 (22.2%)
	Female	17 (34.7%)	10 (34.7%)	7 (77.8%)
Race	Asian	26 (53.0%)	26 (65.0%)	0
	Black	2 (4.0%)	1 (2.5%)	1 (11.1%)
	White	19 (38.8%)	11 (27.5%)	8 (88.9%)
	Other	2 (4.0%)	2 (5.0%)	0
Weight (kg)	Mean (SD)	75.6 (15.48)	74.5 (16.14)	80.49 (12.99)
	Min, Max	44.9, 120.0	44.9, 120.0	61.7, 99.7

Disease Characteristic	Statistic	ITT (N=49)	mITT (N=40)	Excluded site* (N=9)
P-NRS, worst	Mean (SD)	7.83 (1.6)	7.59 (1.6)	8.79 (1.0)
	Median	7.93	7.7	9.1
P-NRS, average	Mean (SD)	6.71 (1.7)	6.58 (1.8)	7.22 (1.1)
	Median	6.79	6.7	7.0
POEM	Mean (SD)	20.59 (5.4)	21.50 (5.2)	16.56 (4.1)
	Median	21.00	23.00	18.00
TARC/CCL17 (pg/mL)	Mean (SD)	6134 (16659)	7360 (18179)	461 (302)
	Median	1684	2262	366
Total IgE (kU/l)	Mean (SD)	10145 (14382)	12225 (15086)	527 (990)
	Median	5010	7095	95

Disease history/ comorbidities		ITT (N=49)	mITT (N=40)	Excluded site* (N=9)
Any		41 (83.7%)	33 (82.5%)	8 (88.9%)
Atopy-associated	Asthma	17 (34.7%)	18 (45.0%)	1 (11.1%)
	Allergy (dust, pet, seasonal, etc.)	12 (24.5%)	12 (30.0%)	0
	Allergic rhinitis	9 (18.4%)	9 (22.5%)	0
	Allergic conjunctivitis/ dry eye	2 (4.1%)	2 (5.0%)	0
	Drug hypersensitivity	7 (14.3%)	8 (20.0%)	0
	Psoriasiform dermatitis	2 (4.1%)	2 (5.0%)	0
	Eczema herpeticum	1 (2.0%)	1 (2.5%)	0
General	Diabetes	4 (8.2%)	0	4 (44.4%)
	Anxiety/depression	6 (12.2%)	4 (10%)	3 (33.3%)
	Hypertension	6 (12.2%)	3 (7.5%)	(44.4%)
Other		25 (51.0%)	22 (55.0%)	5 (55.6%)
None documented		8 (16.3%)	6 (15.0%)	1 (11.1%)

Adverse events

	mITT (N=43)				Excluded site* (N=9)	
	200 mg (N=5)	400 mg (N=8)	600 mg (N=16)	PBO (N=14)	600 mg (N=6)	PBO (N=3)
Any	5 (100%)	8 (100%)	9 (56%)	(N=14)	3 (50%)	0 (0%)
Related	5 (100%)	6 (75%)	6 (38%)	7 (50%)	2 (33%)	0 (0%)
Moderate/severe	2 (40%)	3 (38%)	4 (25%)	5 (36%)	2 (33%)	0 (0%)
Serious adverse event (SAE)	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leading to discontinuation	0 (0%)	1 (13%)	2 (13%)	3 (21%)	0 (0%)	0 (0%)
Drug-related AEs of interest:						
• Injection site reaction	4 (80%)	3 (38%)	3 (19%)	2 (14%)	2 (33%)	0 (0%)
• Allergic conjunctivitis	0 (0%)	1 (13%)	2 (13%)	0 (0%)	0 (0%)	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. Including the Excluded site* data did not change the primary endpoint or conclusions.
- That these significant improvements were seen within the 8-week study period offers the potential for a greater magnitude of effect with prolonged treatment, supporting further investigation in an ongoing Phase 2b clinical trial.