P0343

Eblasakimab improves multiple disease measures in adult patients with moderate-to-severe atopic dermatitis in a randomized, double-blinded, placebo-controlled, Phase 1 study

Karen A. Veverka[1], Josemund Menezes[1], Steven Tien Guan Thng[2], Melinda Gooderham[3], Eric Simpson[4]

1. ASLAN Pharmaceuticals, Menlo Park, CA, and Singapore. 2. Skin Research Institute of Singapore, Agency for Science Technology & Research, Singapore; National Skin Center, Singapore. 3. SKiN Centre for Dermatology, Peterborough, ON, Canada; Queens University, Kingston, ON, Canada; Probity Medical Research, Waterloo, ON, Canada.
4. Department of Dermatology, Oregon Health & Science University, Portland, OR, USA

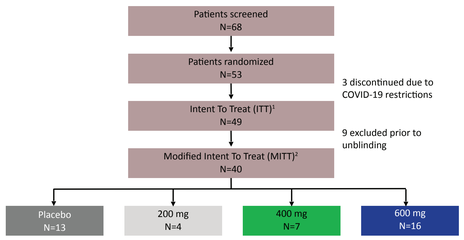
Background

- Interleukin (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. Top line results have been reported previously (Blauvelt 2022, AAD presentation).
- The objective of this study was to further analyze secondary endpoints of clinical relevance and post hoc subgroup analyses. Observations on patient reported outcomes (PROs) and pharmacodynamic (PD) markers and are reported separately [**Posters P0342 & P0243**].

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. Further detail on the methodology has been presented previously (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 med.
- Efficacy assessments included percent change from baseline (%CFBL) in EASI, proportions of patients with 50% or 75% improvement in EASI score (EASI 50 or EASI 75) or IGA 0/1, and %CFBL in percent BSA involvement. Further data are presented from a prespecified subgroup of patients from an excluded site with atypical AD.
- 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 the participants did not have disease characteristics consistent with moderate to severe AD.

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 and BSA. Participants in this site had no atopic disease history but reported other comorbidities including diabetes and hypertension (**Tables of Baseline data**).
- In the mITT analysis set, improvements in EASI score were seen early and progressed over the trial duration with eblasakimab treatment compared with placebo, with the 400 and 600 mg doses producing a great magnitude of response than the 200 mg dose (**Figure 1**).

Figure 2. EASI, mean %CFBL at week 8

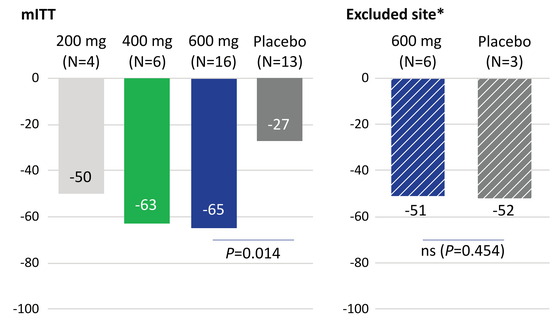


Figure 3. Placebo adjusted means (EASI)

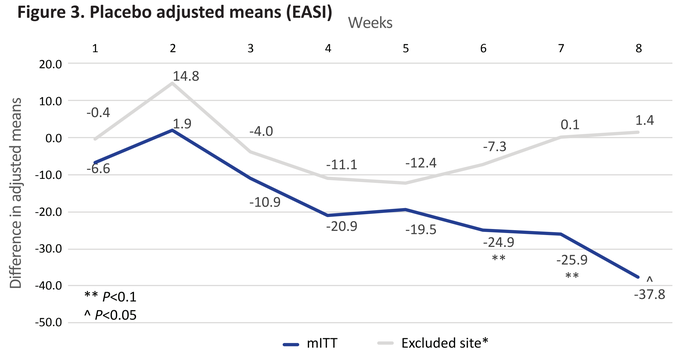


Figure 4. % of patients achieving EASI-50, EASI-75, EASI-90 at week 8

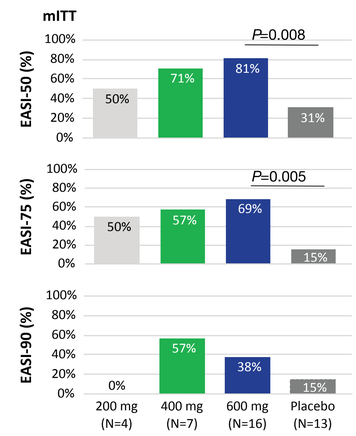


Figure 5. % of patients achieving IGA 0/1 at week 8

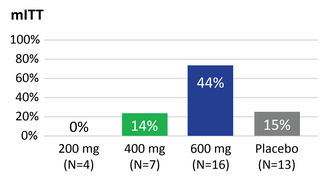


Figure 6. Mean %CFBL in %BSA affected

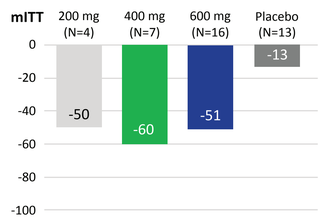
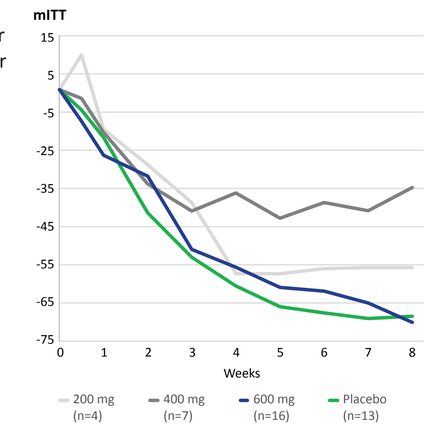


Figure 1. EASI, mean %CFBL



- Significant improvements in %CFBL in EASI score at week 8 were noted for eblasakimab 600 mg vs. placebo in the mITT set (-65% vs. -27%, *P*=0.014), but not the Excluded site population (**Figure 2**). The difference in adjusted means was apparent early for the mITT set by week 6 but not for the Excluded site* set (**Figure 3**).
- Though the study was not powered to achieve statistical significance in any of the binary outcomes, improvements were also observed in the mITT set in the proportions of patients taking eblasakimab who achieved EASI-50, EASI-75 and EASI-90 over time vs. placebo at week 8 (EASI-50: 81% vs. 31%; EASI-75: 69% vs. 15%; EASI-90: 38% vs. 15%) (Figure 4). No such improvement was apparent in the Excluded site* population.
- A higher percentage of patients achieved an IGA 0/1 at week 8 for eblasakimab 600 mg vs placebo in the mITT set (44% vs. 15%, *P*=0.107) but not the Excluded site* population (**Figure 5**).
- Mean %CFBL in BSA at week 8 was -51% for eblasakimab 600 mg vs. -13% for placebo in the mITT set and -39% vs. -44% in the Excluded site* population (**Figure 6**).
- Rescue medication use was low, but higher in the placebo group (data not shown).
- Patients treated with eblasakimab also had reductions in AD pharmacodynamic markers, further supporting its efficacy (**Poster P0243**). Reductions in patient reported outcomes including itch and sleep loss were also observed (**Poster P0342**).
- 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.

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)
EASI	Mean (SD)	29.0 (12.0)	31.2 (12.2)	19.3 (3.5)
	Median	24.8	28.0	18.0
IGA	IGA 3	32 (65.3%)	23 (57.5%)	9 (100%)
	IGA 4	17 (34.7%)	17 (42.5%)	0 (0%)
BSA (%)	Mean (SD)	46.9 (26.2)	51.1 (27.1)	28.4 (8.3)
	Median	17.0	41.0	30.0
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 several efficacy 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.

Acknowledgement: The sponsor gratefully acknowledges the participation of all patients, Investigators and staff who took part in this study. **Sponsor:** ASLAN Pharmaceuticals Pte Ltd.