Potentially Greater Efficacy with CBP-201 for Adults with Severe versus Moderate Atopic Dermatitis at Baseline: Subgroup Analyses from the WW001 Phase 2 Randomized Trial

Abstract #438

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CBP-201 is a next-generation mAb targeting IL-4Rα

- CBP-201 and dupilumab utilize distinct binding epitopes. In studies characterizing the immunological profile of CBP-201, it was demonstrated that amino acid residues crucial for IL-4 binding with CBP-201 had little effect on the affinity for dupilumab; however, the same mutations completely abolished binding of CBP-201.[1,2]
- CBP-201 exhibits higher binding affinity (20.7 pM) to human IL-4Rα than dupilumab (45.8 pM), based on surface plasmon resonance.[1,2]
- CBP-201 downregulates intracellular signalling *in vitro* and cytokine gene expression in human skin *ex vivo* with greater potency than dupilumab.[1,2]

Clinical trials in atopic dermatitis (AD) were positive[3–6]

- Signs and symptoms decreased rapidly, often without plateauing across 16 weeks of treatment with CBP-201.
- In WW001, AD improvements were gained with both Q2W and Q4W dosing.

Objective

It is unknown whether there are differences in clinical response to CBP-201 with moderate versus severe AD. The WW001 phase 2 study with CBP-201 recruited a population with mostly moderate AD patients (~31% vIGA4 and EASI score ~21 [median] and ~25 [mean]) and it was theorized that a more balanced population between moderate and severe patients (ie 50% vIGA4 or an EASI score of ~30) would demonstrate increased levels of efficacy with CBP-201.

Here we report *post hoc* efficacy analyses at Week 16 with CBP-201 300 mg from the global WW001 phase 2 trial with baseline severity subgroups: vIGA 3 (moderate) and 4 (severe).

Methodology

Study design

In WW001 (NCT04444752), 226 adults with moderate-to-severe AD were randomized (1:1:1:1), double-blind, to subcutaneous CBP-201 (300 mg Q2W, 150 mg Q2W, 300 mg Q4W) or placebo.

***Post hoc* efficacy analyses**

CBP-201 300 mg Q2W and 300 mg Q4W data were pooled. Efficacy was assessed per subgroup based on investigator assessments (EASI, SCORAD, percent BSA, vIGA) and PROs (DLQI, POEM).

Statistics used in the *post hoc* analyses

Least squares mean score changes were analyzed using ANCOVA (including treatment, baseline scores, and baseline vIGA in the models), with missing data interpolated by LOCF. Responder endpoints were analyzed using Clopper-Pearson methodology and, for missing values, non-responder imputation.

All statistical analyses reported here are for CBP-201 vs placebo, per baseline severity subgroup, at Week 16

Results

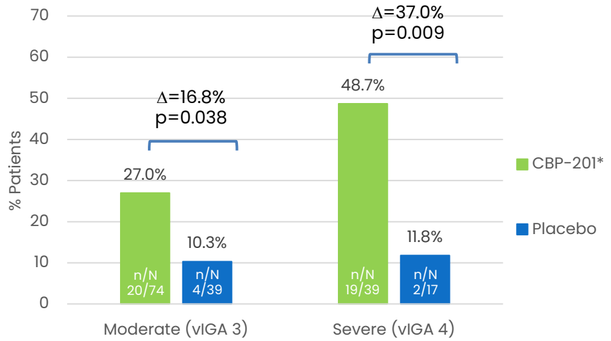
AD and QoL rating scale scores at baseline

Mean (SD) scores	Moderate (vIGA 3)		Severe (vIGA 4)	
	CBP-201* N=74	Placebo N=39	CBP-201* N=39	Placebo N=17
EASI	21.5 (7.0)	22.2 (6.3)	32.6 (11.9)	31.9 (10.8)
BSA	35.1 (16.9)	34.4 (16.5)	49.9 (22.7)	45.3(20.5)
SCORAD	59.4 (9.1)	63.5 (10.5)	72.2 (9.9)	76.7 (8.5)
PP-NRS	6.5 (2.0)	6.8 (1.2)	6.9 (2.2)	7.8 (1.5)
DLQI	13.1 (7.5)	12.6 (5.6)	14.4 (8.3)	16.8 (6.5)
POEM	17.9 (6.5)	18.7 (5.1)	20.7 (6.8)	22.3 (5.3)

*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms.

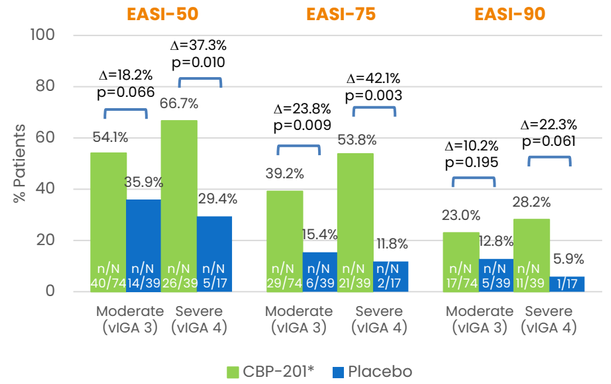
Numerically greater CBP-201 responses at Week 16 for patients with severe (vIGA-AD™ 4) vs moderate (vIGA-AD™ 3) AD at baseline

Percent of patients with vIGA ≥2-point reduction at Week 16



*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n/N = responders at Week 16/patients at baseline.

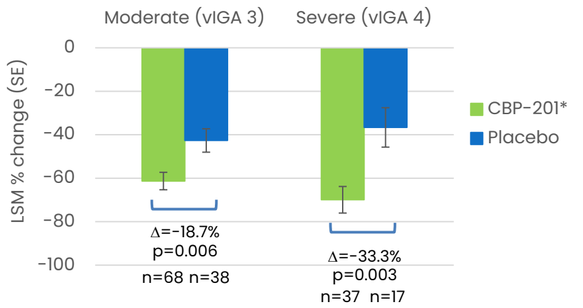
Percent of patients with EASI-50/-75/-90 at Week 16



*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n/N = responders at Week 16/patients at baseline.

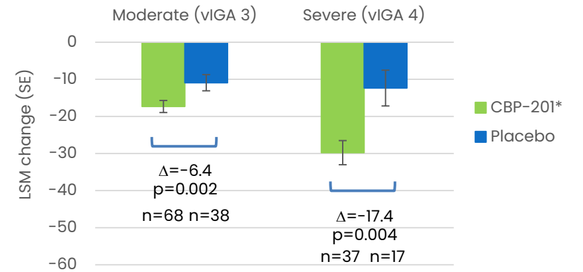
References: 1. Yang et al. Poster LB945, SID 2022, Portland, OR. 2. Manuscript submitted. 3. Zhang et al. Presentation 45874. AAD 2023, New Orleans, LA. 4. Strober et al. Maui Derm 2022, Maui, HI. 5. Silverberg et al. Poster P0214 (Abstract 469), EADV 2022, Milan, Italy. 6. Strober et al. Poster P0215 (Abstract 470), EADV 2022, Milan, Italy.

LSM % reductions in EASI at Week 16



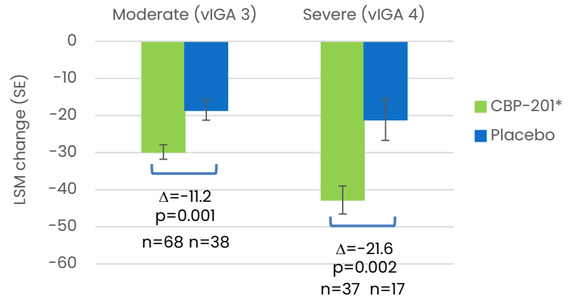
*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n = patients at Week 16.

LSM reductions in BSA at Week 16



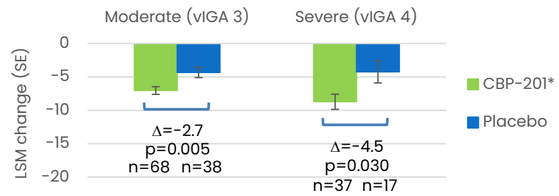
*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n = patients ar Week 16.

LSM reductions in SCORAD at Week 16



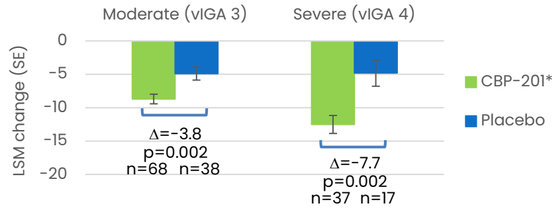
*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n = patients at Week 16.

LSM reductions in DLQI at Week 16



*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n = patients at Week 16.

LSM reductions in POEM at Week 16



*Pooled CBP-201 300 mg Q2W and 300 mg Q4W arms. n = patients at Week 16.

Conclusion

- Improvements were observed in patients with either moderate or severe AD after 16 weeks of treatment with CBP-201 300 mg Q2W and Q4W.
- Numerically greater proportions of patients with severe versus moderate AD on study entry experienced improvements with CBP-201.
- No clear differences in placebo responses were noted between the moderate and severe subgroups.

Future Directions

- In future CBP-201 trials, a more balanced AD severity population needs to be examined to determine if similar observations are noted.
- Collectively, the WW001 findings support further investigation of CBP-201 at both the Q2W and Q4W dosing schedules, enrolling larger numbers of patients with both moderate and severe AD, with prespecified analyses by baseline AD severity.

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Abbreviations: AD, atopic dermatitis; BSA, Body Surface Area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-50, at least 50% decrease from baseline; mAb, monoclonal antibody; POEM, Patient Oriented Eczema Measure; PP-NRS, Peak Pruritus Numerical Rating Scale; PRO, patient-reported outcome; Q2/4W, every 2/4 weeks; QoL, quality of life; SCORAD, Scoring Atopic Dermatitis; SD, standard deviation; SE, standard error; vIGA, validated Investigator Global Assessment.

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