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

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Introduction: CBP-201 is a next-generation monoclonal antibody targeting the IL-4Rα subunit. Rapid efficacy with CBP-201 was demonstrated in global phase 2 (WW001) and China-only pivotal trials (CN002) in patients with moderate-to-severe atopic dermatitis (AD). Previous studies of AD therapy demonstrated similar efficacy between moderate and severe disease, with a trend toward greater improvement in moderate patients.[1,2] It is unknown whether there are differences in clinical response to CBP-201 with moderate versus severe AD.

Objective: We report *post hoc* efficacy analyses at Week 16 with CBP-201 300 mg from WW001 in baseline severity subgroups, based on validated Investigator Global Assessment (vIGA™) scores of 3 (moderate) and 4 (severe).

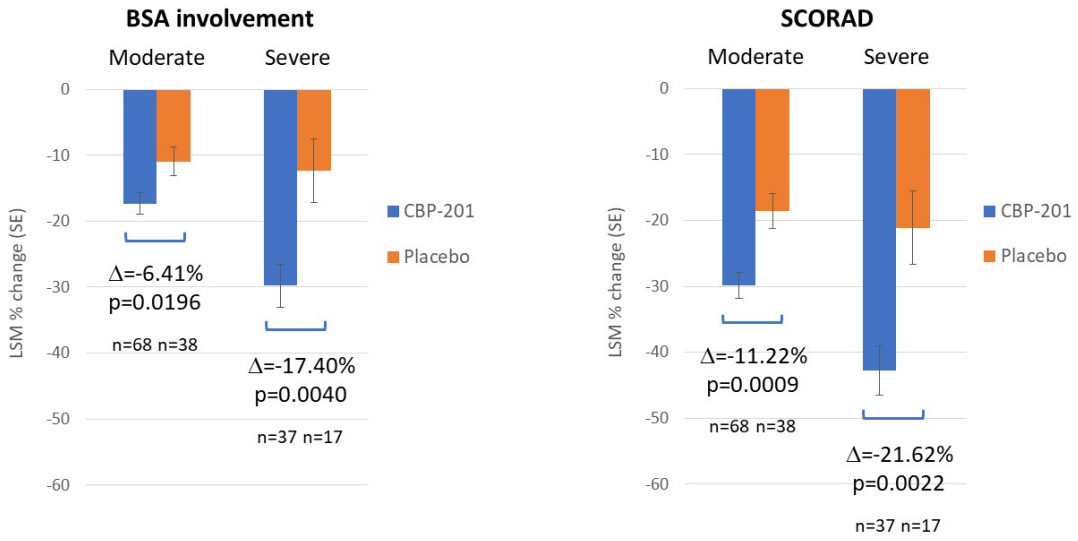
Methods: In WW001 (NCT04444752), adults with moderate-to-severe AD were enrolled in a RDBPC 16-week trial of subcutaneous CBP-201 or placebo. For *post hoc* analysis, data for 300 mg every two- and four-week dose regimens were pooled. Investigators assessed AD severity using Eczema Area and Severity Index (EASI), SCORing AD (SCORAD), percent Body Surface Area (BSA) of AD involvement, and vIGA. Patient reported outcomes were assessed with the Dermatology Life Quality Index (DLQI) and Patient Oriented Eczema Measure (POEM). Least squares mean (LSM) score changes were analyzed using ANCOVA modeling (including treatment, baseline score, baseline vIGA), with missing data interpolated by last observation carried forward. Responder endpoints were analyzed using Clopper-Pearson methodology and, for missing values, non-responder imputation. P-values are for CBP-201 versus placebo, per baseline severity subgroup, at Week 16.

Results: At baseline, 113 patients had moderate AD (n=74 CBP-201, n=39 placebo) and 56 patients had severe AD (n=39 CBP-201, n=17 placebo). Baseline EASI scores were lower in the moderate subgroup (mean [SD]: CBP-201, 21.5 [7.0]; placebo, 22.2 [6.3]) versus the severe subgroup (CBP-201, 33.6 [11.9]; placebo, 31.9 [10.8]). In both the moderate and severe AD subgroups, significant improvements with CBP-201 versus placebo were observed. Except for the proportion of patients achieving vIGA 0/1, numerically greater CBP-201 responses were observed in patients with severe versus moderate AD at Week 16; placebo responses were comparable per subgroup. In the severe and moderate subgroups, LSM SCORAD scores decreased by -42.8% (severe) and -29.8% (moderate) and LSM percent BSA decreased by -29.8% and-17.3%, respectively (Figure). Clinically meaningful 2-point improvement in vIGA

was reported for 48.7% and 27.0% of patients with severe and moderate AD, respectively. The proportions of patients achieving vIGA 0/1, with 2-point improvement, were 20.5% and 27.0% with severe and moderate AD, respectively. Numerically greater proportions of patients with severe versus moderate AD experienced EASI responses with CBP-201: EASI-50, 66.7% vs 54.1%; EASI-75, 53.8% vs 39.2%; EASI-90, 28.2% vs 23.0%. Patients with severe versus moderate AD reported greater improvements in patient reported outcomes with CBP-201: DLQI, -8.7 vs -7.0; POEM, -12.5 vs -8.7.

Conclusions: Clinically meaningful improvements were observed in AD patients with either moderate or severe AD after 16 weeks of treatment with CBP-201 300 mg at either two- or four-week dosing. There were no differences noted between moderate and severe patients in the placebo treatment group. In most severity readouts, greater proportions of AD patients with severe disease on study entry experienced clinically meaningful improvements with CBP-201. In future CBP-201 trials, a more severe AD population needs to be examined to determine if this same observation is also noted. Collectively, the WW001 findings support further investigation of CBP-201, at both the 2- and 4-week dosing schedules enrolling larger numbers of moderate and severe AD patients and with prespecified analyses by baseline AD severity.

Percentage change in BSA involvement and SCORAD scores at Week 16



n = patients with Week 16 data
Numbers of patients at baseline were: moderate (n=74 CBP-201, n=39 placebo), severe (n=39 CBP-201, n=17 placebo)

Keywords: atopic dermatitis, severe, moderate, CBP-201, IL-4Rα

References

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