The Effect of Baseline Disease Characteristics on Efficacy Outcomes: Results from a Phase 2b, Randomized, Double-blind, Placebo-controlled Trial of CBP-201 in Adults with Moderate-to-Severe Atopic Dermatitis (AD)

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Introduction: CBP-201 is a novel monoclonal antibody targeting IL-4Rα. A Phase 2b trial (WW001) in moderate-to-severe patients with AD successfully met its primary and key secondary endpoints, despite the trial recruiting less severe AD patients than phase 3 trials of the approved IL-4Rα agent during the ongoing COVID-19 pandemic (Strober et al, Maui Derm 2022). As such, post-hoc analyses were conducted to determine the relationship between baseline levels of thymus- and activation-regulated chemokine (TARC), a chemokine distinctively expressed on Th2 lymphocytes and a biomarker that correlates with AD disease activity, and efficacy outcomes.

Methods: In this double-blind, placebo-controlled, international trial (NCT04444752), with 16-week treatment and 8-week follow-up periods, 226 adults with moderate-to-severe AD were randomized (1:1:1:1) to subcutaneous CBP-201 (300mg Q2W, 150mg Q2W, 300mg Q4W) or placebo. The overall trial population was stratified into three subgroups according to baseline TARC; “low” (≤116.74 pg/ml), “mid” (>116.74 to ≤291 pg/ml), “high” (>291 pg/ml) and the relationship with disease severity and effect on other biomarkers and efficacy outcomes was determined.

Results: Each subgroup included 74 patients. The “high” subgroup had higher baseline EASI (median 27.8) compared with either the “low” (median EASI, 18.4) or “mid” (median EASI, 19.9) subgroups.

Across all CBP-201 doses, Week 16 clinical responses were greatest in the “high” subgroup with numerically larger absolute reductions in EASI scores compared to the “low” subgroup (300 mg Q4W: “high” -25 vs “low” -12; 300 mg Q2W: -20 vs -11; 150 mg Q2W: -20 vs -10 respectively). Similar Week 16 trends were noted for placebo-adjusted LS mean percent EASI reductions (-54% vs -19%; -33% vs -18%; -35% vs -11%), absolute reductions in PP-NRS (-4.3 vs -2.4; -4.0 vs -3.4; -3.2 vs -2.5) and percent PP-NRS change (-24% vs +8.3%; -19% vs -16%; -8.1% vs +2.8%).

When comparing baseline EASI tertiles, clinical response was also greater in the most severe (EASI ≥26.4) vs least severe (EASI ≤18.4) subgroup as expected from the correlation between baseline TARC and baseline EASI.

Mean TARC levels themselves were unchanged from baseline at Week 16 for the “low” subgroup but decreased by 54–76% across the treatment arms in the “high” subgroup. IgE levels showed a greater reduction in the “high” vs the “low” subgroup.

Patients randomized in China (N=32) had both higher baseline TARC levels (median 457.6 pg/mL) and EASI scores (median 26.9) and experienced greater clinical responses compared with the overall trial population (Strober et al, Maui Derm 2022), consistent with the effects seen in the high TARC group of the whole population.

Conclusion: This post-hoc analysis of the Phase 2b trial of CBP-201 in patients with moderate-to-severe AD, showed that higher baseline TARC levels correlated with higher baseline EASI and that CBP-201 in patients with higher baseline TARC achieved greater placebo adjusted clinical responses. These results highlight the relationship of baseline disease characteristics on efficacy outcomes and the difficulties in making comparisons across trials and patients with distinct immunology and baseline severity.

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