Disease Control and Quality of Life: Efficacy Outcomes from the Phase 2b Trial of CBP-201 in Patients with Atopic Dermatitis (CBP-201-WW001)

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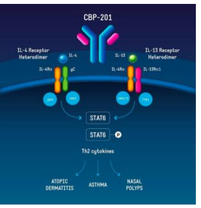
Abstract # 108-1000252



CBP-201 is a novel monoclonal antibody targeting IL-4Rα.

In a Phase 2b trial (WW001), all three doses of CBP-201 met the primary endpoint in the treatment of moderate-to-severe AD, with significant percent reductions in LS mean EASI scores observed at Week 16 with CBP-201 300mg Q2W (-63.0%; p=0.001), 150mg Q2W (-57.5%; p=0.01), and 300mg Q4W (-65.4%; p=0.0002) vs placebo (-40.7%).[1]

Key secondary endpoints were also met.[1]

Here, we report additional efficacy outcomes from WW001, including investigator-assessed AD severity, patient-reported disease control and QoL.

Methodology

Study design

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

Patients were recruited across the USA (N=172), China (N=32), New Zealand (N=19), and Australia (N=3). A China subgroup analysis was specifically conducted to address local health authority requirements necessary for future regulatory review.

The full trial design, key eligibility criteria, results for the primary and key secondary endpoints, and post hoc analyses, were presented previously.[1,2]

Endpoints and statistics

During the 16-week treatment period, AD symptoms and QoL were assessed using the investigator-assessed SCORAD (total score 0–103), patient-reported POEM (total score 0–28) and DLQI (total score 0–30). Higher scores indicate worse AD severity and QoL impact.

Changes in LS mean scores were analyzed using an ANCOVA model (including treatment, baseline score, and baseline IGA) and LOCF methodology. All other analyses presented here for SCORAD, POEM and DLQI were performed post hoc.

DLQI scores for each life quality domain (symptoms & feelings, daily activities, leisure, work & school, personal relationships, and treatment) were expressed as a percentage of the maximum possible score for the domain. This method has previously been used to assess QoL in real-life clinical practice.[3] Lower DLQI scores represent improved QoL.

For POEM sleep disturbance and itch, percentage point response rate differences were calculated based on the percentages of patients with scores of 0 at baseline and Week 16.

For subjective, patient-reported SCORAD sleep loss and itch (0–10 on a VAS), a clinically meaningful score was defined as <2 points (among patients with ≥2 points at baseline).

Results

Baseline characteristics

SCORAD, POEM, DLQI total, and EASI scores (Table 1) and other baseline characteristics[1,2] were generally well balanced across the treatment arms.

Table 1: Mean (SD) SCORAD, POEM, DLQI, and median (IQR) EASI scores, at baseline

Assessment	300 mg Q2W N=57	150 mg Q2W N=57	300 mg Q4W N=56	Placebo N=56
SCORAD total	65.9 (12.1)	62.8 (12.5)	61.8 (9.7)	67.5 (11.6)
POEM total	20.1 (6.6)	17.9 (6.4)	17.6 (6.6)	20.0 (5.5)
DLQI total	13.6 (7.8)	12.1 (6.1)	13.5 (7.9)	13.9 (6.2)
EASI	20.8 (16.8, 35.2)	21.2 (17.6, 28.2)	20.1 (17.6, 26.2)	22.1 (18.3, 30.9)

In the overall population (N=226), notable baseline differences compared with Phase 3 trials of the currently approved anti-IL-4Rα agent[4] included less severe AD (median EASI 21.2; 31% with IGA score of 4), shorter AD duration (median 13.0 years), lower BSA (median 35.1%), and higher BMI (median 28.4 kg/m^2).

In China (N=32), AD was more severe (median EASI 26.9; 38% IGA 4), BSA was higher (median 42.5%), and BMI was lower (median 25.6 kg/m^2) than in the overall population. In China, median EASI per CBP-201 arm was 26.6 (300mg Q2W), 26.6 (150mg Q2W), and 25.9 (300mg Q4W) vs 32.9 (placebo).

Improvements in SCORAD, POEM and DLQI total scores in the overall and China populations

In the overall population (N=226), mean SCORAD, POEM, and DLQI total scores improved rapidly by Week 2 with each CBP-201 dose, decreasing by 16.7–29.8% from baseline vs 9.5–18.0% with placebo and, at Week 16, by 49.2–61.8% vs 32.0–38.1% with placebo.

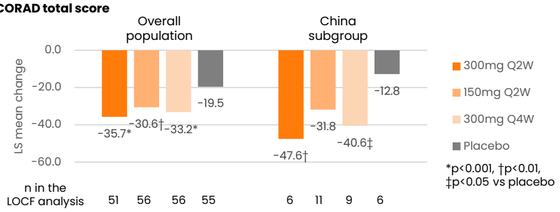
LS mean reductions in SCORAD, POEM, and DLQI total scores were statistically significant with all CBP-201 doses vs placebo at Week 16 (Fig 1).

Greatest improvements in AD symptoms and QoL were seen with the 300mg Q2W and 300mg Q4W doses, indicating possible dosing options with CBP-201.

Among patients in China (N=32), who had higher baseline EASI scores than in the overall population at baseline (median 26.9 vs 21.2), changes in SCORAD, POEM, and DLQI total scores with CBP-201 at Week 16 tended to be greater than in the overall population (Fig 1).

Fig 1: Changes in LS mean SCORAD, POEM and DLQI total scores at Week 16 (LOCF)

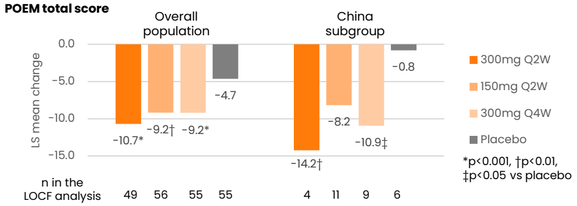
SCORAD total score



*p<0.001, †p<0.01, ‡p<0.05 vs placebo

Investigator-assessed symptoms of AD, as measured by SCORAD, were significantly reduced at Week 16 vs placebo. Greater efficacy was seen with greater AD severity at baseline, as indicated by the China subgroup.

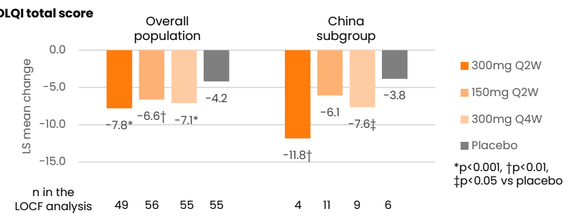
POEM total score



*p<0.001, †p<0.01, ‡p<0.05 vs placebo

Subjective patient-reported symptoms of AD were also significantly improved at Week 16 vs placebo. Patients with more severe AD at baseline (China subgroup) demonstrated greater overall patient-reported improvement than the overall population.

DLQI total score



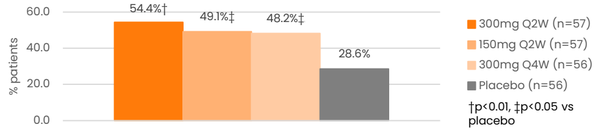
*p<0.001, †p<0.01, ‡p<0.05 vs placebo

Patient-reported QoL significantly improved following 16 weeks of treatment with CBP-201.

Greater proportions of patients with DLQI ≤5 points with CBP-201 vs placebo, and improvements across DLQI life quality domains

Greater proportions of patients had DLQI ≤5 points ("No effect" or "Small effect" on patient's life) following treatment with each CBP-201 dose vs placebo at Week 16 (Fig 2).

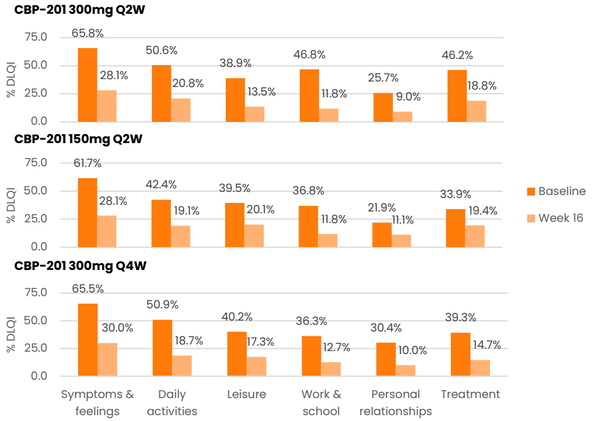
Fig 2: Percentages of patients with DLQI ≤5 points at Week 16



†p<0.01, ‡p<0.05 vs placebo

Improvements were observed across the DLQI life quality domains from baseline to Week 16 with each CBP-201 dose (Fig 3).

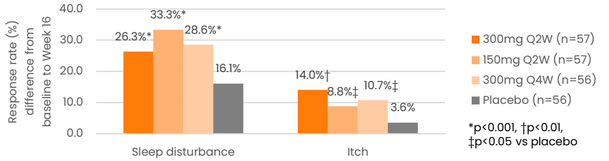
Fig 3: DLQI scores, expressed as a percentage of maximum possible scores, for life quality domains at baseline and at Week 16 (lower scores reflect improved QoL)



Improvements in POEM sleep and itch

Greater improvements in POEM sleep disturbance and itch responses were observed at Week 16 of treatment with each CBP-201 dose vs placebo (Fig 4).

Fig 4: Response rate differences from baseline to Week 16 for POEM sleep disturbance and itch (based on percentages of patients with a score of 0)



*p<0.001, †p<0.01, ‡p<0.05 vs placebo

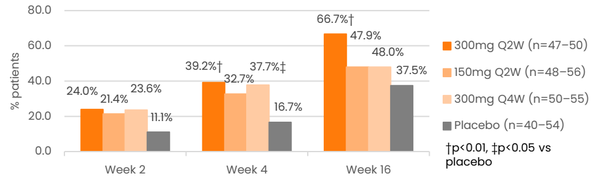
When compared to baseline, more CBP-201 treated patients reported itch and sleep scores of '0' at Week 16 than placebo treated patients

Clinically meaningful improvements in SCORAD sleep and itch

Greater proportions of patients achieved clinically meaningful improvements in SCORAD sleep loss and SCORAD itch VAS scores at Week 2, and at all subsequent time points, with each CBP-201 dose vs placebo (Fig 5).

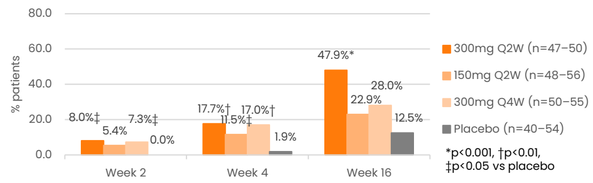
Fig 5: Percent of patients with clinically meaningful improvements in SCORAD sleep and itch VAS scores (<2 points, among patients with ≥2 points at baseline) at Weeks 2, 4 and 16

SCORAD sleep



†p<0.01, ‡p<0.05 vs placebo

SCORAD itch



*p<0.001, †p<0.01, ‡p<0.05 vs placebo

Conclusion

- In the WW001 Phase 2b trial, patients with moderate-to-severe AD experienced rapid and clinically meaningful reductions in the symptoms and burden of AD, based on patient-reported assessments (POEM, DLQI, and subjective SCORAD sleep and itch scores), during 16 weeks of treatment with CBP-201.
- These patient-reported improvements were mirrored by rapid reductions in investigator-assessed AD severity (SCORAD) and are compatible with previously reported investigator-assessed findings in this trial, including reductions in the primary endpoint (EASI scores at Week 16).[1,2]
- Thus, CPB-201 demonstrated rapid onset of efficacy in skin lesion clearance, with improvements in itch and sleep starting at the earliest assessed timepoint (Week 2) in patients with moderate-to-severe AD.
- CBP-201 potentially fulfills an unmet need by providing a convenient, reliably efficacious 2- and 4-week dosing option for both induction and maintenance of response not available with other biologics.
- Based on the China subgroup, patients with greater baseline AD severity may experience greater improvements in symptoms and QoL (assessed with SCORAD, POEM, and DLQI), consistent with previously reported analyses demonstrating greater improvements in symptoms (assessed with outcome measures such as EASI) in patients with more severe AD at baseline in the WW001 trial.[1,2]
- The results presented here and previously reported findings from the WW001 trial[1,2] support further investigation of CBP-201 in larger Phase 3 trials, particularly 300mg Q2W and 300mg Q4W dosing.

Funding: Connect BioPharma

References: 1. Strober et al. 18th Maui Derm 2022, Maui, HI, USA. 2. Silverberg et al. 18th Maui Derm 2022, Maui, HI, USA. 3. Kurwa & Finlay. Br J Dermatol. 1995;133:575–8. 4. Thaçi et al. J Dermatol Sci. 2019;94:266–75.

Abbreviations: AD, atopic dermatitis; ANCOVA, analysis of covariance; BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; LOCF, last observation carried forward; LS, least squares; POEM, Patient Oriented Eczema Measure; QoL, quality of life; Q2W, every 2 weeks; Q4W, every 4 weeks; SCORAD, SCORing Atopic Dermatitis; VAS, visual analog scale.