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A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTIPLE ASCENDING DOSE STUDY OF THE SAFETY, PHARMACOKINETICS AND PRELIMINARY EFFICACY OF CBP-201 IN ADULT PATIENTS WITH MODERATE TO SEVERE ATOPIC DERMATITIS (CBP-201AU002)

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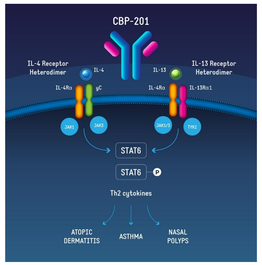
Poster #P0269
Abstract #2647

- Atopic dermatitis (AD) is a chronic inflammatory skin condition primarily characterized by intense pruritis and recurrent eczematous skin lesions.
- Connect Biopharma is developing CBP-201, a novel recombinant human mAb that binds human IL-4Rα, a common subunit of both Type I and Type II IL-4 receptors, as well as the IL-13 receptor.
- These receptors are known to play a role in the pathogenesis of AD and other Type II mediated inflammatory diseases.



METHODOLOGY

Design:

Thirty one (31) patients with moderate-to-severe AD, between 20 and 65 years, were enrolled at 13 sites in Australia and New Zealand for this randomized, double-blind, multiple ascending dose (MAD) study.

Patients were randomized in 3 separate cohorts, in a 4:1 ratio to receive CBP-201 (75, 150, and 300mg subcutaneously (SC)) or matching placebo, once a week (QW) for 4 doses, with approximately 10 patients randomized in each cohort (Figure 1). All dose escalations were subject to Safety Review Committee blinded review.

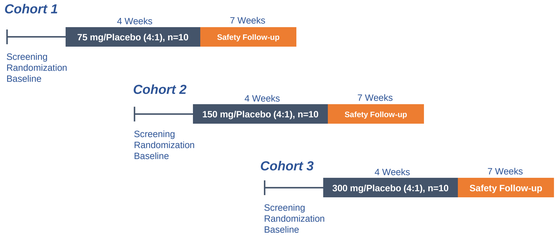
Standard safety endpoints, serum biomarker levels, and PK characteristics were evaluated. Exploratory efficacy endpoints included the Eczema Area and Severity Index (EASI) score, Investigator's Global Assessment (IGA), and Pruritus Numeric Rating Scale (P-NRS). Study treatment for each of 3 cohorts was administered QW on Days 1, 8, 15, 22 with follow-up visits on Days 29, 36, 50, 64 and 78.

Here we report safety data through to day 78 and efficacy data for the initial 4 weeks of treatment. PK and serum biomarker data will be reported separately.

Safety Monitoring:

History, vital signs, physical examinations, electrocardiograms (ECGs), clinical safety laboratory tests and adverse events (AEs).

Figure 1. Study Design



RESULTS

Demographics:

A total of 83 patients were screened, 32 who met eligibility criteria were randomized (Table 1). One patient in the CBP-201 300 mg group withdrew consent prior to dosing.

Table 1. Demographics of Study Participants

Parameter		75 mg CBP-201 (n = 8)	150 mg CBP-201 (n = 8)	300 mg CBP-201 (n = 7)	Pooled CBP-201 (n = 23)	Placebo (n = 8)	All Patients (n = 31)
Age in years	Median (Min – Max)	38.0 (23-65)	24.5 (20-36)	42.0 (28-55)	33.0 (20-65)	45.0 (27-56)	35.0 (20-65)
Sex	M/F N	6/2	3/5	2/5	11/12	5/3	16/15
Race	White	5 (62.5%)	7 (87.5%)	6 (85.7%)	18 (78.3%)	8 (100%)	26 (83.9%)
	Asian	2 (25.0%)	1 (12.5%)	1 (14.3%)	4 (17.14%)	0	4 (12.9%)
	Other	1 (12.5%)	0	0	1 (4.3%)	0	1 (3.2%)
Weight (kg)	Mean (SD)	74.36 (9.22)	74.14 (20.37)	80.54 (23.91)	76.17 (17.94)	75.86 (13.4)	76.0 (16.72)
Baseline EASI Total Score	Mean (SD)	29.42 (16.64)	20.68 (6.63)	23.21 (6.24)	24.49 (11.28)	33.36 (15.27)	26.78 (12.78)
Baseline BSA AD (%)	Mean (SD)	60.31 (31.76)	30.09 (12.50)	29.90 (11.68)	39.65 (24.25)	47.57 (26.53)	41.56 (24.57)
Baseline IGA N (%)	0 – Clear	0	0	0	0	0	0
	1 – Almost Clear	0	0	0	0	0	0
	2 – Mild	0	0	0	0	0	0
	3 – Moderate	5 (62.5%)	8 (100.0%)	5 (71.4%)	18 (78.3%)	6 (75.0%)	24 (77.4%)
	4 - Severe	3 (37.5%)	0	2 (28.6%)	5 (21.7%)	2 (25.0%)	7 (22.6%)
Baseline P-NRS Mean (SD)	Severity	7.14 (2.38)	6.74 (2.20)	7.10 (1.00)	6.99 (1.91)	7.53 (2.01)	7.13 (1.92)
	Frequency	6.96 (2.32)	6.89 (2.31)	6.50 (1.52)	6.80 (2.02)	7.46 (2.28)	6.97 (2.02)
Baseline DLQI	Mean (SD)	14.1 (6.3)	17.5 (5.5)	14.7 (4.9)	15.5 (5.6)	16.4 (6.7)	15.7 (5.8)

Safety Results:

- Safety and tolerability CBP-201 findings were based on 23 patients administered CBP-201 and 8 patients administered placebo (Table 2):
- There were no SAEs, TEAEs that were life-threatening, or deaths reported
- There were no TEAEs leading to the discontinuation from the study
- There were no clinically significant injection site reactions that were reported as AEs
- The majority (35/51 events in 65.2% patients in the pooled CBP-201 group and 7/11 events in 37.5% of patients in the placebo group) of TEAEs were mild, 18/62 TEAEs reported (15 events in 43.5% of patients on CBP-201 and 3 events in 25.0% of patients on placebo) were moderate; there were two severe TEAEs.
- The number and severity of TEAEs and treatment related TEAEs did not increase with increasing CBP-201 dose level. Of 51 TEAEs reported across the pooled CBP-201 group, 9 events were deemed by the Investigator to be related to CBP-201 and 3/11 TEAEs in the placebo group were deemed related to placebo treatment. There were no treatment-related severe TEAEs reported.

- The most common TEAEs reported in the study by PT were dermatitis atopic (6 events in 6 patients in the pooled CBP-201 group; 4 events in 3 placebo patients), headache (7 events in 4 patients in the pooled CBP-201 group and 0 events in placebo patients), and URTI (3 events in 2 patients in the pooled CBP-201 group and 0 events in placebo patients). The most frequent SOC for TEAEs was Skin and Subcutaneous Tissue Disorders, likely related to the underlying AD of patients.
- There were no apparent differences between the CBP-201 dose cohorts and placebo cohort in terms of study treatment-related TEAEs.
- There were no changes in vital signs, ECG parameters, or physical examination findings that were clinically significant or related to study treatment.

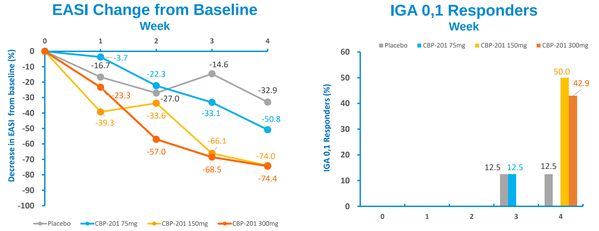
Table 2. Treatment Emergent Adverse Events (Safety Population)

Patients With	75 mg CBP-201 N = 8 n (%) Event	150 mg CBP-201 N = 8 n (%) Event	300 mg CBP-201 N = 7 n (%) Event	Pooled CBP-201 N = 23 n (%) Event	Placebo Group N = 8 n (%) Event
≥ one TEAE	7 (87.5%) 12	7 (87.5%) 22	6 (85.7%) 17	20 (87.0%) 51	5 (62.5%) 11
≥ one serious TEAE	0	0	0	0	0
≥ one severe TEAE	0	0	1 (14.3%) 1	1 (4.3%) 1	1 (12.5%) 1
≥one IP: CBP-201 related TEAE	1 (12.5%) 2	2 (25.0%) 4	1 (14.3%) 3	4 (17.4%) 9	1 (12.5%) 3
≥ one TEAE leading to IP: CBP-201 withdrawal	1 (12.5%) 1	0	0	1 (4.3%) 1	1 (12.5%) 1
≥ one TEAE pertaining to injection site reactions	0	0	0	0	0
≥ one TEAE leading to premature withdrawal	0	0	0	0	0

Efficacy Results:

- Overall, efficacy assessments including total EASI score, IGA of severity of AD, BSA affected by AD, severity and frequency of pruritus assessed by P-NRS, and quality of life determined by DLQI, demonstrated improvement of AD in patients.

Figure 2. EASI Change from Baseline and IGA 0,1 over Time



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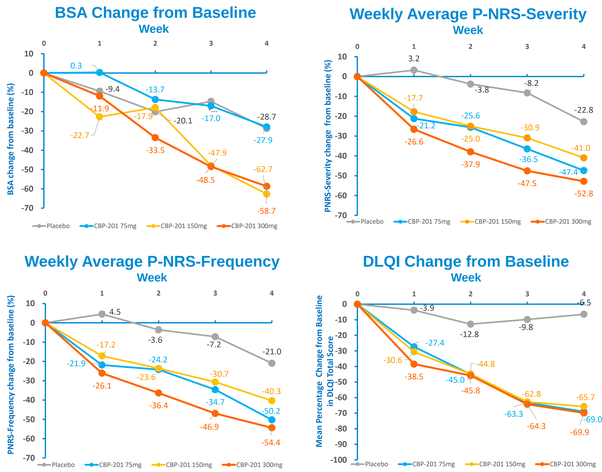
- Responses in investigator assessed (EASI, IGA 0,1, BSA) and patient reported outcome measures (P-NRS) generally showed a dose dependent response and consistent improvements over baseline to week 4, with separation as early as week 1, primarily at higher doses of CBP-201 (150 mg and 300 mg) vs. placebo.
- All doses of CBP-201 studied showed rapid improvements in Quality of Life as assessed by DLQI at week 1, and this continued to improve out to week 4.

Figure 3. BSA, P-NRS and DLQI over Time



CONCLUSIONS & DISCUSSION

- In conclusion, the results of this phase 1b study of CBP-201 in patients with moderate-to-severe AD, showed that multiple SC doses of CBP-201 up to 300 mg, administered QW for 4 weeks, were safe and well tolerated.
- There were no reported serious adverse events (SAEs), no AEs of injection site reaction or conjunctivitis/keratitis and no change in peripheral blood eosinophil counts compared to baseline or placebo.
- Preliminary efficacy assessments suggest that CBP-201 at 150 and 300 mg, improved patients' total EASI scores, IGA 0,1 response, BSA affected and severity and frequency of pruritus, with responses seen from week 1, and no evidence of a plateauing of efficacy effect during the week 4 dosing.
- Quality of Life assessed by DLQI improved across all CBP-201 dose cohorts.
- These data support further exploration of CBP-201's effects in an ongoing dose-ranging study in moderate-to-severe AD (NCT04444752)