

Efficacy and Safety of CBP-201 in Adults with Moderate-to-Severe Atopic Dermatitis (AD): A Phase 2b, Randomized, Double-blind, Placebo-controlled Trial (CBP-201-WW001)

Bruce Strober,^{1,2} Brian Feinstein,³ Jinhua Xu,^{4,5} Emma Guttman-Yassky,⁶ Jonathan I. Silverberg,⁷ Eric Simpson,⁸ Pauline Li,⁹ Malinda Longphre,⁹ Jing Song,⁹ John Guo,⁹ Maryam Yaghini,⁹ Belinda Williams,⁹ Zheng Wei,⁹ Selwyn Ho⁹

¹Yale University, New Haven, CT, USA; ²Central Connecticut Dermatology, Cromwell, CT, USA; ³Encore Medical Research LLC, FL, USA; ⁴Department of Dermatology, Huashan Hospital, Fudan University, Shanghai, China. ⁵Shanghai Institute of Dermatology, Shanghai, China; ⁶Department of Dermatology and Laboratory of Inflammatory Skin Diseases, Icahn School of Medicine at Mount Sinai, New York, NY; ⁷Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA; ⁸Department of Dermatology, Oregon Health and Science University, Portland, OR, USA; ⁹Connect Biopharma, San Diego, CA, USA and Suzhou, China.

Introduction: CBP-201 is a novel monoclonal antibody that binds to a region of IL-4R α that is different than dupilumab. Early phase trial data suggest potential for efficacy and safety in AD, with more convenient dosing frequency than currently available biologics. This Phase 2b trial assessed three regimens of CBP-201 in adults with moderate-to-severe AD.

Methods: This randomized, double-blind, placebo-controlled, international trial (NCT04444752) comprised 16-week treatment and 8-week follow-up periods. Patients were randomized (1:1:1:1) to subcutaneous CBP-201 (300mg Q2W, 150mg Q2W, 300mg Q4W) or placebo. Eligible patients had moderate-to-severe AD (IGA \geq 3, EASI \geq 16, BSA \geq 10%) inadequately controlled with, or not suitable for, topical treatments; no prior anti-IL-4R α /IL-13 therapies; and no concomitant topical AD treatment except for bland emollient and rescue medication.

Results: A total of 226 patients received \geq 1 dose of CBP-201 or placebo (median [range] EASI 21.15 [16.0–68.4], age 38.5 [18–73] years; 31% of patients had IGA 4, 54% were female). As expected during the COVID-19 pandemic, trial conduct was impacted, with higher discontinuation rates (12.5–19.3% across CBP-201 groups) compared with Phase 3 trials of the approved anti-IL-4R α (6.3–9.5%).

The trial successfully met its primary endpoint: significant percent reductions in least squares (LS) mean EASI at Week 16 were observed with all CBP-201 doses (300mg Q2W: -63.0% [$P=0.001$]; 150mg Q2W: -57.5% [$P=0.01$]; 300mg Q4W: -65.4% [$P=0.0002$]) versus placebo (-40.7%). Median EASI percent reductions at Week 16 (300mg Q2W: -79.3%; 150mg Q2W: -64.7%; 300mg Q4W: -72.4%) were greater than LS mean percent reductions, with a similar placebo response (-41.0%). Patients in China (N=32) had higher baseline EASI (median 26.9), and no discontinuations in CBP-201 groups, which may have contributed to greater CBP-201 responses (300mg Q2W:

LS mean -82.9% [$P<NS$]; 150mg Q2W: -59.1% [$P=NS$]; 300mg Q4W: -76.1% [$P<0.05$] and lower placebo response (-34.9%).

Significant improvements with CBP-201 were observed for secondary endpoints, including proportions of EASI-50, -75, -90 and IGA 0/1 responders and pruritus scores. Rescue medication use by Week 16, imputed as non-responders, ranged from 3.5% (150mg Q2W) to 12.5% (placebo), lower than in Phase 3 trials for the approved anti-IL-4R α ; range, 17.1% (Q2W 300mg) to 51.7% (placebo). Clinical improvements with CBP-201 were particularly notable in patients with higher AD severity biomarker levels at baseline (Silverberg et al, Maui Derm 2022).

CBP-201 and placebo had similar incidence of TEAEs (48% vs 54%), serious TEAEs (1.8% vs 3.6%), TEAEs leading to discontinuation (1.2% vs 1.8%) and injection site reactions (1.8% vs 1.8%). Incidence of conjunctivitis with CBP-201 was 3.5%.

Conclusion: Clinical outcomes were significantly improved in patients randomized to CBP-201, despite the challenges of COVID-19 restrictions. The trial met primary and key secondary endpoints, supporting the potential of both 300mg Q2W and 300mg Q4W. The safety profile of CBP-201 was similar to placebo, except for a low incidence of conjunctivitis consistent with IL-4R α inhibition. Further investigation of CBP-201 300mg in moderate-to-severe AD is warranted, in larger trials that take into consideration how differences in trial design and the patient populations recruited may impact efficacy and safety outcomes.

Funding: Connect Biopharma.

Financial disclosures

BS:

- *Consultant (honoraria):* AbbVie, Almirall, Amgen, Arcutis, Arena, Aristeia, Asana, Boehringer Ingelheim, Immunic Therapeutics, Bristol-Myers-Squibb, Connect Biopharma, Dermavant, EPI Health, Evelo Biosciences, Janssen, Leo Pharma, Eli Lilly, Maruho, Meiji Seika Pharma, Mindera Health, Novartis, Ono, Pfizer, UCB Pharma, Sun Pharma, Regeneron, Sanofi-Genzyme, Union Therapeutics, Ventyx bio, vTv Therapeutics
- *Stock Options:* Connect Biopharma, Mindera Health
- *Speaker:* AbbVie, Eli Lilly, Incyte, Janssen, Regeneron, Sanofi-Genzyme
- *Scientific Co-Director (consulting fee):* CorEvitas (formerly Corrona) Psoriasis Registry
- *Investigator:* Dermavant, AbbVie, CorEvitas Psoriasis Registry, Dermira, Cara, Novartis
- *Editor-in-Chief (honorarium):* Journal of Psoriasis and Psoriatic Arthritis

JIS:

- *Stock ownership*: AbbVie, Arcutis, Eli Lilly
- *Consultant (honoraria)*: AbbVie, Afyx, Aobiome, Arena Pharmaceuticals, Asana, Aslan, BioMX, Bluefin, Bodewell, Boehringer Ingelheim, Celgene, Connect Biopharma, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo Pharma, Luna, Menlo, Novartis, Pfizer, RAPT, Regeneron, Sanofi-Genzyme
- *Research grants*: Galderma, Pfizer

BF, JX: No financial disclosures

EGY:

- *Consultant (honoraria)*: : AbbVie, Almirall, Amgen, Arena Pharmaceuticals, Asana Biosciences, AstraZeneca, Boehringer-Ingelheim, Bristol Meyers Squibb, Cara Therapeutics, Celgene, DBV, DS Biopharma, Eli Lilly, EMD Serono, Galderma, Ichnos Sciences (Glenmark), Incyte, Janssen Biotech, Kyowa, Kirin, Leo Pharmaceuticals, Pandion Therapeutics, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, UCB, Union Therapeutics, Connect, Biopharm, SATO, Siolta Therapeutics, Target Pharma Solutions, Ventyx, Novartis, Boston Pharmaceuticals, Evidera, Principia, Bluefin Biomedicine
- *Investigator*: AbbVie, AstraZeneca, Eli Lilly, Kyowa Kirin, Leo Pharmaceuticals, Pfizer, Regeneron
- *Advisory Boards*: AbbVie, Aditum Bio, Aena Pharmaceuticals, Asana Biosciences, AstraZeneca, Boehringer-Ingelheim, Bristol Meyers Squibb, Cara Therapeutics, DBV, Eli Lilly, Galderma, Ichnos Sciences (Glenmark), Incyte, Janssen Biotech, Kyowa Kirin, Leo Pharmaceuticals, Pfizer, RAPT Therapeutics (Flx Bio), Regeneron, Sanofi, Union Therapeutics, Connect Biopharma, SATO, Siolta Therapeutics, Target Pharma Solutions, Ventyx, Novartis, Bluefin Biomedicine.
- *Research Grants*: Almirall, Amgen, AnaptysBio, Asana Bioscience, AstraZeneca, Bristol Meyers Squibb, Cara Therapeutics, DS Biopharma, Galderma, Innovaderm, Janssen Biotech, Kiniska, Kyowa Kirin, Leo Pharmaceuticals, Pfizer, Regeneron, UCB, and KAO
- *Stockholder*: RAPT

ES:

- *Personal fees*: AbbVie, Amgen, Arena Pharmaceuticals, Aslan Pharma, Boston Consulting Group, Collective Acumen, LLC (CA), Dermira, Eli Lilly, Evidera, ExcerptaMedica, Forte Bio RX, Galderma, GlaxoSmithKline, Incyte, Janssen, Kyowa Kirin Pharmaceutical Development, Leo Pharma, Medscape LLC, Pfizer, Physicians World LLC, Regeneron, Sanofi-Genzyme, Trevi therapeutics, WebMD. *These potential conflicts of interest have been reviewed and managed by OHSU.*
- *Grants (or Principal investigator role)*: AbbVie, Amgen, Arcutis, Aslan, Corevita, Dermira, Eli Lilly, Incyte, Kyowa Hakko Kirin, Leo Pharma, Merck, Novartis, Pfizer, Regeneron, Sanofi, and TARGET-DERM. *These potential conflicts of interest have been reviewed and managed by OHSU.*

PL, ML, JS, JG, MY, BW, ZW and SH are employees of Connect Biopharma.

Keywords

Atopic dermatitis, IL-4, CBP-201, biologics, monoclonal antibody, phase 2, efficacy, safety