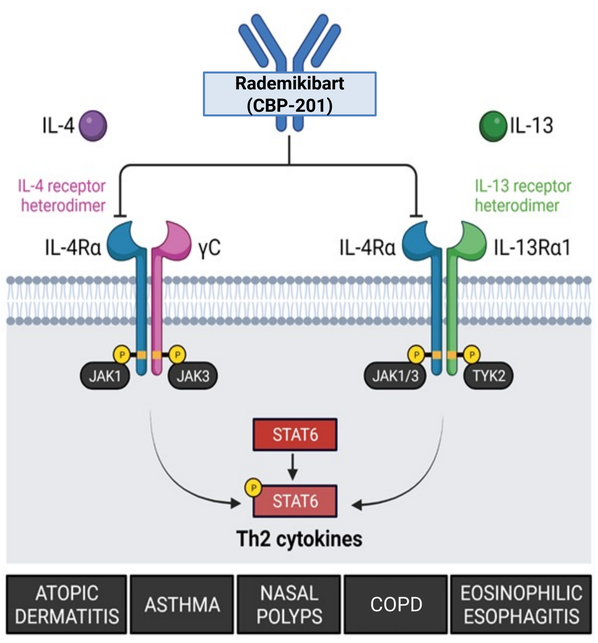
# Eczema Area and Severity Index (EASI) scores improved, and encouraging safety and tolerability were observed, across 16 weeks of treatment with rademikibart (CBP-201) for moderate-to-severe atopic dermatitis (AD): A pivotal trial in China (CBP-201-CN002)

**Jianzhong Zhang,[1] Pauline Li,[2] Jiawang Guo,[2] Jili Yun,[2] Jang Yun,[3] Chin Lee,[3] Zheng Wei,[3] Wubin Pan,[2] Raúl Collazo[3]**

[1]Peking University People's Hospital, Department of Dermatology, Beijing, China;
[2]Suzhou Connect Biopharmaceuticals Ltd, Taicang, China; [3]Connect Biopharma LLC, San Diego, USA

Poster 3242




- Rademikibart (formerly CBP-201), a next-generation mAb, inhibits both IL-4 and IL-13 mediated responses.
- In preclinical experiments, rademikibart bound to IL-4Rα and reduced intracellular signaling and cytokine mRNA levels with greater potency than dupilumab.[1,2]
- In the previously reported WW001 global Phase 2 trial with rademikibart, significant improvements in primary and key secondary endpoints (on skin clearance, AD severity, and itch) were observed.[3,4]
- Also in WW001, low rates of TEAEs, including conjunctivitis and injection site reactions, suggest safety results that are similar to placebo.[3]

## Objective

In the ongoing CN002 pivotal trial in China (NCT05017480), rademikibart is being investigated primarily in adults with moderate-to-severe AD. Assessments are also being conducted in adolescents.

Rademikibart achieved significance across all primary and secondary endpoints during the initial 16-week treatment period in the adult population, as reported in three other posters by Zhang et al. at this meeting (WCD2023, posters 3240, 3243, 3247).

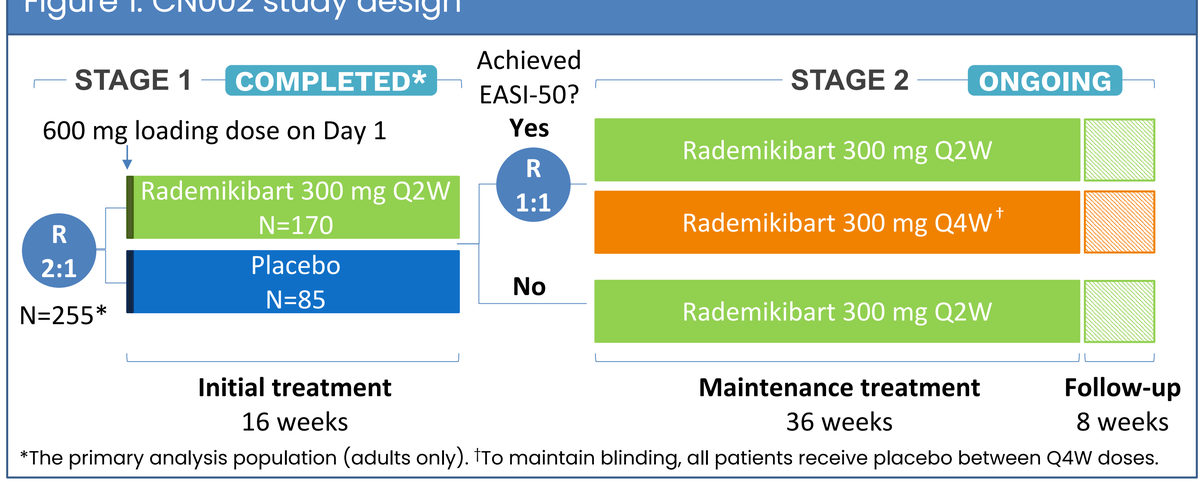
Here, we report change in EASI total scores across the 16-week treatment period (a secondary endpoint at Week 16) and in EASI scores per AD sign, as well as safety outcomes, for adult patients in CN002.

## Methodology

### Study design

CN002 is a randomized, double-blind, placebo-controlled, pivotal trial of subcutaneous rademikibart conducted across 48 centers in China (Figure 1). Stage 1 has completed in adults; Stage 2 is ongoing. Patients had moderate-to-severe AD (IGA ≥3, EASI ≥16, BSA ≥10%) inadequately controlled topically, no prior anti-IL-4Rα/IL-13s, and no concomitant topical AD treatment except rescue medication and emollient.

Figure 1: CN002 study design




*The primary analysis population (adults only). †To maintain blinding, all patients receive placebo between Q4W doses.

### Statistics

EASI score was analyzed by MMRM. EASI total score was calculated by adding subscores for four body regions (each subscore was calculated by adding the severity for AD signs [score = 0-3 per sign], multiplying by AD area [score = 0-6], and then by a multiplier per region [x0.1 head/neck, x0.3 trunk, x0.4 lower and x0.2 upper extremities]).

## Results

### Baseline characteristics, including EASI scores

All 255 adult patients had moderate-to-severe AD at baseline (median EASI 26.9; 54.5% with IGA score of 4; median BSA 44.5%; median PP-NRS 7.0). These disease characteristics were generally comparable to trials of dupilumab in China and globally.[5–7]

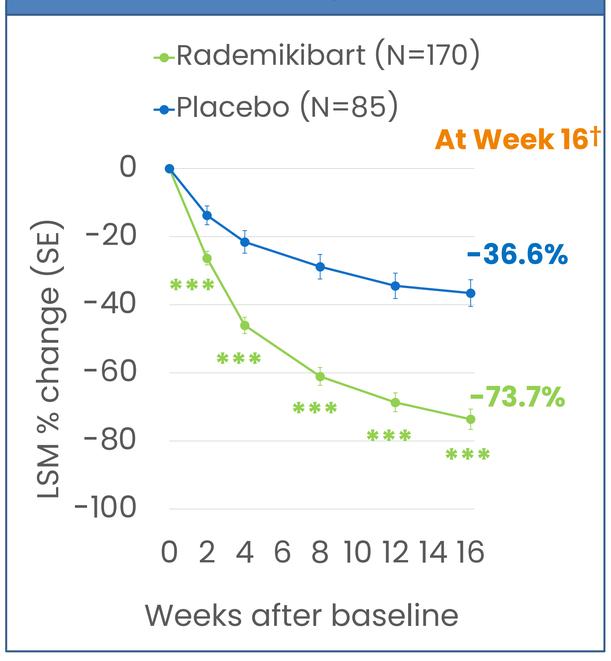
Baseline EASI total scores, rademikibart vs placebo arm respectively, were: mean (SD), 29.6 (11.9) vs 29.3 (12.0); median (min, max), 27.3 (16.0, 72.0) vs 26.3 (16.0, 66.9).

### EASI score reductions across the initial 16-week treatment period

Highly significant improvements in EASI total scores with rademikibart versus placebo occurred at the earliest assessment (Week 2) and throughout the 16-week treatment period ($p<0.001$; Figure 2).

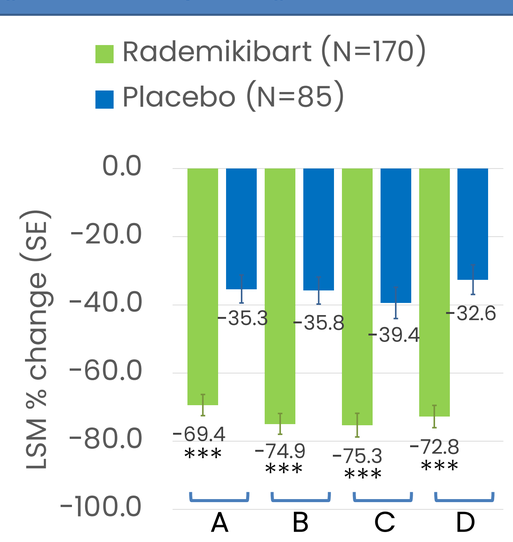
Based on EASI scores, highly significant reductions were also observed in each AD sign throughout the 16-week treatment period ($p<0.001$ at Week 16; Figure 3)

Figure 2: EASI total by visit




†Secondary endpoint at Week 16.

Figure 3: EASI per sign at Week 16




A. Erythema; B. Edema/Papulation; C. Excoriation; D. Lichenification

***$P<0.001$ vs placebo

### Safety and tolerability across the initial 16-week treatment period

Rademikibart was well tolerated, with no new safety signals. For rademikibart vs placebo, lower or similar proportions of patients reported any TEAEs (73.5% vs 72.9%), serious TEAEs (0.6% vs 3.5%), and severe TEAEs (2.4% vs 5.9%) (Table 1). No serious TEAEs were related to study treatment. There were no deaths.

One patient discontinued due to a TEAE (AD in the rademikibart arm; Table 1); 95.3% and 92.9% of patients completed to Week 16 in the rademikibart and placebo arms.

Other notable TEAEs, in the rademikibart vs placebo arm, included: conjunctivitis (4.7% vs 3.5%), keratitis (1.2% vs 0%), anaphylaxis (0.6% vs 0%), injections site reactions (10.0% vs 1.2%), and injections site reactions lasting >24 hours (6.5% vs 0%) (Table 1).

The case of anaphylaxis was mild, not related to study treatment, and the patient continued with rademikibart therapy in the trial.

All injection site reactions were mild, did not result in discontinuation, and were mainly erythema, induration, inflammation, and edema (Tables 1 and 2).

Few TEAEs were observed in ≥5% of patients in either treatment arm (Table 2).

**Table 1: Overview of TEAEs**

| n (%) patients | Rademikibart N=170 | Placebo N=85 |
|---|---|---|
| Any TEAEs | 125 (73.5%) | 62 (72.9%) |
| TEAEs related to study drug | 54 (31.8%) | 20 (23.5%) |
| Serious TEAEs (none related to treatment) | 1 (0.6%) | 3 (3.5%) |
| Severe TEAEs | 4 (2.4%) | 5 (5.9%) |
| TEAEs leading to study drug discontinuation | 1 (0.6%) | 0 |
| Herpes virus infection* | 1 (0.6%) | 1 (1.2%) |
| Conjunctivitis† | 8 (4.7%) | 3 (3.5%) |
| Keratitis† | 2 (1.2%) | 0 |
| Anaphylaxis (mild, not related to treatment)† | 1 (0.6%) | 0 |
| Injection site reactions (all mild)<br>Any<br>Lasting longer than 24 hours† | <br>17 (10.0%)<br>11 (6.5%) | <br>1 (1.2%)<br>0 |

*Other herpes TEAEs were: 'herpes simplex', 'herpes simplex reactivation', and 'oral herpes' (all n=1 in the rademikibart arm); 'herpes zoster' (n=1 in the placebo arm).

†Prespecified TEAEs of special interest. None of the following TEAEs of special interest were observed: 'AST/ALT elevated >5×ULN', 'parasitic and opportunistic infections', 'pregnancy', 'symptomatic overdose'.

**Table 2: TEAEs in ≥5% of patients in either treatment group**

| n (%) patients with… | Rademikibart N=170 | Placebo N=85 |
|---|---|---|
| Hyperlipidemia | 21 (12.4%) | 5 (5.9%) |
| Hyperuricemia | 16 (9.4%) | 5 (5.9%) |
| Atopic dermatitis | 16 (9.4%) | 15 (17.6%) |
| Injection site erythema | 10 (5.9%) | 1 (1.2%) |
| Upper respiratory tract infection | 10 (5.9%) | 6 (7.1%) |
| Blood lactate dehydrogenase increased | 2 (1.2%) | 5 (5.9%) |

## Conclusions

In a large China-specific pivotal trial, in the primary analysis population of adults with moderate-to-severe AD receiving rademikibart for 16 weeks:

- 73.7% improvement in AD severity and extent (EASI total scores), and large improvements per AD sign, were gained at Week 16 in the rademikibart arm.
- EASI scores (total and per AD sign) decreased rapidly at the first assessment (Week 2).
- EASI total score improvements with rademikibart were comparable to those with dupilumab in global and China-specific trials;[5–7] they did not plateau by Week 16 with rademikibart.
- In addition to EASI reductions, rademikibart achieved its primary and other secondary efficacy endpoints, reported in three other posters by Zhang et al at this meeting (WCD2023, posters 3240, 3243, 3247), reflecting rapid and sustained improvements in AD and QoL.

Rademikibart was well tolerated.

- Most TEAEs were mild to moderate in severity, and one of 170 patients (0.6%) discontinued rademikibart due to a TEAE.
- Safety results were consistent with targeting the IL-4Rα pathway, including low incidence of conjunctivitis of any cause in the radimikibart arm (4.7%) vs placebo (3.5%).
- All injection site reactions were mild and did not lead to discontinuation of rademikibart.

The ongoing maintenance treatment period may result in greater/sustained efficacy with rademikibart.

**Presented at:** 25th World Congress of Dermatology (WCD2023), July 3rd–8th, 2023, Singapore

**Funding:** Connect Biopharma

**References:** 1. Yang et al. SID 2022, Portland, OR (Poster LB945). 2. Manuscript submitted. 3. Strober et al. Maui Derm 2022, Maui, HI. 4. Strober et al. Poster P0215 (Abstract 470), EADV 2022, Milan, Italy. 5. Zhao et al. Br J Dermatol 2022;186:633-41. 6. Thaçi et al. The Lancet 2016;387:40-52 7. Simpson et al. NEJM 2016;375:2335-48.

**Abbreviations:** AD, atopic dermatitis; BSA, Body Surface Area; EASI, Eczema Area and Severity Index; EASI, Eczema Area and Severity Index; EASI-50, at least 50% decrease from baseline; IGA, Investigator Global Assessment; LSM, least squares mean; mAb, monoclonal antibody; MMRM, Mixed-Effect Model for Repeated Measures; PP-NRS, Peak Pruritus Numeric Rating Scale; QoL, quality of life; Q2/4W, every 2/4 weeks; R, randomized; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event.