Rademikibart (CBP-201), a next-generation IL-4Rα antibody, achieved all primary and secondary endpoints in a randomized pivotal trial for moderate-to-severe atopic dermatitis (AD) in China (CBP-201-CN002)

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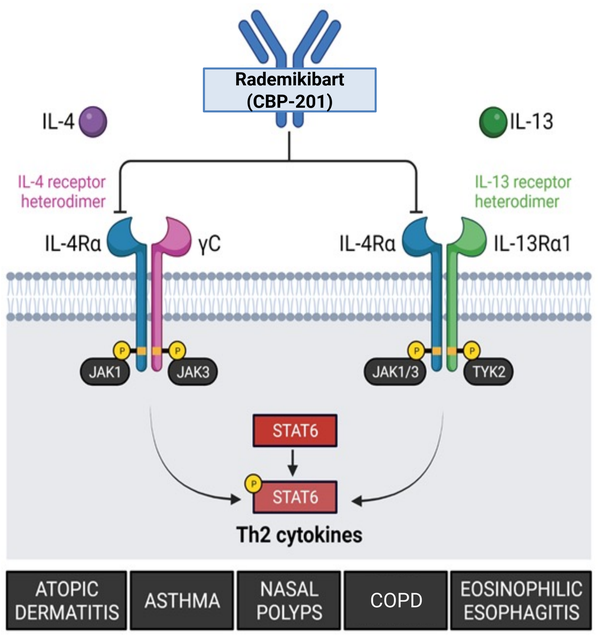


- Rademikibart (formerly CBP-201) is a next-generation mAb, inhibiting the actions of both IL-4 and IL-13.
- In preclinical studies, rademikibart bound with higher affinity to a distinct IL-4Rα epitope, and downregulated intracellular signaling and cytokine gene expression with greater potency than dupilumab.[1,2]
- In clinical trials of rademikibart in adults with moderate-to-severe AD, including the WW001 global Phase 2 study:[3–6]
  - AD signs and symptoms decreased rapidly.
  - In WW001, AD improvements with Q2W and Q4W dosing often did not plateau across 16 weeks of treatment.
  - Rademikibart and placebo had similar, low incidence of TEAEs in WW001.

Objective

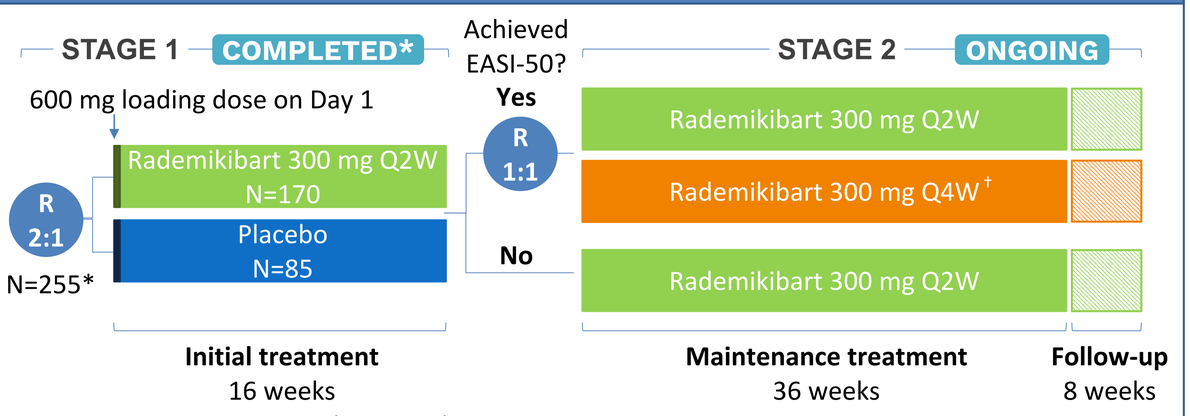
Rademikibart is being evaluated in CN002 (NCT05017480), a pivotal trial in China, in adults and adolescents with moderate-to-severe AD. For adult patients, we report the primary and secondary efficacy outcomes, as well as key safety data, at Week 16.

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

Binary endpoints were analyzed by CMH test; missing data were imputed by jump to reference (after the rule of intercurrent event) and multiple imputation for rademikibart and placebo, respectively. Continuous score changes were analyzed using MMRM.

Results

Baseline characteristics and patient disposition

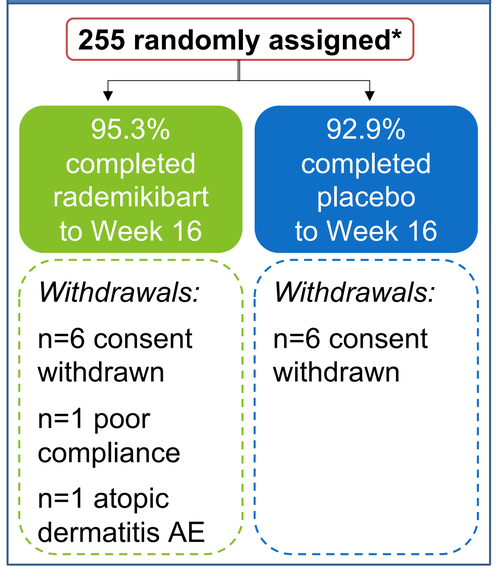
All 255 adult patients had moderate-to-severe AD at baseline (Table 1), with generally comparable disease characteristics per treatment arm and also versus late phase trials of dupilumab in China[7] and globally.[8] Rademikibart treatment was completed to Week 16 by 95.3% of patients (Figure 2).

Table 1: Baseline characteristics*

Median (min, max), unless stated otherwise	Rademikibart N=170	Placebo N=85
Age (years)	36.0 (18, 74)	36.0 (18, 74)
Female, n (%)	57 (34%)	33 (39%)
BMI (kg/m²)	23.6 (14.8, 47.1)	24.6 (18.1, 46.9)
IGA, n (%) 3 (moderate) 4 (severe)	 78 (45.9%) 92 (54.1%)	 38 (44.7%) 47 (55.3%)
EASI score	27.3 (16.0, 72.0)	26.3 (16.0, 66.9)
PP-NRS score	7 (2, 10)	7 (2, 10)
DLQI score	16 (1, 30)	14 (5, 30)

*The primary analysis population (adults only). All patients received ≥1 dose.

Figure 2: Patient disposition*



Safety outcomes

Rademikibart was well tolerated, with no new safety signals (Table 2).

Table 2: Overview of treatment-emergent adverse events

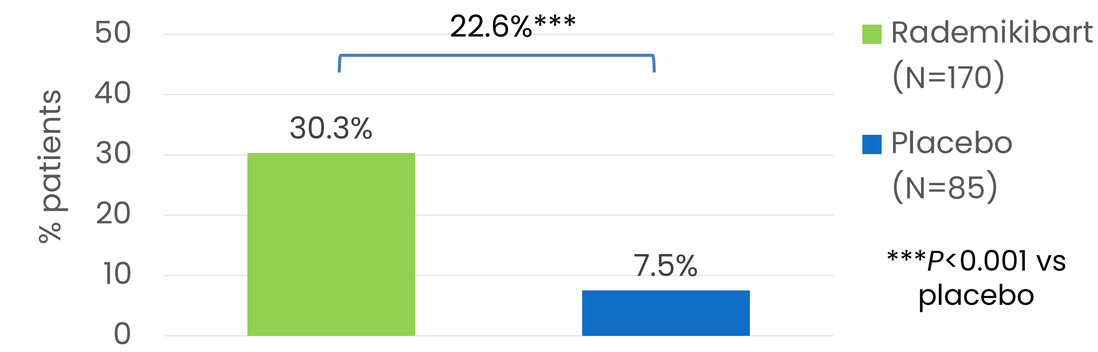
n (%) patients	Rademikibart N=170	Placebo N=85
Any TEAEs	125 (73.5%)	62 (72.9%)
TEAEs related to study drug	54 (31.8%)	20 (23.5%)
Serious TEAEs (none related to treatment)	1 (0.6%)	3 (3.5%)
Severe TEAEs	4 (2.4%)	5 (5.9%)
TEAEs leading to study drug discontinuation	1 (0.6%)	0
Herpes virus infection*	1 (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) Any Lasting longer than 24 hours	 17 (10.0%) 11 (6.5%)	 1 (1.2%) 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).

Primary efficacy endpoint

The IGA 0/1 response rate at Week 16 was highly significant with rademikibart versus placebo (Figure 3).

Figure 3: Primary efficacy endpoint

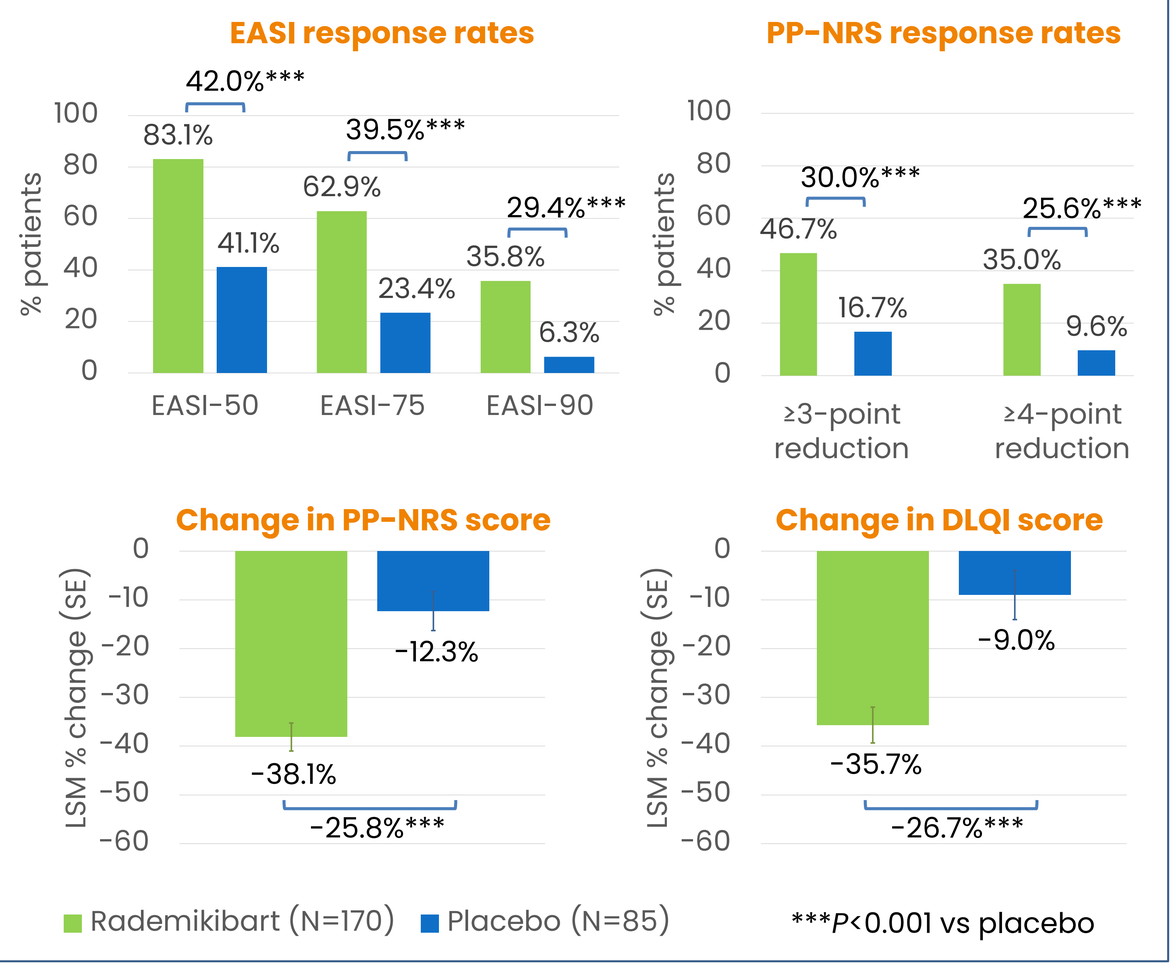


The placebo-adjusted response rate was based on the multiple imputation inference.

Secondary efficacy endpoints

Improvements were observed in all secondary efficacy endpoints (Figure 4).

Figure 4: Secondary efficacy endpoints (all at Week 16)



Conclusions

- Rademikibart achieved all primary and secondary endpoints at Week 16, in a large China-specific pivotal trial, in the primary analysis population of adults with moderate-to-severe AD.
- Improvements in AD symptoms at Week 16 with rademikibart included:
  - 83% of patients achieved 50% clearance (EASI-50).
  - 63% of patients achieved 75% clearance (EASI-75).
- Efficacy responses were sustained through to Week 16 and were generally comparable to those with dupilumab in a similar patient population in China[7] and in global Phase 3 trials.[8]
- In three other posters at this meeting (WCD2023, posters 3242, 3243, 3247), we demonstrate that rademikibart efficacy responses occurred rapidly (often at the first observation, Week 1 or 2), **without plateauing at Week 16**.
- Rademikibart was well tolerated, with no new safety signals.
  - Most TEAEs were mild to moderate in severity, and one of 170 patients (0.6%) discontinued due to a TEAE.
  - Rademikibart treatment completion at Week 16 (95.3%) was comparable to placebo (92.9%).
  - All injection site reactions were mild and did not lead to discontinuation of rademikibart.
- The ongoing maintenance period will potentially demonstrate sustained efficacy with rademikibart Q2W, as well as with a more convenient Q4W dose.

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References: 1. Yang et al. SID 2022, Portland, OR (Poster LB945). 2. Manuscript submitted. 3. Strober et al. Maui Derm 2022, Maui, HI. 4. Silverberg et al. Poster P0214 (Abstract 469), EADV 2022, Milan, Italy. 5. Strober et al. Poster P0215 (Abstract 470), EADV 2022, Milan, Italy. 6. Wang et al. Poster P0269 (Abstract 2647), EADV 2020, Vienna, Austria. 7. Zhao et al. Br J Dermatol 2022;186:633-41. 8. Simpson et al. NEJM 2016;375:2335-48.

Abbreviations: AD, atopic dermatitis; AE, adverse event; BMI, body mass index; BSA, Body Surface Area; CMH, Cochran-Mantel-Haenszel; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-50/75/90, at least 50%/75%/90% decreases 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; SE, standard error; TEAE, treatment-emergent adverse event.