Improvements in investigator-rated outcomes across 16 weeks of treatment with rademikibart (CBP-201) for moderate-to-severe atopic dermatitis (AD): Results from a pivotal trial in China (CBP-201-CN002)

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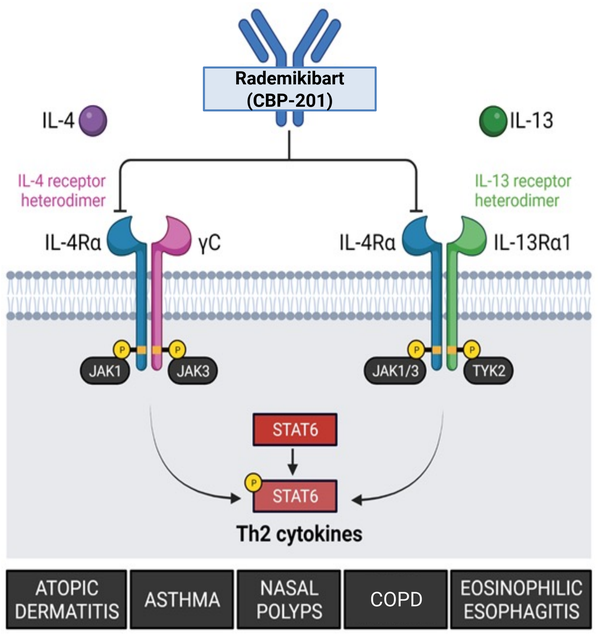
Poster 3247



- Rademikibart (formerly CBP-201) is a next-generation mAb, inhibiting the actions of both IL-4 and IL-13.
- In preclinical studies, rademikibart was shown to bind with higher affinity to a distinct IL-4Rα epitope, and downregulates STAT6 signalling and Th2 cytokine gene expression with greater potency than dupilumab.[1,2]
- The WW001 global Phase 2 trial of rademikibart demonstrated improvements in AD signs and symptoms across a range of investigator and PRO rating scales.[3–5]
- Investigator assessments provide particularly objective and reliable measurement of improvements in AD severity.

Objective

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

In three other posters at this meeting (WCD 2023, posters 3240, 3242, 3243), we report that the CN002 trial achieved all primary and secondary efficacy endpoints at Week 16, and rademikibart was well tolerated.

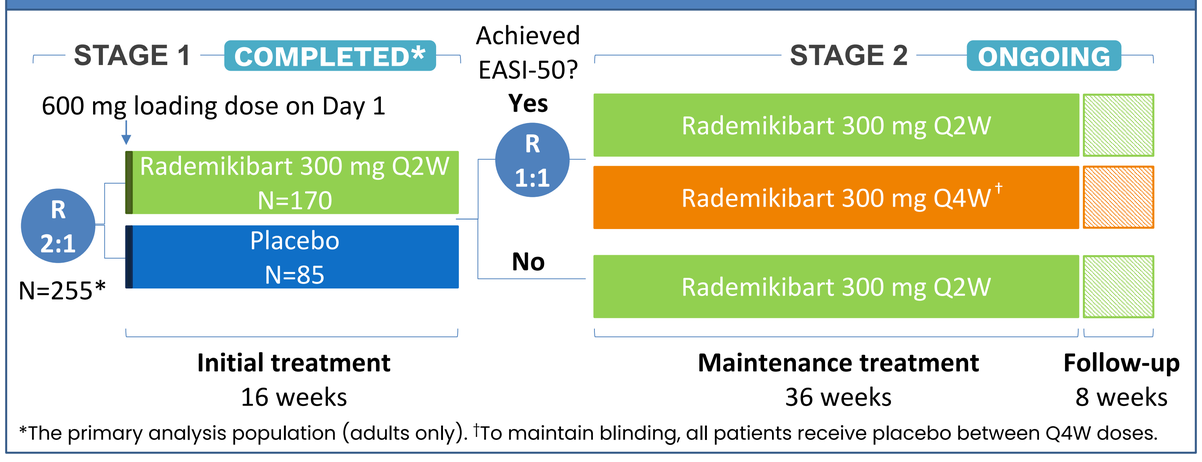
Here, we report the time course of improvements in investigator-assessed outcomes with rademikibart across the initial 16-week treatment period in the adult population.

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

Disease characteristics at baseline were well balanced for the 255 adults (Table 1), and generally comparable to dupilumab trials in China and globally.[6–8] All patients received ≥1 dose; 95.3% and 92.9% completed rademikibart and placebo, respectively, to Week 16.

Table 1: Disease characteristics at baseline*

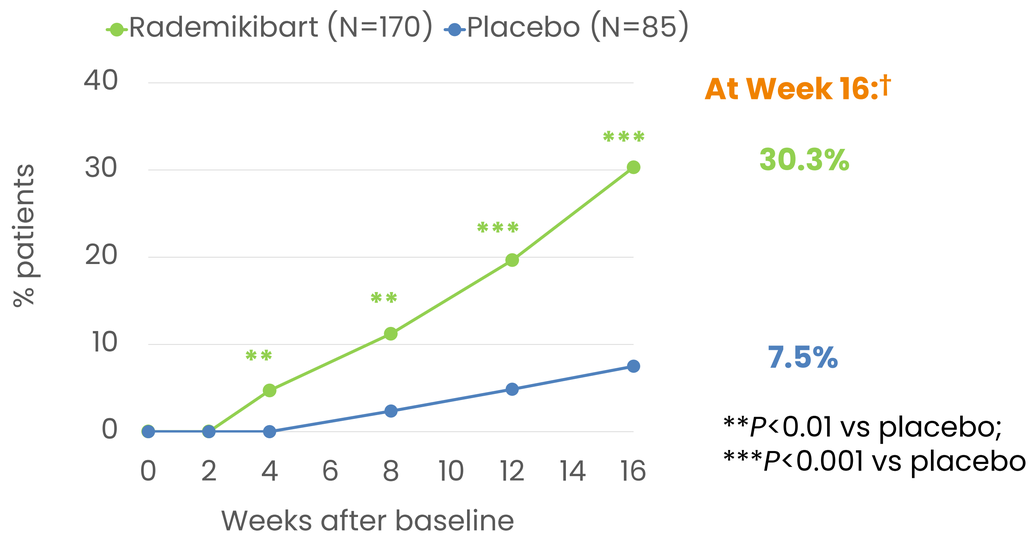
Median (min, max), unless stated otherwise	Rademikibart N=170	Placebo N=85
IGA, n (%) 3 (moderate) 4 (severe)	 78 (45.9%) 92 (54.1%)	 38 (44.7%) 47 (55.3%)
EASI score	27.3 (16.0, 72.0)	26.3 (16.0, 66.9)
BSA score	44.3 (13.5, 100.0)	45.0 (18.0, 100.0)
SCOARD score	66.7 (39.7, 101.7)	64.5 (40.6, 97.8)

*For the primary analysis population (adults only).

IGA across the initial 16-week treatment period

The proportion of patients achieving IGA 0/1 response *improved without plateauing* (Figure 2). IGA 0/1 response at Week 16 was the primary endpoint; 22.6% of patients responded to rademikibart (adjusted for placebo with multiple imputation inference).

Figure 2: Patients achieving IGA 0/1 and ≥2-point reduction from baseline



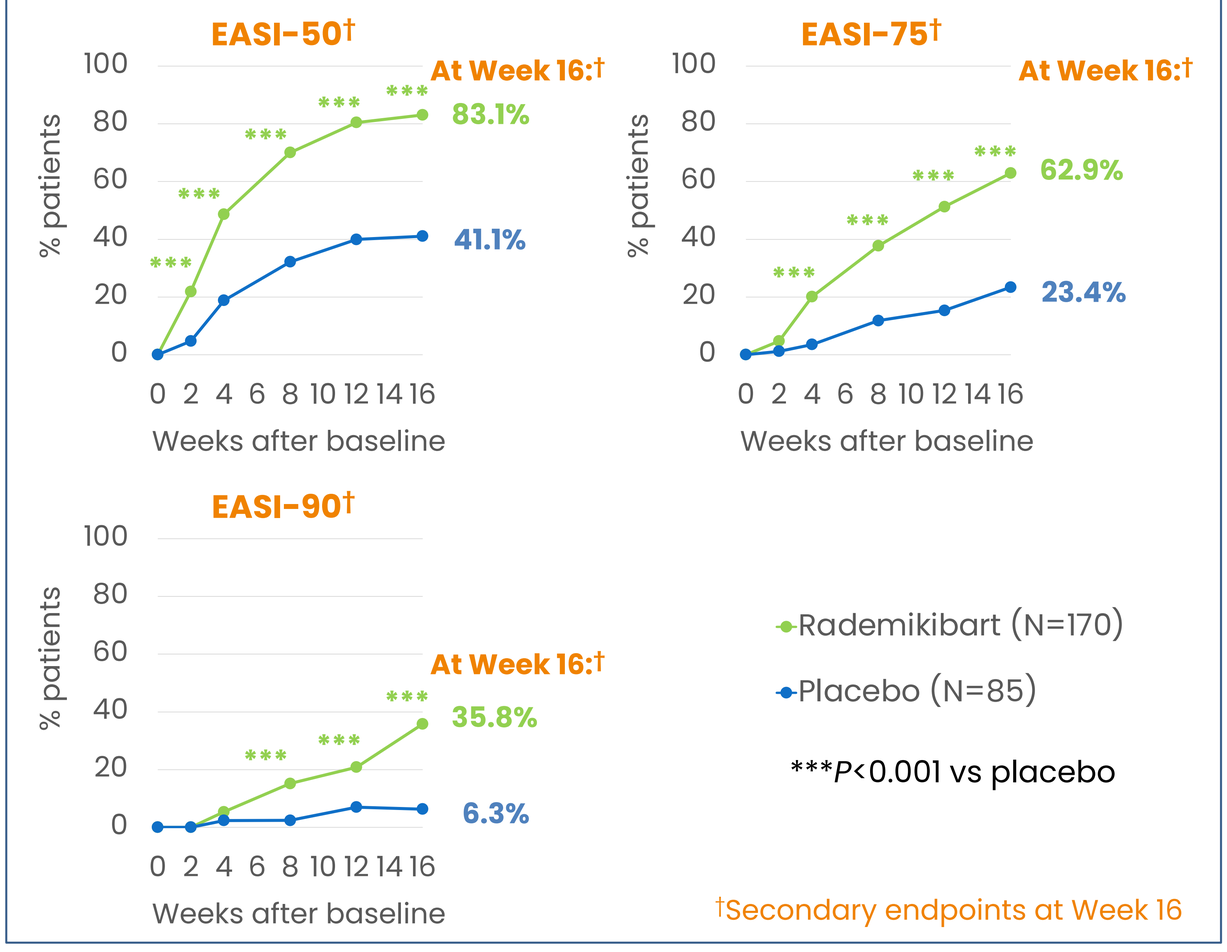
**P<0.01 vs placebo; ***P<0.001 vs placebo

†Primary endpoint at Week 16

EASI category scores across the initial 16-week treatment period

Categorical EASI response rates increased rapidly, generally *without plateauing* by Week 16 (Figure 3).

Figure 3: Patients achieving EASI responses†



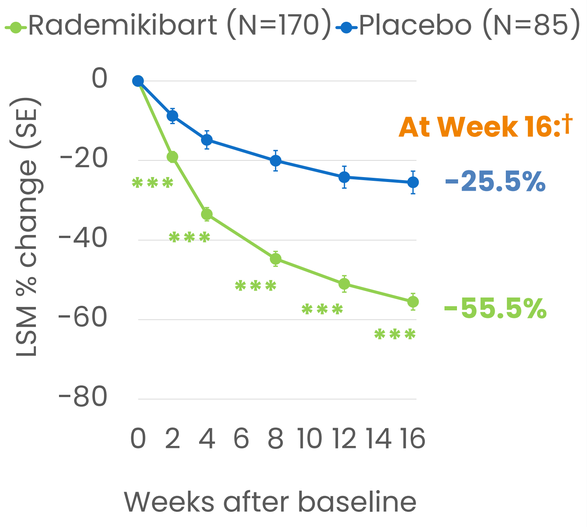
†Secondary endpoints at Week 16

SCORAD and BSA across the initial 16-week treatment period

Rapid improvements in AD, *without plateauing* by Week 16, were observed based on SCORAD* and BSA scores (Figures 4 and 5). Placebo-adjusted improvements in SCORAD* and BSA were -30.0% and -33.1%, respectively, at Week 16.

*The SCORAD scale mainly reflects investigator-assessed AD extent and severity (~20% of the scale is based on patient-reported sleep disturbance and pruritus).

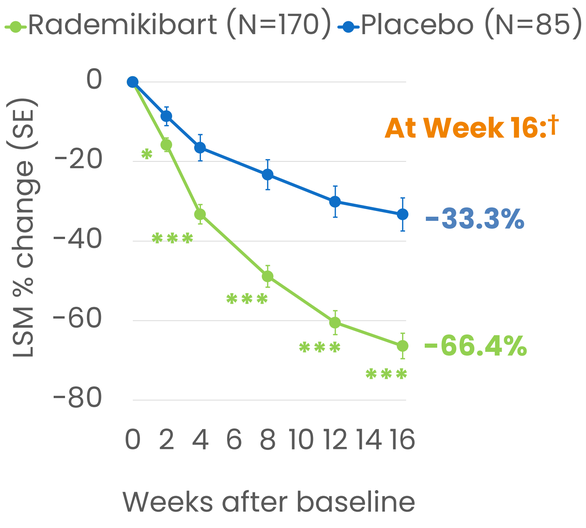
Figure 4: Change in SCORAD scores†



***P<0.001 vs placebo

†Secondary endpoint at Week 16

Figure 5: Change in BSA scores†



*P<0.05 vs placebo; ***P<0.001 vs placebo

†Secondary endpoint at Week 16

Conclusions

- The pivotal CN002 trial in China achieved its primary endpoint (IGA 0/1 response), <u>without plateauing of this efficacy response</u> by Week 16, in adults with moderate-to-severe AD.
- Rapid improvements were also observed with EASI, BSA, and SCORAD, <u>all without plateauing</u> by Week 16.
- We also report efficacy in the CN002 trial, including rapid improvements in PROs, in three other posters at this meeting (WCD2023, posters 3240, 3242, 3243).
- These findings are confirmatory of rapid and sustained improvements in AD signs and symptoms during the WW001 global Phase 2 trial of rademikibart.[3–5]
- Efficacy responses at Week 16 in CN002 were generally comparable to global and China-specific trials of dupilumab[6–9]
- Further clinical improvements may be gained during 36 weeks of maintenance treatment with rademikibart.

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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. Thaçi et al. The Lancet 2016;387:40-52. 7. Zhao et al. Br J Dermatol 2022;186:633-41. 8. Simpson et al. NEJM 2016;375:2335-48. 9. Thaçi et al. J Dermatol Sci 2019;94:266-72.

Abbreviations: AD, atopic dermatitis; BSA, Body Surface Area; CMH, Cochran-Mantel-Haenszel; 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; Q2/4W, every 2/4 weeks; PRO, patient rated outcomes; R, randomized; SCORAD, SCORing Atopic Dermatitis; SE, standard error.