Positive 52-Week Maintenance Data Observed with Rademikibart in Patients with Moderate-to-Severe Atopic Dermatitis (S*EASI*DE CHINA)

Jianzhong Zhang,[1] Jonathan I. Silverberg,[2] Jiawang Guo,[3] Jili Yun,[3] Wuban Pan,[3] Zheng Wei,[4] Raúl Collazo[4]

[1]Peking University People's Hospital, Department of Dermatology, Beijing, China; [2]Department of Dermatology, George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [3]Suzhou Connect Biopharmaceuticals Ltd, Taicang, China; [4]Connect Biopharma LLC, San Diego, CA, USA

Rademikibart

Rademikibart is a next-generation mAb, optimized for high affinity binding to the IL-4Rα subunit, potentially allowing **convenient monthly dosing** intervals.[1,2]

S*EASI*DE CHINA

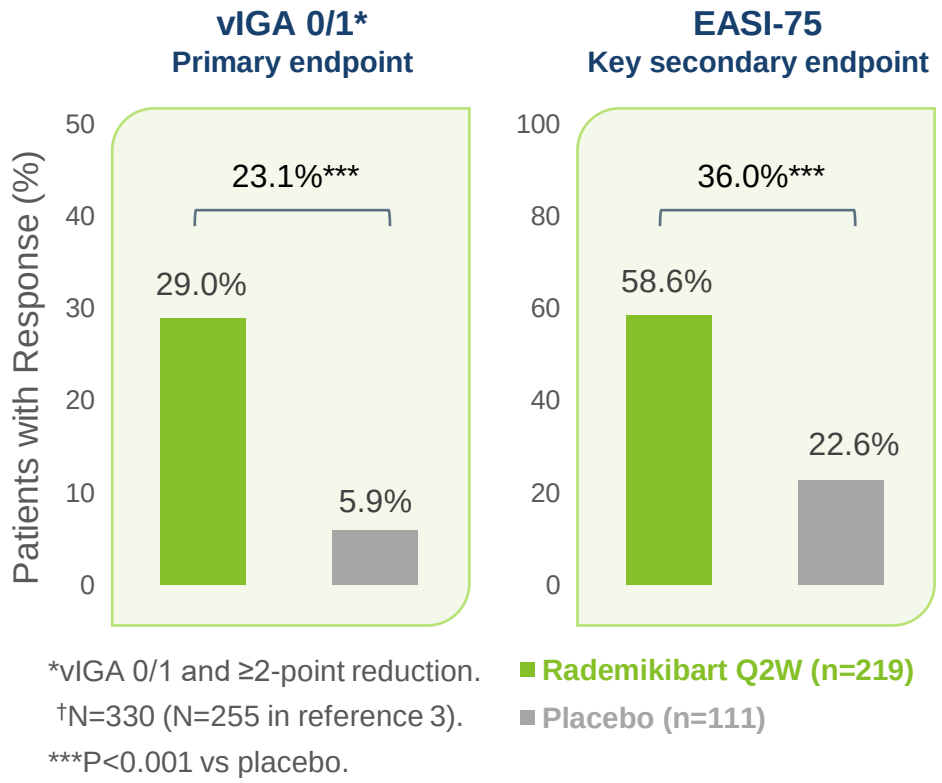
In **Stage 1** of S*EASI*DE CHINA (CN-002), patients with moderate-to-severe AD, all primary and secondary endpoints (e.g. vIGA 0/1, EASI, PP-NRS) were achieved at Week 16 with Q2W dosing

Stage 2 assessments were conducted across an additional 36 weeks following re-randomization with either Q2W or Q4W dosing

Objective

To report efficacy and safety from **Stage 2** across 52 weeks in S*EASI*DE CHINA.

Week 16 in S*EASI*DE CHINA[3,†]

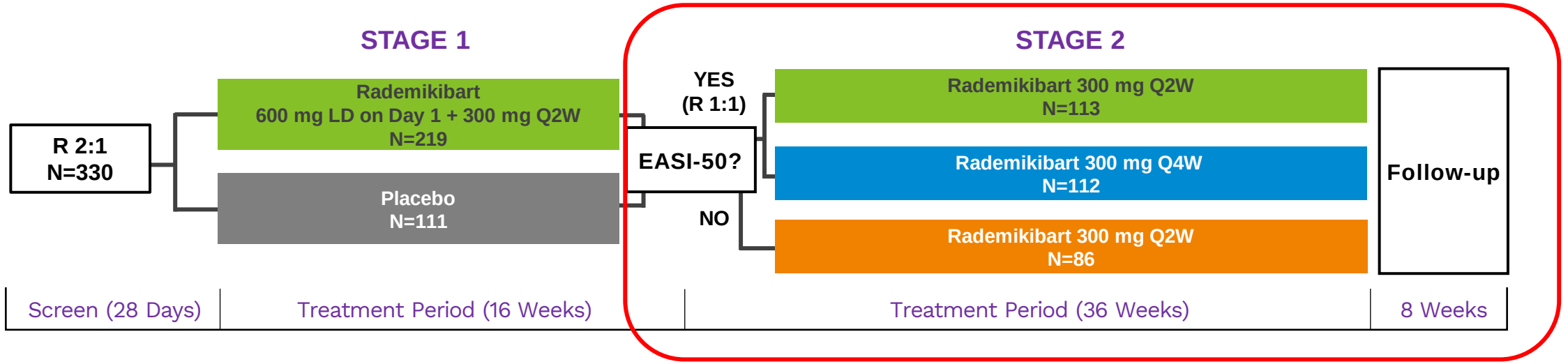


References: 1. Zhang L, et al. Sci Rep. 2023;13:12411. 2. Silverberg JI, et al. J Allergy Clin Immunol. 2024:153:1040-1049.e12. 3. Zhang J, et al. Oral presentation #45874, AAD 2023, New Orleans, LA, USA.

Abbreviations: AD = atopic dermatitis. EASI = Eczema Area and Severity Index. EASI-75 = at least 75% decrease from baseline. IL, interleukin. IL-4Rα = IL-4-receptor alpha. mAb = monoclonal antibody. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

RAD 2024, June 8th–10th, Chicago, IL, USA
Abstract #712

*SEASI*DE CHINA:
Study Design, Inclusion Criteria, Endpoints, and Treatment Completion Rates



Key inclusion criteria:

- 12–75 years of age
- Atopic dermatitis for ≥1 year
- EASI ≥16
- vIGA ≥3 (5-point scale [0-4])
- ≥10% BSA involvement
- PP-NRS ≥4

Week 16 EASI-50 responders were re-randomized 1:1 to rademikibart 300 mg Q2W or Q4W

Primary endpoint:

- vIGA 0/1 (including ≥2-point reduction) response at Week 16

Other efficacy endpoints included:

- EASI-75 and EASI-90 response at Week 16
- PP-NRS ≥3- and ≥4-point response at Week 16
- % changes from baseline in EASI and PP-NRS scores at Week 16
- These efficacy outcomes during the 36-week treatment period

Patients completing treatment:

At Week 16

- 94.2% (rademikibart Q2W or placebo)

At Week 52

- 92.4% of Week 16 EASI-50 responders (Q2W or Q4W)
- 89.5% of Week 16 EASI-50 non-responders (Q2W)

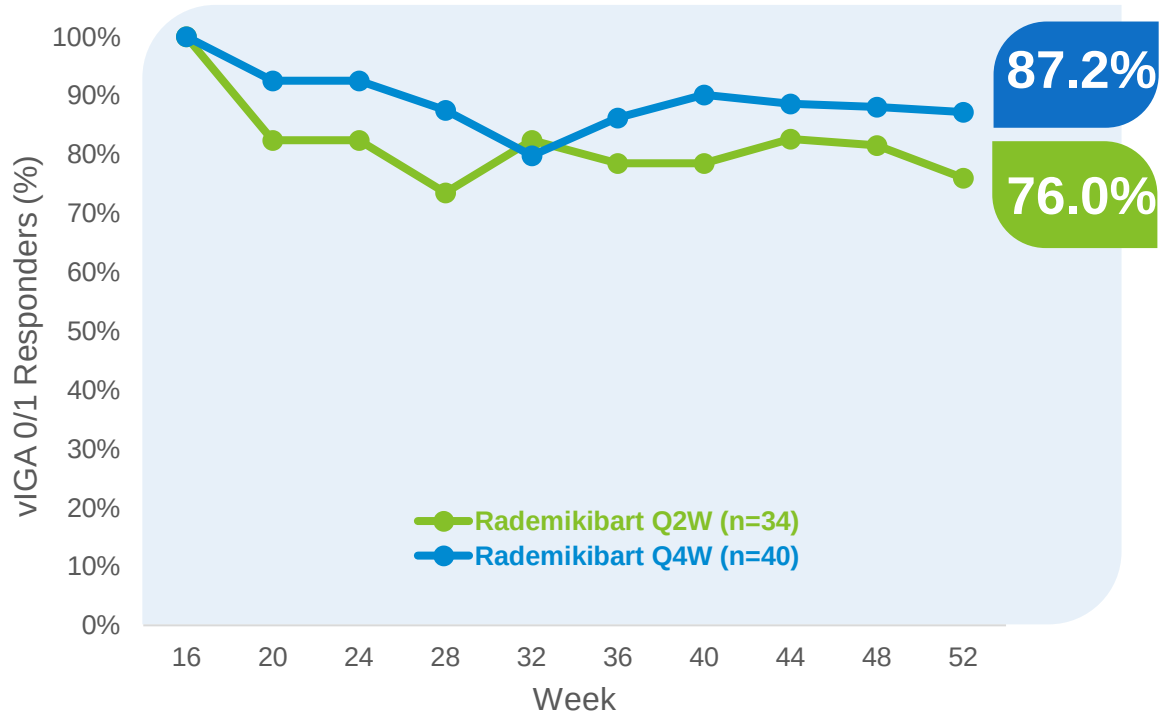
To maintain blinded state, all patients received placebo between Q4W doses of rademikibart 300 mg.

Abbreviations: BSA = Body Surface Area. EASI = Eczema Area and Severity Index. EASI-50, EASI-75, and EASI-90 = at least 50%, 75%, and 90% decrease from baseline. LD = Loading Dose. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. R = randomized. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

Maintenance of IGA 0/1 and EASI-75 Responses Observed at Week 16 were Sustained Through Week 52

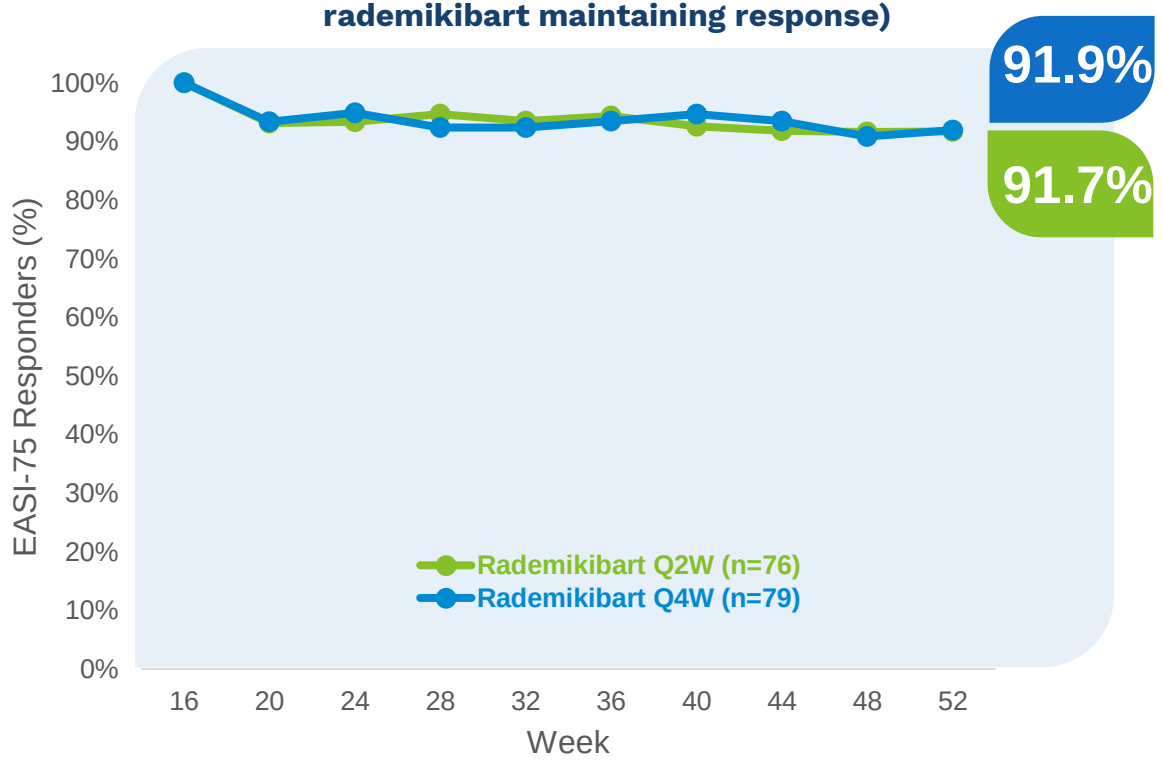
vIGA 0/1 and ≥2-Point Reduction

(Percentage of Week 16 vIGA 0/1 responders to rademikibart maintaining response)*



EASI-75

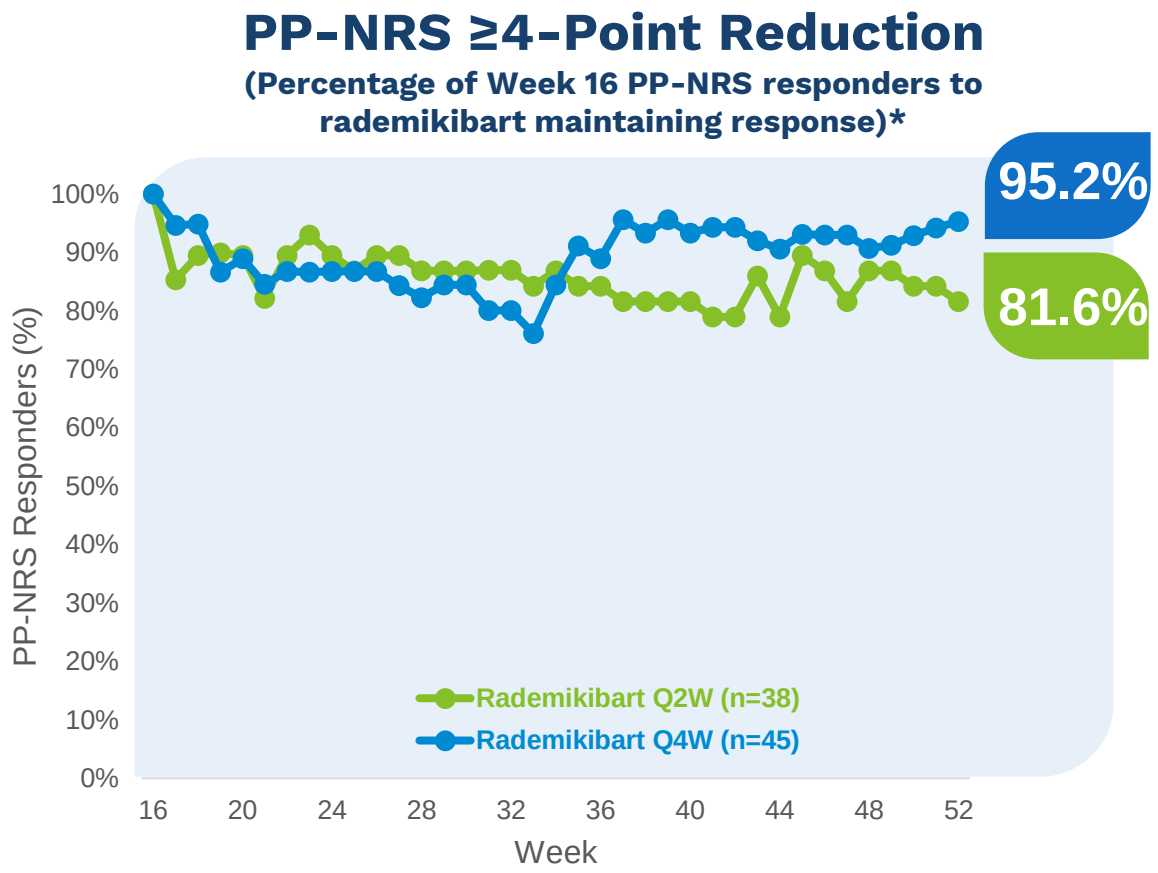
(Percentage of Week 16 EASI-75 responders to rademikibart maintaining response)



*Patients with both EASI-50 and IGA 0/1 responses at Week 16

Q2W = Continued on Q2W dosing from Week 16. Q4W = Switched from Q2W to Q4W dosing at Week 16.
Data were analyzed by NRI-MI (non-responder imputation for rescue medications and multiple imputation for remaining missing data).
Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

PP-NRS ≥4-Point Responses were also Highly Maintained from Week 16 Through Week 52

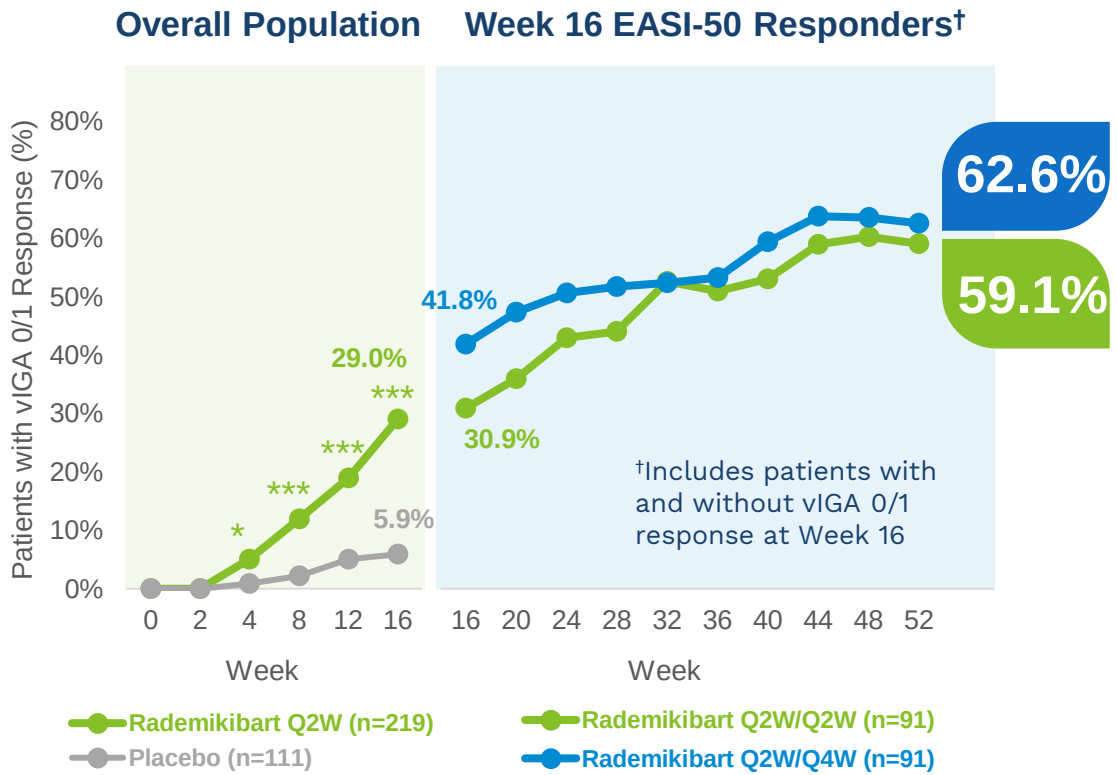


*Patients with both EASI-50 and PP-NRS responses at Week 16

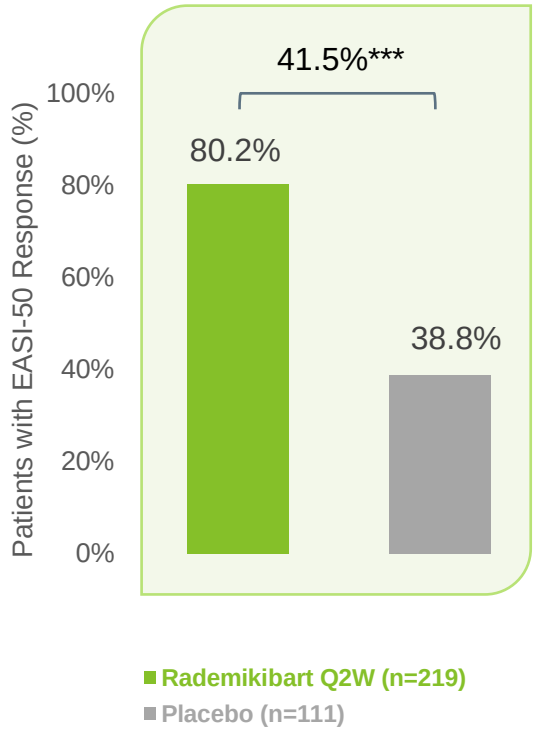
Q2W = Continued on Q2W dosing from Week 16. Q4W = Switched from Q2W to Q4W dosing at Week 16.
Data were analyzed by NRI-MI (non-responder imputation for rescue medications and multiple imputation for remaining missing data).
Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. PP-NRS = Peak Pruritus Numerical Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks.

Among EASI-50 Responders, Continued Improvement of IGA 0/1 Response was Observed with Rademikibart (through Week 52)

vIGA 0/1 and ≥2-point reduction



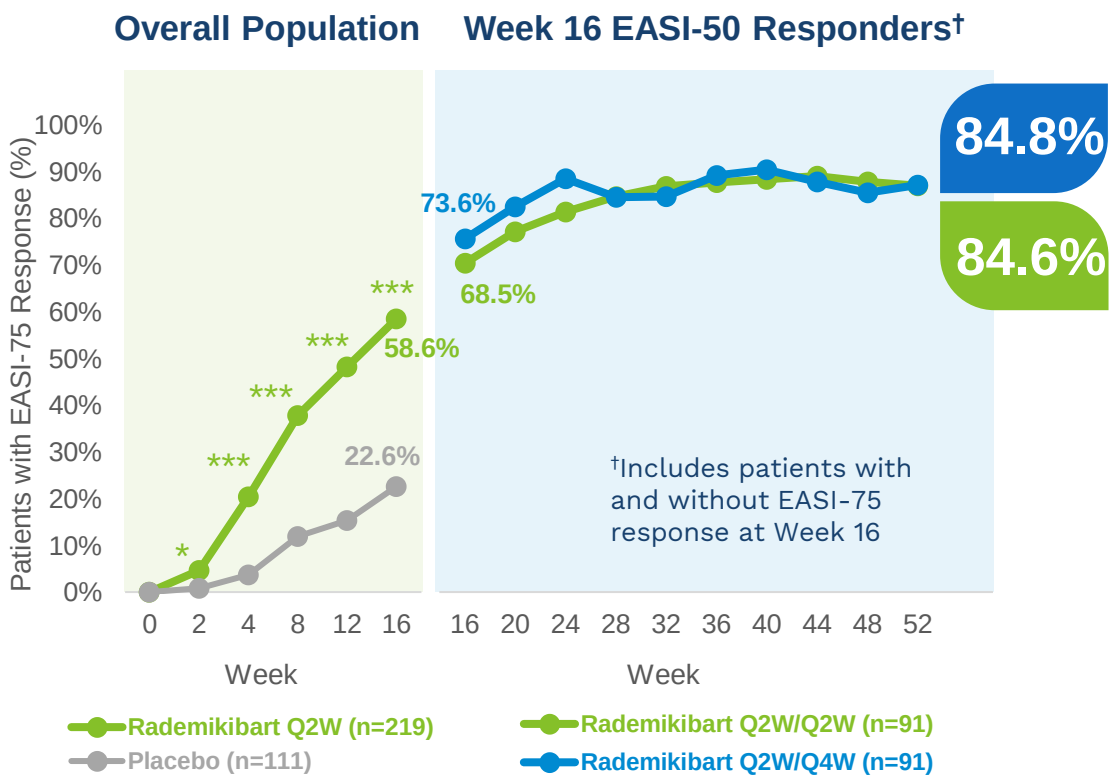
EASI-50 Response at Week 16



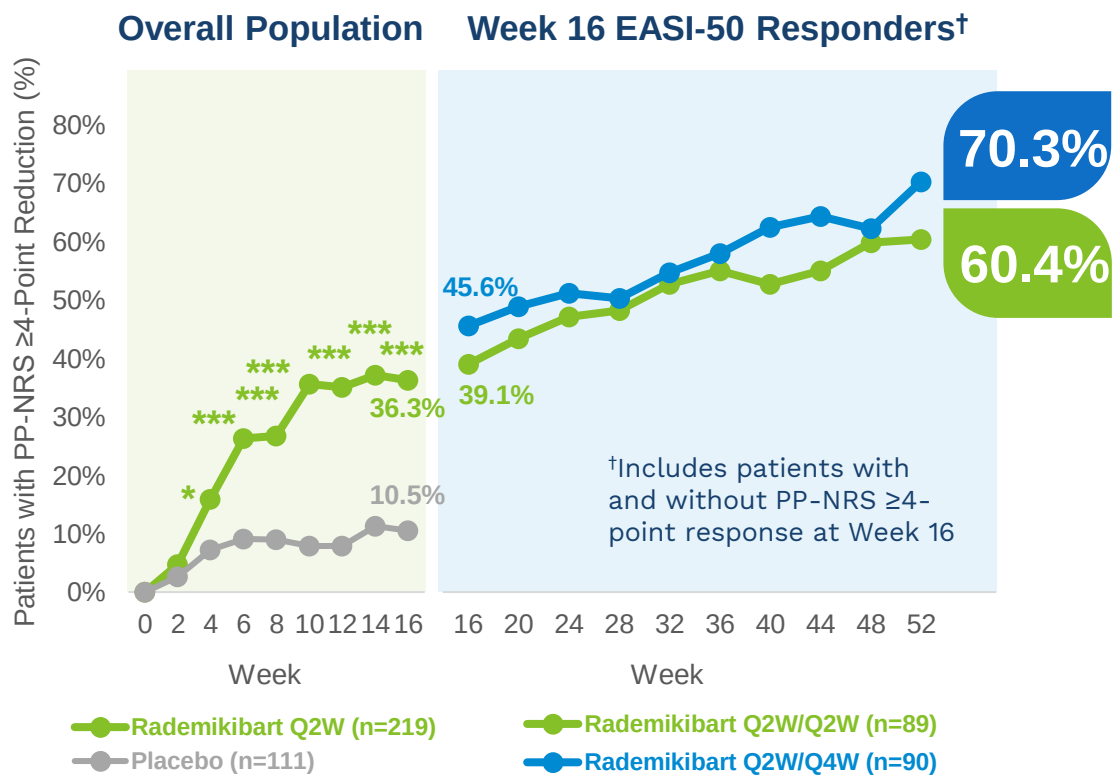
Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo.
Missing data in the rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent events; multiple imputation was used for the placebo arm. From Week 16, binary response data were analyzed by non-responder imputation and multiple imputation. **Abbreviations:** EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear).

Continued Improvement of EASI-75 and PP-NRS were Observed with Rademikibart Treatment (Baseline through Week 52)

EASI-75



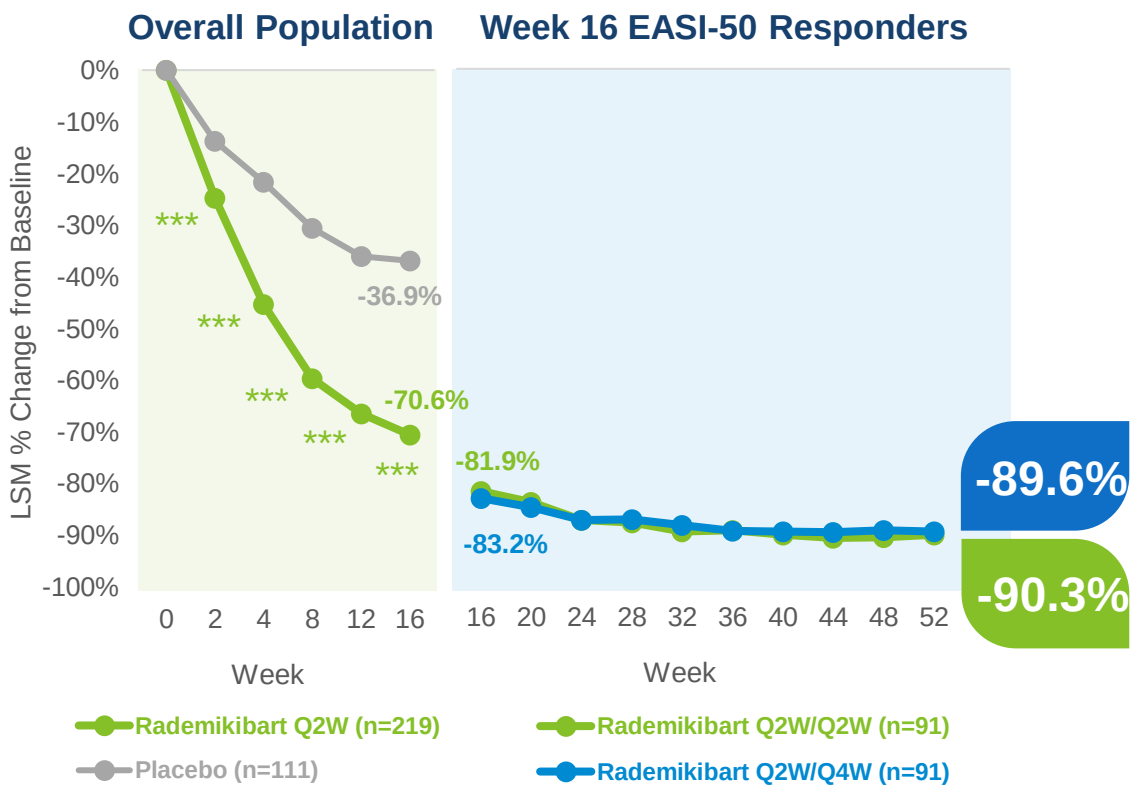
PP-NRS ≥4-Point Reduction



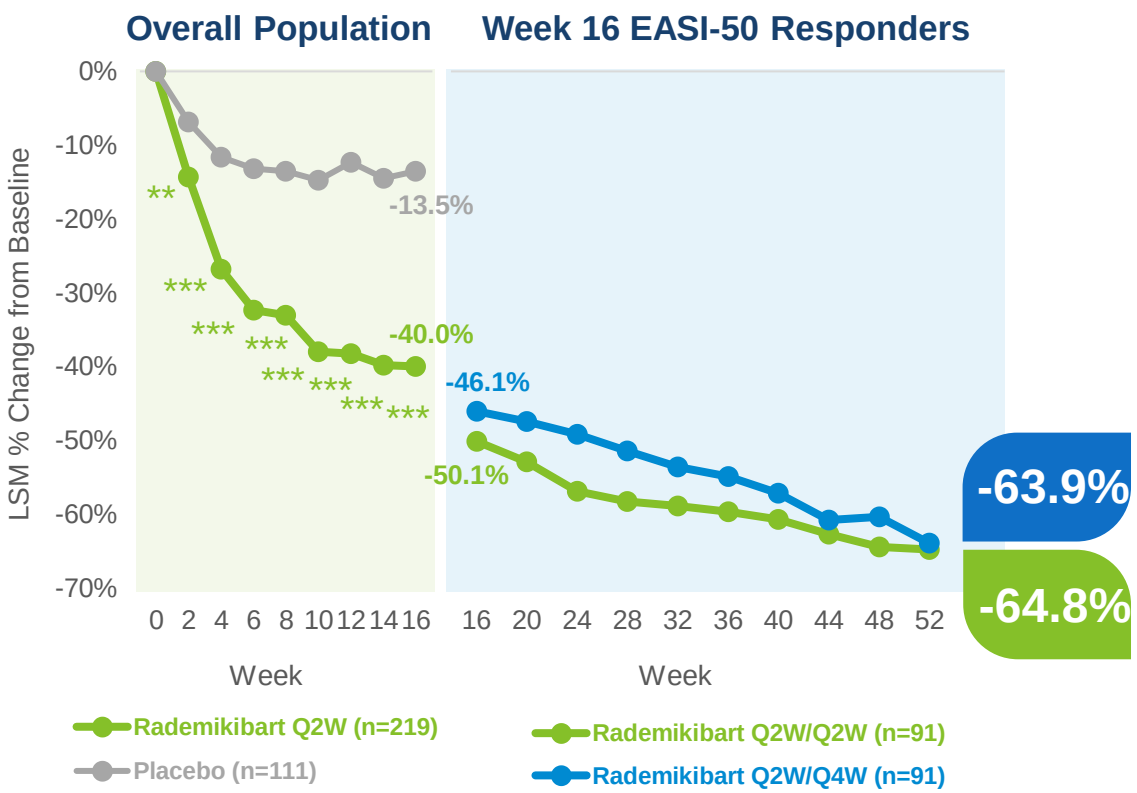
Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo.
Missing data in rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. From Week 16, binary response data were analyzed by non-responder imputation and multiple imputation. **Abbreviations:** EASI = Eczema Area and Severity Index. EASI-75/90 = at least 75/90% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks.

Continued Improvement of EASI and PP-NRS Scores were Observed with Rademikibart (Baseline through Week 52)

EASI Score



PP-NRS Score



Q2W/Q2W = Continued on Q2W dosing from Week 16. Q2W/Q4W = Switched from Q2W to Q4W dosing at Week 16. ***, **, * for P<0.001, <0.01, <0.05, respectively, vs placebo.
Missing data in the rademikibart group up to Week 16 was imputed by jump to reference imputation (J2R) after applying the rule of intercurrent event; multiple imputation was used for the placebo arm. From Week 16, score change data were analyzed by ANCOVA and multiple imputation. **Abbreviations:** ANCOVA = Analysis of Covariance. EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. LSM, least squares mean. PP-NRS = Peak Pruritus Numerical Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks.

No new safety signals compared with previous rademikibart trials,[1,2] including no treatment-related serious events

n (%) patients with…	Stage 1 (Weeks 0–16)		Stage 2 (Weeks 16–60)		
	Rademikibart Q2W N=219	Placebo N=111	Rademikibart Q2W (W16 responders)* N=113	Rademikibart Q4W (W16 responders)* N=112	Rademikibart Q2W, (W16 non-responders)* N=85
Any TEAE	166 (75.8%)	80 (72.1%)	93 (82.3%)	95 (84.8%)	71 (83.5%)
Serious TEAEs – none were related to study treatment and no deaths	1 (0.5%)	3 (2.7%)	1 (0.9%)	3 (2.7%)	6 (7.1%)
Severe (Grade 3) TEAEs	4 (1.8%)	5 (4.5%)	3 (2.7%)	5 (4.5%)	6 (7.1%)
TEAEs leading to treatment discontinuation†	2 (0.9%)	1 (0.9%)	0	0	1 (1.2%)
Injection site reaction – all mild (Grade 1)	20 (9.1%)	3 (2.7%)	6 (5.3%)	8 (7.1%)	6 (7.1%)
Conjunctivitis‡	12 (5.5%)	3 (2.7%)	6 (5.3%)	6 (5.4%)	7 (8.2%)
Herpes infection#	4 (1.8%)	2 (1.8%)	0	0	3 (3.5%)

*Week 16 EASI-50 responders or non-responders.

†Discontinuations were due to atopic dermatitis flare in the rademikibart Q2W (Grade 2) and placebo (Grade 3) during Stage 1, pregnancy (classified as a TEAE) in Stage 2, and vitiligo (Grade 2) that developed in Stage 1 (rademikibart 300 mg Q2W arm) and discontinuation occurred in Stage 2.

‡Conjunctivitis includes the preferred terms conjunctivitis, allergic conjunctivitis, conjunctival injection, bacterial conjunctivitis, viral conjunctivitis, giant papillary conjunctivitis, eye irritation, and eye inflammation.

#Herpes infections includes the preferred terms herpes virus infection, herpes zoster, herpes simplex, herpes simplex reactivation, oral herpes.

References: 1. Wang J, et al. Clin Transl Sci. 2023;16:2614-2627. 2. Silverberg JI, et al. J Allergy Clin Immunol. 2024:153:1040-1049.e12.

Abbreviations: EASI = Eczema Area and Severity Index. EASI-50 = at least 50% decrease from baseline. Q2W = every 2 weeks. Q4W = every 4 weeks. TEAE = treatment-emergent adverse event.

Conclusion:
*SEASI*DE CHINA supports long-term monthly dosing of rademikibart

Efficacy continuously improved through Week 52

- Skin clearance (IGA0/1, EASI) and pruritus (PP-NRS) improvements at Week 16 in S*EASI*DE CHINA (dosed Q2W) were compatible with WW001 global Phase 2 trial results (dosed Q2W and Q4W).[1]
- Efficacy continued to improve between Weeks 16 and 52 and was comparable with rademikibart Q2W and Q4W.

Binary responses at Week 16 were highly maintained through Week 52

- Most patients with response at Week 16 maintained them through Week 52.
- Maintenance rates were comparable with rademikibart Q2W and Q4W: IGA0/1 (76.0%, 87.2%), EASI-75 (91.7%, 91.9%), PP-NRS ≥4-point reduction (81.6%, 95.2%).
- Maintenance rates were higher than reported for approved AD biologic therapies (dupilumab and tralokinumab).[2,3]

Well tolerated through Week 52

- No new safety signals.
- Few TEAEs led to discontinuation.
- No serious TEAEs were related to study treatment.

References: 1. Silverberg JI, et al. J Allergy Clin Immunol. 2024:153:1040-1049.e12. 2. Wollenberg A, et al. Br J Dermatol. 2021;184:437-449. 3. Worm M, et al. JAMA Dermatol. 2020;156:131-143.

Abbreviations: EASI = Eczema Area and Severity Index. EASI-75 = at least 75% decrease from baseline. PP-NRS = Peak Pruritus Numeric Rating Scale. Q2W = every 2 weeks. Q4W = every 4 weeks. TEAE = treatment-emergent adverse event. vIGA 0/1 = validated Investigator Global Assessment of 0 (clear skin) or 1 (almost clear) and ≥2-point reduction.