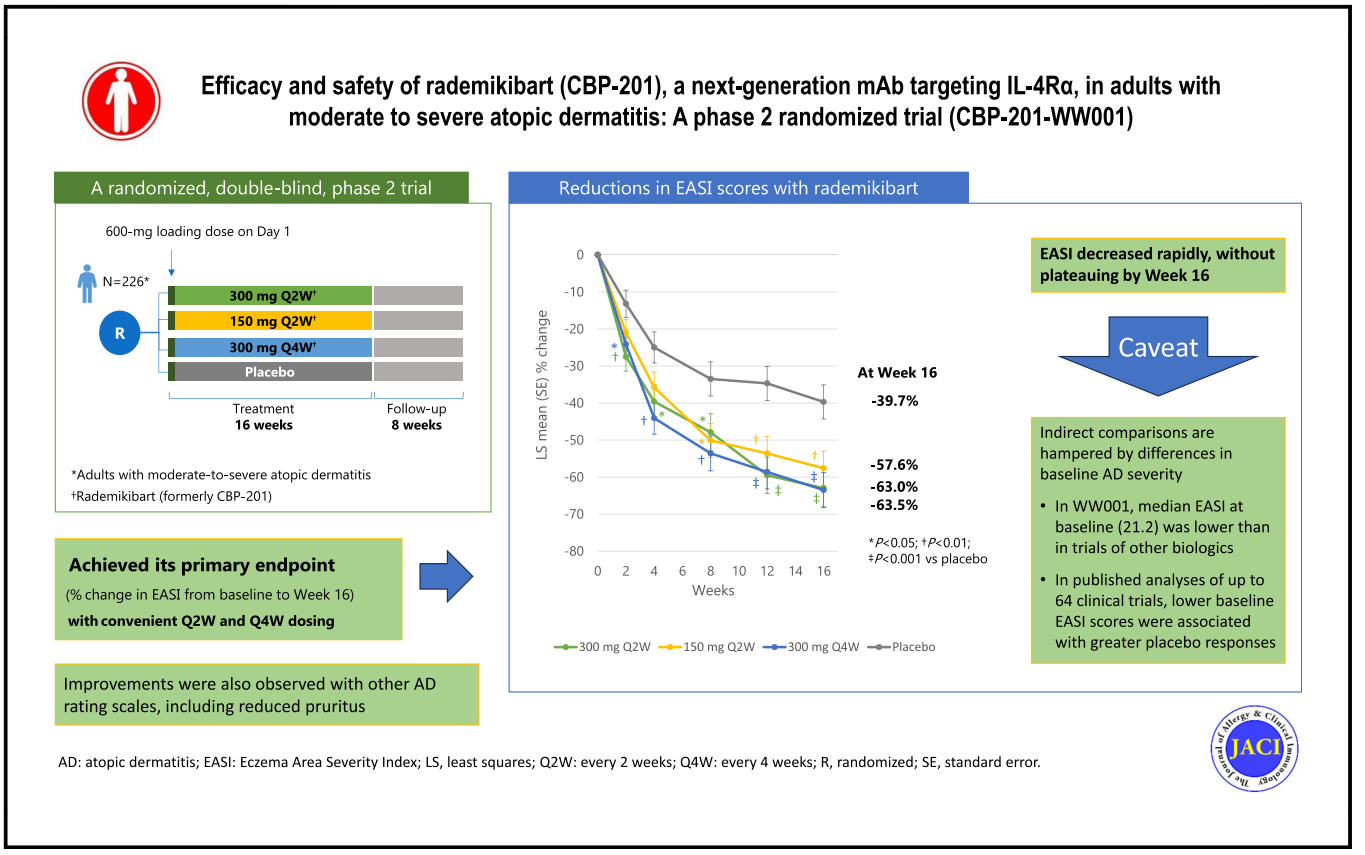
Efficacy and safety of rademikibart (CBP-201), a next-generation mAb targeting IL-4Rα, in adults with moderate to severe atopic dermatitis: A phase 2 randomized trial (CBP-201-WW001)

Jonathan I. Silverberg, MD, PhD, MPH, Bruce Strober, MD, PhD, Brian Feinstein, DO, Jinhua Xu, MD, PhD, Emma Guttman-Yassky, MD, PhD, Eric L. Simpson, MD, MCR, et al

GRAPHICAL ABSTRACT



Capsule summary: Atopic dermatitis treatments are associated with variable efficacy, tolerability, and safety concerns. The IL-4 receptor alpha antagonist rademikibart (CBP-201) may be reliably efficacious, with convenient 2- and 4-week dosing options, for adults with moderate to severe atopic dermatitis.

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Efficacy and safety of rademikibart (CBP-201), a next-generation mAb targeting IL-4Rα, in adults with moderate to severe atopic dermatitis: A phase 2 randomized trial (CBP-201-WW001)

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Background: Rademikibart (CBP-201) is a next-generation IL-4 receptor alpha–targeting antibody.

Objective: We sought to evaluate rademikibart in adults with moderate to severe atopic dermatitis.

Methods: A total of 226 patients were randomized, double-blind, to subcutaneous rademikibart (300 mg every 2 weeks [Q2W], 150 mg Q2W, 300 mg every 4 weeks [Q4W]; plus 600-mg loading dose) or placebo. Randomization began in July 2020. The trial was completed in October 2021.

Results: The WW001 phase 2 trial achieved its primary end point: significant percent reduction from baseline in least-squares mean Eczema Area Severity Index (EASI) to week 16 with rademikibart 300 mg Q2W (−63.0%; $P = .0007$), 150 mg Q2W (−57.6%; $P = .0067$), 300 mg Q4W (−63.5%; $P = .0004$) versus placebo (−39.7%). EASI scores decreased significantly with 300 mg Q2W and Q4W at the earliest assessment (week 2), with no evidence of plateauing by week 16. Significant improvements were also observed in secondary end points, including pruritus. Across the primary and secondary end points, efficacy tended to be comparable with 300 mg Q2W and Q4W dosing. Rademikibart and placebo had similar, low incidence of treatment-emergent adverse events (TEAEs) (48% vs 54%), serious TEAEs (1.8% vs 3.6%), TEAEs leading to treatment discontinuation (1.2% vs 1.8%), conjunctivitis of unspecified cause (2.9% vs 0%), herpes (0.6% vs 1.8%), and injection-site reactions (1.8% vs 1.8%). Although no discontinuations were attributed to coronavirus disease 2019, pandemic-related restrictions likely had an impact on trial conduct.

Conclusions: Rademikibart was efficacious and well tolerated at Q2W and Q4W intervals. Q4W dosing is a more convenient frequency than approved for current therapies. (J Allergy Clin Immunol 2024;153:1040-9.)

Key words: *Atopic dermatitis, rademikibart, CBP-201, dosing frequency, efficacy, tolerability, safety*

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease that affects up to 12% of adults and 25% of children.[1-4] Among other bothersome signs and symptoms, AD is characterized by intense pruritus and eczematous skin lesions.[4] Severe and unrelenting pruritus, sleeplessness, and embarrassment can lead to depression and other psychological disturbances in patients with moderate to severe AD.[5-9]

Topical treatments for AD may be hampered by variable efficacy, and oral systemic immunosuppressants are associated with safety concerns including serious infection, cancer risk, renal insufficiency, and hepatotoxicity.[10-17] More recently approved treatment options include multiple oral Janus kinase inhibitors and 2 biologics—dupilumab, an mAb directed against IL-4 receptor alpha (IL-4Rα), and tralokinumab, an mAb directed against the free IL-13 cytokine.[18-29] Other potential treatments targeting IL-13 and other immune pathways are in clinical development.[30-32] Janus kinase inhibitors are associated with herpes zoster and other serious infections, malignancy, thrombosis, major adverse cardiovascular events, and mortality.[18-21,33,34] The Food and Drug Administration–approved biologics dupilumab and tralokinumab have reported a higher risk of conjunctivitis and subcutaneous (SC) injection-site reactions than placebo.[22-29,35-37] For dupilumab and tralokinumab, the recommended dosing frequency is every other week (Q2W)[35-37]; tralokinumab may be administered every fourth week (Q4W) as a maintenance dose to a subset of patients—those below 100 kg who achieve clear or almost clear skin after 16 weeks of Q2W treatment.[36,37] Although Q4W dosing has been studied for both dupilumab and tralokinumab, substantial proportions of patients (42% and 51% at week 52, respectively) did not maintain their week 16 responses.[29,38]

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Abbreviations used

AD: Atopic dermatitis
BSA: Body surface area
COVID-19: Coronavirus disease 2019
DLQI: Dermatology Life Quality Index
EASI: Eczema Area and Severity Index
EASI-50/75/90: ≥50%/75%/90% improvement from baseline in Eczema Area and Severity Index
FAS: Full analysis set
IL-4Rα: IL-4 receptor alpha
LOCF: Last observation carried forward
LS: Least-squares
POEM: Patient-Oriented Eczema Measure
PP-NRS: Peak Pruritus Numerical Rating Scale
PPS: Per-protocol set
Q2W: Every 2 weeks
Q4W: Every 4 weeks
QoL: Quality of life
SC: Subcutaneous
SCORAD: SCORing Atopic Dermatitis
TEAE: Treatment-emergent adverse event
vIGA-AD: Validated Investigator Global Assessment Scale for Atopic Dermatitis

Rademikibart (CBP-201) is a next-generation human IgG4 kappa mAb directed against human IL-4Rα, blocking signaling from T_H2 inflammatory cytokines IL-4 and IL-13, which both interact with the receptor subunit. In preclinical experiments, rademikibart bound with high specificity to a unique epitope on human IL-4Rα and, compared with dupilumab, was associated with higher binding affinity and similar or more potent downregulation of T_H2-driven inflammatory responses *in vitro*, *in vivo*, and *ex vivo*.[39] In transgenic mice expressing human IL-4Rα and IL-4, rademikibart eliminated antigen-specific IgE and eosinophilic lung infiltration, and in human skin explants, rademikibart downregulated IL-4 and IL-13 expression with greater effectiveness than dupilumab.[39] Early-phase clinical trials of rademikibart demonstrated efficacy across a range of rating scales in patients with AD, as well as few SC injection-site reactions and low incidence of conjunctivitis versus placebo.[40]

We report the primary analysis of the WW001 phase 2 trial, in which the efficacy and safety of 2 Q2W and 1 Q4W dose regimens of rademikibart were assessed in adults with moderate to severe AD.

METHODS

Study design

This phase 2, randomized, double-blind, placebo-controlled trial (NCT04444752) was conducted across 59 sites in the United States (38), China (9), Australia (8), and New Zealand (4). The trial comprised a 45-day screening period, a 16-week treatment period, and an 8-week follow-up period (see Fig E1 in this article's Online Repository at www.jacionline.org). Patients were randomized (1:1:1:1) to SC rademikibart (300 mg Q2W, 150 mg Q2W, or 300 mg Q4W) or matching placebo, administered up to and including day 113 (week 16), preceded on day 1 by a 600-mg loading dose of rademikibart or placebo. The first patient was randomized in July 2020, and the trial was completed in October 2021.

Patients

All patients were adults with moderate to severe AD (validated Investigator Global Assessment Scale for Atopic Dermatitis [vIGA-AD] ≥ 3, Eczema Area and Severity Index [EASI] ≥ 16, ≥10% body surface area [BSA] involvement of AD) inadequately controlled with, or not suitable for, topical treatments (see Table E1 in this article's Online Repository at www.jacionline.org). AD must have been present for 1 year or more before baseline. No previous treatment with anti–IL-4Rα/IL-13 agents and no concomitant topical AD treatment was allowed, except for emollient and permitted rescue medications for AD flares (creams/lotions and low- to medium-potency topical corticosteroids). If a patient received any other rescue medication, study treatment was immediately discontinued, and the patient was asked to continue with the study assessments.

Procedures and assessments

The trial complied with the Good Clinical Practice guidelines and the Declaration of Helsinki. Patients provided written informed consent. Informed consent forms and the study protocol were approved by appropriate institutional review boards and ethics committees.

Patients were randomly assigned to the rademikibart arms or placebo using a central randomization scheme, provided by a web-based interactive response system. The patient, site personnel, sponsor, and designees directly involved in the conduct and/or monitoring of the study were fully blinded to the treatment group assignments.

Rademikibart was provided in 1-mL (150-mg/mL) SC injections. The number, frequency, and volume of the injections were identical in each rademikibart and placebo arm. All patients were asked to apply emollient, twice daily, except for 4 hours before evaluation of dryness and scaling.

AD severity and extent were analyzed by the investigator using EASI, percent BSA of AD involvement, SCORing Atopic Dermatitis (SCORAD), and vIGA-AD. Patient-reported outcome measures were the Peak Pruritus Numerical Rating Scale (PP-NRS), the Dermatology Life Quality Index (DLQI), and the Patient-Oriented Eczema Measure (POEM). The PP-NRS is a visual analog scale used to determine the peak severity of pruritus over the previous 24-hour period, ranging from 0 ("no itch") to 10 ("worst itch imaginable"). All efficacy outcomes were assessed predose at visits throughout the study (Fig E1).

Outcomes

The primary end point was percent EASI change from baseline to week 16. Secondary end points included the proportions of patients achieving vIGA-AD response (clear [0] or almost clear skin [1], and a reduction of ≥2 points), EASI-50/75/90 (≥50%/75%/90% reductions in EASI score), and change in weekly average PP-NRS to week 16. Other end points included changes in POEM, BSA of AD involvement, SCORAD, and DLQI scores to week 16.

Safety assessments included adverse events, vital signs, physical examinations, injection-site changes, laboratory parameters, and electrocardiograms. Adverse events were classified by Medical Dictionary for Regulatory Activities terminology.

Statistical analysis

Efficacy and safety analyses were conducted using the full analysis set (FAS), comprising all randomized patients who received at least part of an SC dose of study treatment, and for the subgroup of patients enrolled in China because of local authority requirements. In the overall population, the primary end point was also analyzed in the per-protocol set (PPS), comprising FAS patients without major protocol deviations, such as use of restricted medication. Patients were included in the FAS after use of any rescue medication (permitted or prohibited), and in the PPS after use of permitted rescue medication, with subsequent assessments treated as missing in efficacy analyses.

The primary and other continuous efficacy end points were assessed using the analysis of covariance models with treatment group, baseline score, and baseline vIGA-AD (moderate, severe). Missing postbaseline scores (eg, if a patient discontinued treatment) were imputed using last observation carried forward (LOCF) in the FAS. For the primary end point, sensitivity analyses were also conducted for the FAS, comprising of worst observation carried forward, multiple imputation of missing data using the Markov-chain Monte-Carlo method, and observed cases.

Responder end points were analyzed using the Clopper-Pearson method; missing values (eg, if a patient discontinued treatment) were imputed by nonresponder imputation. For the primary end point, pairwise comparisons for each rademikibart arm versus placebo were performed and a serial gatekeeping procedure was used for multiplicity adjustment. Starting with the 300-mg Q2W dose, followed by the 150-mg Q2W dose, and ending with the 300-mg Q4W dose, each rademikibart group was compared with the placebo group, until statistical significance at the .05 level was not achieved.

A sample size of 220 patients (assuming ≥176 completers) would provide 95% power to detect a treatment effect on the primary end point between the rademikibart 300-mg Q2W and placebo arms. The sample size was based on a 2-sided, 2-sample independent t test with a 5% significant level ($\alpha = 0.05$). The mean between-group difference was assumed to be 35 percentage points and the pooled SD of 45%, on the basis of preliminary results at week 4 and other empirical data.

RESULTS

Patient characteristics

From July 2020 to April 2021, 226 patients were randomly assigned to the 3 rademikibart dose regimens or placebo (see Fig E2 in this article's Online Repository at www.jacionline.org) in the United States (n = 172), China (n = 32), New Zealand (n = 19), and Australia (n = 3). Baseline characteristics were generally well balanced across the treatment arms (Table I; see also Tables E2 and E3 in this article's Online Repository at www.jacionline.org). Approximately one-third of patients had severe AD at baseline, on the basis of 31% having an vIGA-AD score of 4, median BSA of 35.1%, and a median EASI score of 21.2. Patients in China, included as a subgroup for *a priori* efficacy analyses conducted because of local authority requirements, had more severe AD (38% had an vIGA-AD score of 4, median BSA of 42.5%, and a median EASI score of 26.9) compared with the overall population (Table I; see also Table E2).

Trial conduct was likely affected by movement restrictions during the pandemic, although no discontinuations were attributed directly to coronavirus disease 2019 (COVID-19). In the overall population, 13% to 19% of patients discontinued study treatment across the rademikibart arms and 29% in the placebo arm (Fig E2). Thirty-two (71%) of the 45 patients who discontinued were either lost to follow-up or withdrew consent. Rescue medication rates were as follows: 5.3% (300 mg Q2W), 8.8% (150 mg Q2W), 16.1% (300 mg Q4W), and 14.3% (placebo) across the 16-week treatment period, and 10.5% (300 mg Q2W), 14.5% (150 mg Q2W), 25.0% (300 mg Q4W), and 16.1% (placebo) across the study.

Reductions in EASI scores at week 16

In the FAS, when analyzed by LOCF, all 3 rademikibart dose regimens met the primary end point. Least-squares (LS) mean percent reductions in EASI scores were significantly greater with 300 mg Q2W (−63.0%; $P = .0007$), 150 mg Q2W (−57.6%; $P = .0067$), and 300 mg Q4W (−63.5%; $P = .0004$) versus placebo (−39.7%) at week 16 (Figs 1 and 2; see Table E4 in this article's Online Repository at www.jacionline.org). EASI responses at week 16 were similar with 300 mg Q2W and Q4W, and numerically greater than with 150 mg Q2W. As expected, given the nonnormally distributed baseline EASI scores (Table I), median EASI percent reductions (300 mg Q2W, −79.3%; 150 mg Q2W, −64.7%; 300 mg Q4W, −70.0%) were numerically greater than LS mean percent reductions, with a similar median placebo response (−41.0%) to the LS mean at week 16 (Fig 1).

Across the sensitivity analyses in the FAS, and also in the PPS, the pattern of the EASI results was similar to that in the FAS LOCF findings (see Table E5 in this article's Online Repository at www.jacionline.org). In the PPS, LS mean percent reductions at week 16 were as follows: 300 mg Q2W (−67.9%; $P = .0123$), 150 mg Q2W (−63.5%; $P = .0553$), 300 mg Q4W (−72.2%; $P = .0015$) versus placebo (−50.2%).

In an *a priori* analysis, with the LOCF methodology, the China subgroup experienced reductions in EASI scores at week 16 that were numerically greater in the rademikibart arms and less in the placebo arm than in the overall population (Fig 1; Table E4). In the China subgroup, LS mean percent reductions at week 16 were as follows: 300 mg Q2W (−81.9%; $P = .0566$), 150 mg Q2W (−59.3%; $P = .1857$), 300 mg Q4W (−75.1%; $P = .0445$) versus placebo (−33.9%).

Rapid reductions in EASI scores, without plateauing by week 16

LS mean percent reductions in EASI scores occurred early, were significant with rademikibart versus placebo, and did not plateau throughout the 16-week treatment period (Fig 2). Across the 3 rademikibart dose regimens, LS mean EASI score reductions ranged from −21.0% to −27.5% at week 2 and from −35.8% to −44.1% at week 4.

Improvements in other efficacy outcomes

Rapid and sustained significant improvements were also observed across a range of other investigator-assessed and patient-reported measures of AD and quality of life (QoL). Rademikibart was associated with greater proportions of vIGA-AD 0/1 and EASI-50/75/90 responders, and greater reductions in PP-NRS, SCORAD, BSA, POEM, and DLQI scores during the 16-week treatment period, than placebo (Figs 3 and 4 and Table

TABLE I. Patient demographic and disease characteristics at baseline in the overall population

Characteristics*	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	All rademikibart (N = 170)	Placebo (N = 56)	Total (N = 226)
Age (y)	38.0 (19, 70)	35.0 (19, 73)	43.0 (18, 73)	38.5 (18, 73)	40.0 (18, 67)	38.5 (18, 73)
Sex: female, n (%)	27 (47)	30 (53)	28 (50)	85 (50)	36 (64)	121 (54)
Race, n (%)†						
White	38 (67)	30 (53)	32 (57)	100 (59)	32 (57)	132 (58)
Asian	9 (16)	17 (30)	12 (21)	38 (22)	14 (25)	52 (23)
Black/African American	7 (12)	8 (14)	10 (18)	25 (15)	6 (11)	31 (14)
Not Hispanic/Latino, n (%)	33 (58)	40 (70)	29 (52)	102 (60)	32 (57)	134 (59)
Country, n (%)						
United States	47 (82)	40 (70)	41 (73)	128 (75)	44 (79)	172 (76)
China	6 (11)	11 (19)	9 (16)	26 (15)	6 (11)	32 (14)
New Zealand	3 (5)	5 (9)	5 (9)	13 (8)	6 (11)	19 (8)
Australia	1 (2)	1 (2)	1 (2)	3 (2)	0	3 (1)
BMI (kg/m^2)	29.10 (20.0, 57.8)	26.90 (17.6, 57.5)	29.75 (18.3, 66.4)	28.50 (17.6, 66.4)	28.05 (14.8, 57.2)	28.40 (14.8, 66.4)
AD duration (y)	10.5 (1, 53)	11.0 (1, 56)	14.0 (1, 58)	13.0 (1, 58)	13.5 (2, 51)	13.0 (1, 58)
vIGA-AD, n (%)						
3 (moderate)	34 (60)	43 (75)	40 (71)	117 (69)	39 (70)	156 (69)
4 (severe)	23 (40)	14 (25)	16 (29)	53 (31)	17 (30)	70 (31)
EASI score	20.75 (16.0, 53.8)	21.20 (16.0, 68.4)	20.10 (16.0, 48.5)	20.88 (16.0, 68.4)	22.10 (16.3, 55.2)	21.15 (16.0, 68.4)
EASI score, mean ± SD	27.57 ± 11.8	24.61 ± 10.5	23.08 ± 8.2	25.10 ± 10.4	25.16 ± 9.0	25.11 ± 10.0
% BSA involvement	37.00 (14.9, 85.0)	36.10 (12.0, 94.0)	32.50 (11.0, 89.5)	35.40 (11.0, 94.0)	35.10 (11.5, 87.0)	35.10 (11.0, 94.0)

BMI, Body mass index.
*Median values (min, max) unless otherwise stated.
†Eleven patients, not shown under "Race" in the table, were Native Hawaiian/Pacific Islander (n = 3), Native American/Alaskan (n = 1), multiple (n = 3), or other (n = 4); 4 in the placebo arm, ≤3 per rademikibart dose arm.

E4; see also Fig E3 in this article's Online Repository at www.jacionline.org). These responses were generally similar in magnitude with rademikibart 300-mg Q2W and Q4W dosing and numerically greater than with 150-mg Q2W dosing. After receiving the final dose of rademikibart or placebo at week 16, the key efficacy responses of vIGA-AD 0/1 and EASI-75 were sustained for most patients until final assessment at week 24 (see Table E6 in this article's Online Repository at www.jacionline.org).

Safety

There were no remarkable findings regarding vital signs, physical examinations, laboratory parameters, and electrocardiograms. Rademikibart and placebo had similar incidences of patients with treatment-emergent adverse events (TEAEs; 48.2% vs 53.6%), serious TEAEs (1.8% vs 3.6%), and TEAEs leading to discontinuation of study treatment (1.2% vs 1.8%; Table II; see also Tables E7 and E8 in this article's Online Repository at www.jacionline.org). Most TEAEs (≥94.4%) were mild or moderate in each treatment group. One patient in the 300-mg Q4W arm died from cardiac arrest that was deemed by the investigator to be unrelated to study treatment because it occurred 56 days after the last dose. No serious TEAEs or TEAEs leading to discontinuation of study treatment were related to study treatment. Rademikibart versus placebo had low rates of herpes (0.6% vs 1.8%), conjunctivitis of unspecified cause (2.9% vs 0%), allergic conjunctivitis (0.6% vs 0%), headache (5.3% vs 0%), and injection-site reactions (1.8% vs 1.8%).

DISCUSSION

In the WW001 phase 2 trial, clinical outcomes were significantly improved for all 3 dose regimens of rademikibart, meeting the primary and key secondary efficacy end points to week 16. Rapid and sustained improvements were observed in skin lesions (measured objectively with EASI, SCORAD, vIGA-AD, and BSA), in pruritus (PP-NRS), and in overall AD symptoms and QoL aspects such as sleeplessness (measured by POEM and/or DLQI). EASI responses did not plateau by week 16. Rademikibart was also associated with low incidence of herpes, conjunctivitis, injection-site reactions, and headache, relative to placebo. There was no evidence of an increase in susceptibility to COVID-19 infection with rademikibart versus placebo. Efficacy responses were generally comparable with 300-mg Q2W and Q4W dosing, possibly related to the high binding affinity for IL-4Rα,[39] thus supporting the use of rademikibart at convenient 2- and 4-week dosing intervals for adults with moderate to severe AD.

Indirect comparisons of AD clinical trial outcomes may be hampered by significant variation in factors such as the populations recruited and aspects of study design.[41] In the WW001 trial, the efficacy results may have been negatively affected by the patients' baseline characteristics. In particular, only one-third of patients in the WW001 trial had severe AD at baseline, compared with approximately half the patients in the phase 2 and 3 trials of the currently approved anti–IL-4Rα, dupilumab.[23-27] A recent mini review article demonstrated that baseline mean EASI scores have decreased across AD clinical trials conducted during the last decade.[42] As discussed in detail in the mini review, this may be related to approval of AD medications; in the present study, no previous treatment with anti–IL-4Rα/IL-13 agents was allowed, perhaps resulting in a trial population with more moderate disease. Relationships between baseline AD severity and EASI responses were observed in the recent mini review and also in a dupilumab phase 3 study and meta-analysis of 64 randomized controlled trials; in each instance, less severe patients experienced greater EASI responses in placebo arms than more severe patients, and the dupilumab analysis suggested that

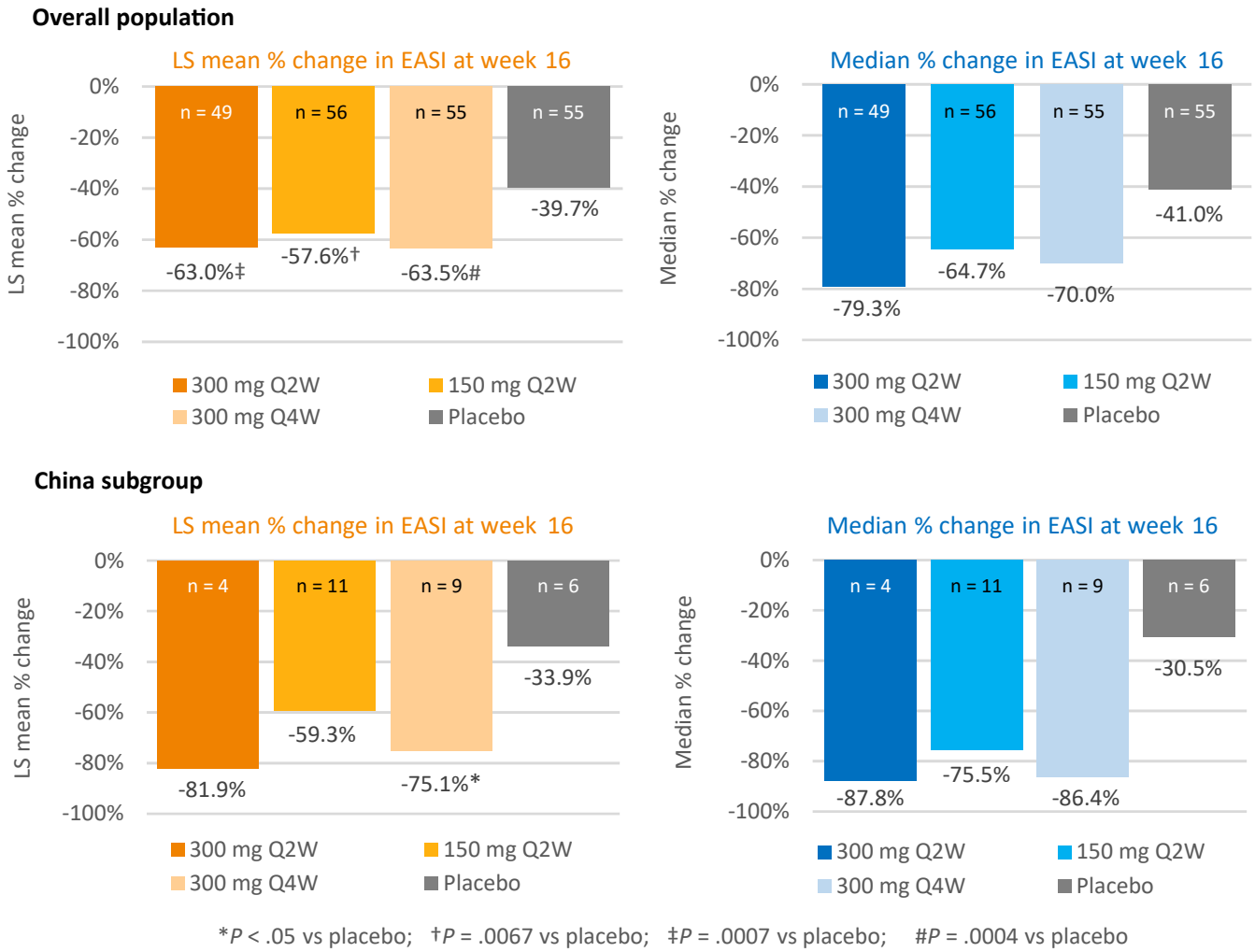

FIG 1. LS mean % change and median % change in EASI score at week 16 in the overall population and China subgroup, and LS mean % change in EASI score across 16 weeks in the overall population (FAS; LOCF analysis). No statistical comparisons of median % change in EASI score were planned or conducted.

baseline AD severity may not have an impact on responses to the same extent in placebo and active treatment arms.[42-44] Notably, the magnitudes of clinical responses were often greater and less in the rademikibart and placebo arms, respectively, of the WW001 China subgroup versus the overall population. Although we cannot discount the possibilities that increased responses in the rademikibart arms in China were related to lower body mass and an element of chance in this small subgroup (n = 32), baseline disease severity also tended to be greater than in the overall population. Baseline AD severity and the magnitude of clinical responses in the WW001 China subgroup resemble those in other Chinese populations, including an ongoing pivotal trial of rademikibart (NCT05017480) and a phase 3 trial of 300-mg Q2W dupilumab.[27]

In addition to baseline AD severity, the efficacy results of the WW001 trial may have been influenced by a lower incidence of comorbid allergic diseases and less rescue medication use than in AD trials of other medications and conduct of the WW001 trial during the COVID-19 pandemic. A low incidence of allergic comorbidities (eg, 4.4% of patients reported history of food allergy, compared with 29.1% in the phase 3 dupilumab trial in China[27]) indicates less T_H2-type disease in the WW001 trial. Patients with rescue medication use by week 16 in the WW001 phase 2 trial, imputed as nonresponders, ranged from 5.3% to 16.1% across the active arms; this was lower than in the phase 3 dupilumab trial (15.0%-23.3%) and substantially lower than in the phase 3 tralokinumab (22.8%-35.8%) and baricitinib (32.9%-68.0%) trials.[24,26,27,29,30,45,46] The WW001 trial was also likely to have been affected by movement restrictions during the COVID-19 pandemic, with patients choosing not to be exposed to social situations, possibly contributing to higher discontinuation rates by week 16 (13%-29% per treatment arm) relative to the dupilumab phase 2 (3%-18%)[23] and phase 3 (6%-19%) trials.[24,26,27] Although no discontinuations were attributed directly to COVID-19 infection in the WW001 trial, most patients who discontinued (71%) were either lost to follow-up or withdrew consent. As well as limiting the patients' ability to attend clinic visits, movement restrictions during the pandemic may have influenced behavior (eg, more self-moisturizing) and disease (eg, less exposure to external irritants). Other notable design aspects of the WW001 trial versus trials of dupilumab include a shorter (≥1 year) history of AD, longer screening (45 days; potentially influencing AD severity and rescue medication use), and differences in participating countries,[23-27] although it

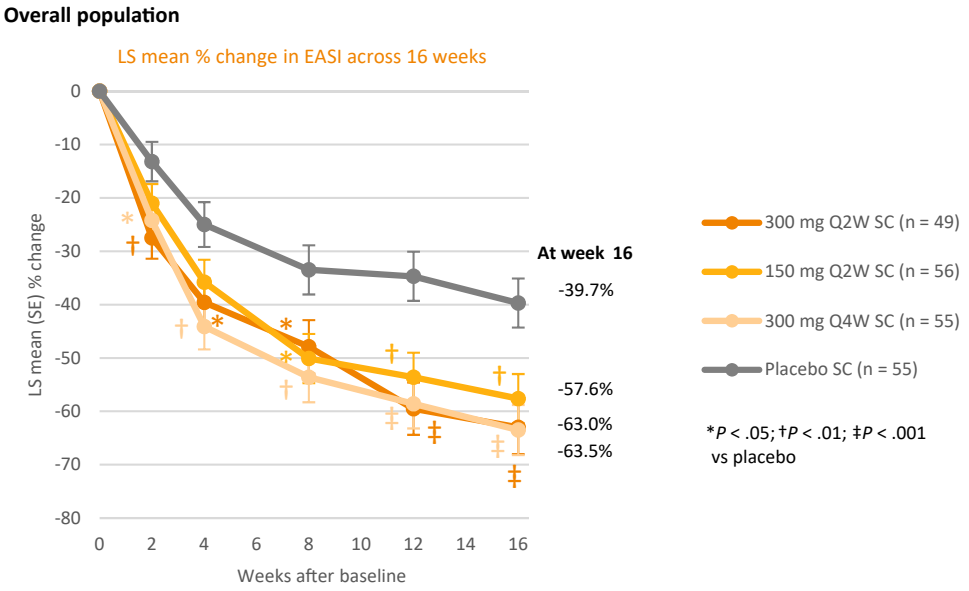

FIG 2. LS mean % change in EASI score across 16 weeks in the overall population (FAS; LOCF analysis). The % change in EASI score from baseline to week 16 was the prespecified primary end point (changes at earlier time points were not prespecified end points).

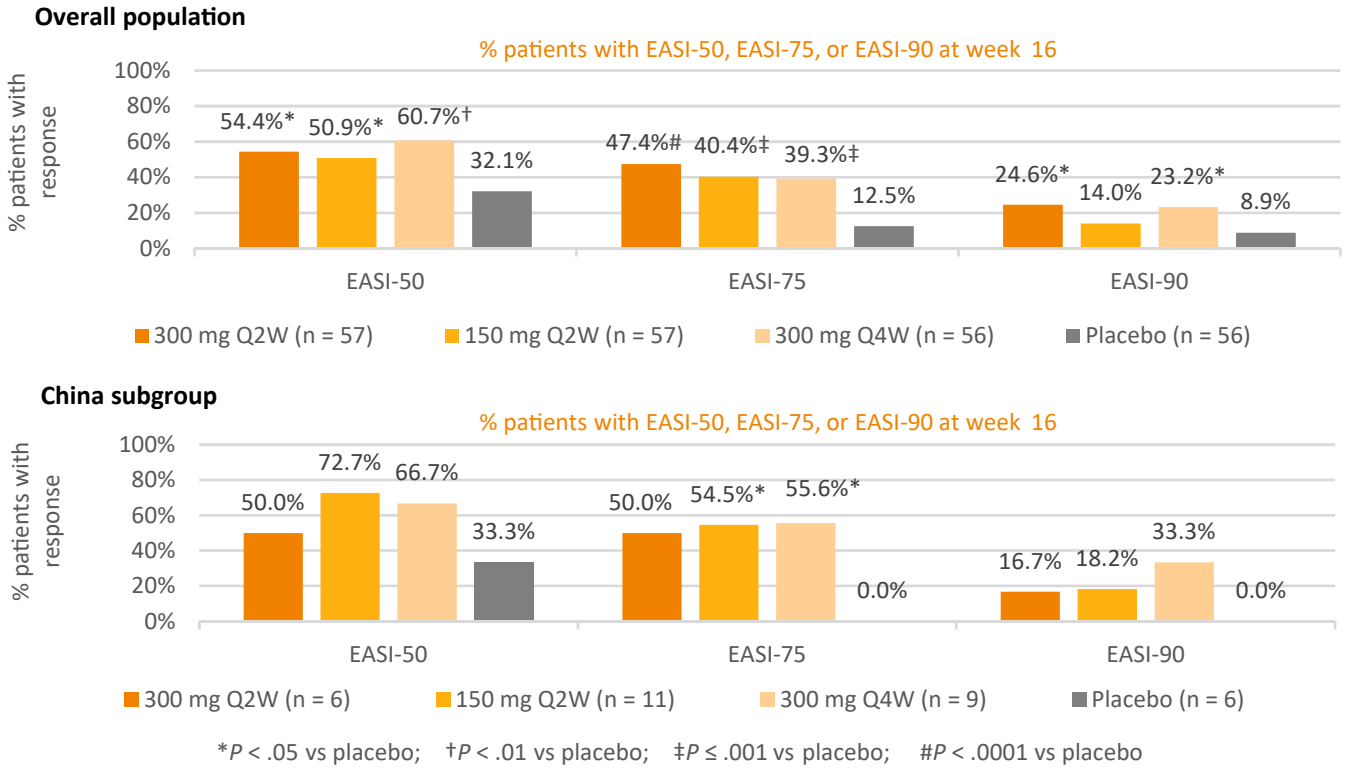

FIG 3. EASI-50/75/90 responder rates at week 16 in the overall population and China subgroup (FAS; NRI analysis). *NRI,* Nonresponder imputation.

is uncertain whether the efficacy outcomes of biologic treatments for AD are likely to vary by race or geography.[47]

The safety profile of rademikibart was similar to placebo, except for a low incidence of conjunctivitis (consistent with studies of other biologics)[22-30] and headache (consistent with dupilumab trials),[23-26,48,49] with no new safety signals. Most TEAEs were mild or moderate in severity, and no patients experienced treatment-related TEAEs leading to discontinuation of study treatment or treatment-related serious TEAEs. The incidence of injection-site reactions in the rademikibart arms (1.8%) was comparable with placebo (1.8%), whereas higher incidence rates have been reported for other biologics versus placebo, including dupilumab in phase 2 (6.9% vs 3.3%) and phase 3 (14.5% vs 7.2%) trials.[23-27]

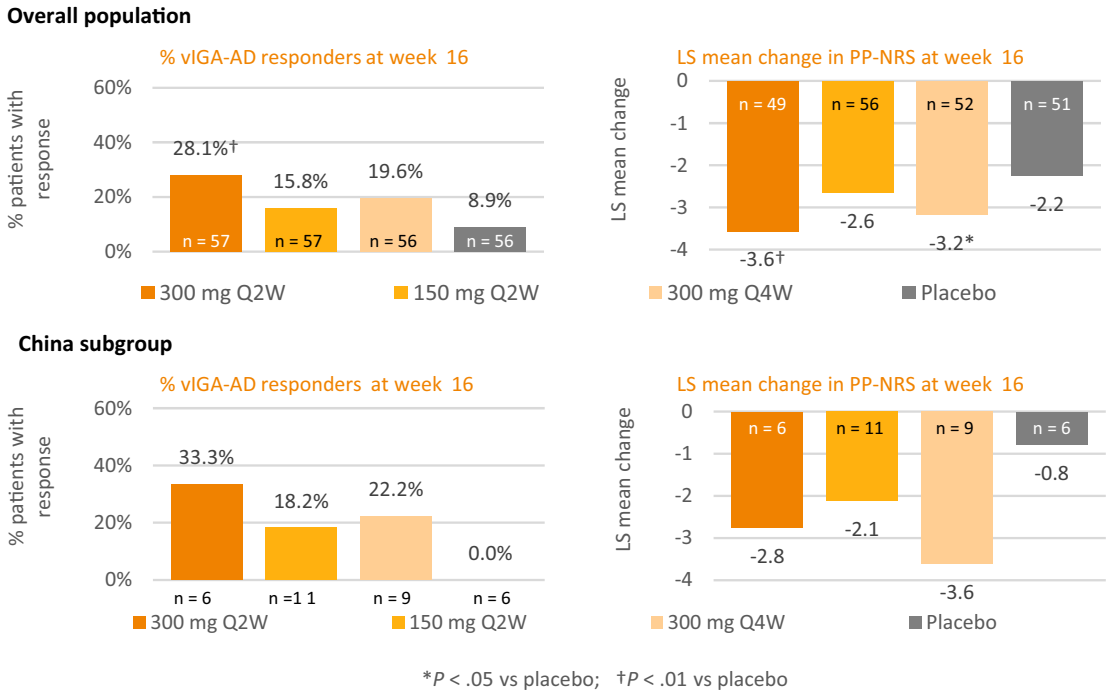

FIG 4. vIGA-AD responder rates (FAS; NRI analysis) and LS mean change in PP-NRS (FAS; LOCF analysis) at week 16 in the overall population and China subgroup. IGA response defined as IGA score of 0 (clear) or 1 (almost clear) and a greater than or equal to 2-point reduction from baseline. *NRI*, Nonresponder imputation.

TABLE II. Summary of TEAEs in the overall population (FAS)

Patients, n (%)	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	All rademikibart (N = 170)	Placebo (N = 56)
Any TEAE	26 (45.6)	24 (42.1)	32 (57.1)	82 (48.2)	30 (53.6)
Serious TEAE	0	1 (1.8)	2 (3.6)	3 (1.8)	2 (3.6)
Grade ≥3 TEAE*	1 (1.8)	1 (1.8)	4 (7.1)	6 (3.5)	1 (1.8)
Discontinuation of study treatment because of TEAE	0	1 (1.8)	1 (1.8)	2 (1.2)	1 (1.8)
COVID-19 infection	2 (3.5)	4 (7.0)	1 (1.8)	7 (4.1)	4 (7.1)
Conjunctivitis of unspecified cause†	2 (3.5)	2 (3.5)	1 (1.8)	5 (2.9)	0
Conjunctivitis allergic†	0	0	1 (1.8)	1 (0.6)	0
Injection-site reaction†	1 (1.8)	1 (1.8)	1 (1.8)	3 (1.8)	1 (1.8)
Oral herpes	0	0	0	0	1 (1.8)
Ophthalmic herpes simplex	0	0	1 (1.8)	1 (0.6)	0

*All grade 3 (severe), except for 1 patient in the 300-mg Q4W arm, who died from cardiac arrest that was deemed by the investigator to be unrelated to study treatment because it occurred 56 d after the last dose.
†All mild except for 2 patients with moderate conjunctivitis, 1 in the 300-mg Q2W group and 1 in the 300-mg Q4W group.

The WW001 trial had several strengths and limitations. Only adults were included (no data were collected in a pediatric population) and, as in phase 2 studies of other biologics,[23,25,28,30] long-term efficacy was not investigated. The China subgroup analyses, conducted on the basis of local regulatory authority requirements, were not powered to definitively determine statistical differences between the placebo and rademikibart treatment arms.

In summary, the WW001 phase 2 trial achieved its primary and key secondary efficacy end points to week 16, and rademikibart was well tolerated, with low incidence of injection-site reactions, herpes, and conjunctivitis across all 3 dose regimens. Rapid and sustained improvements were observed in AD extent and severity, on the basis of several rating scales including EASI, accompanied by better QoL. EASI responses did not plateau by week 16. Efficacy responses were generally comparable with 300-mg Q2W and Q4W dosing. The findings of the WW001 trial support further investigation of rademikibart 300 mg in moderate to severe AD in phase 3 trials, at Q2W and Q4W dosing frequencies, and beyond 16 weeks to determine whether additional efficacy can be achieved with a longer duration of treatment.

DISCLOSURE STATEMENT

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Kiniksa Pharmaceuticals, Leo Pharma, Luna, Menlo Therapeutics, Novartis, Pfizer, RAPT, Regeneron Pharmaceuticals, and Sanofi; and is a researcher for Galderma. B. Strober has received honoraria for serving as a consultant, advisory board member, and/or speaker for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Connect Biopharma, Dermavant, Dermira, Janssen, Eli Lilly, Leo Pharma, Medac, Meiji Seika Pharma, Sebela Pharmaceuticals, Menlo Therapeutics, Novartis, Pfizer, GlaxoSmithKline, UCB, Sirtris, Sun Pharma, Ortho Dermatologics/Valeant, Regeneron Pharmaceuticals, and Sanofi-Genzyme. B. Feinstein and J. Xu have acted as investigators for Connect Biopharma. E. Guttman-Yassky is an employee of Mount Sinai Medical Center; has received research funds paid to the institution from AbbVie, Almirall, Amgen, AnaptysBio, Asana BioSciences, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Celgene, Dermira, Eli Lilly, Galderma, Glenmark/Ichnos Sciences, Innovaderm Research, Janssen, Kao, Kiniksa Pharmaceuticals, Kyowa Kirin, Leo Pharma, Novan, Novartis, Pfizer, Ralexar Therapeutics, Regeneron Pharmaceuticals, Sanofi, and UCB; is an investigator for AbbVie, Bristol-Myers Squibb, Eli Lilly, Galderma, Glenmark, GlaxoSmithKline, Leo Pharma, Pfizer, Regeneron Pharmaceuticals, and Sanofi; and is a consultant for AbbVie, Almirall, Amgen, Anacor Pharmaceuticals, Arena Pharmaceuticals, Asana BioSciences, Aslan Pharmaceuticals, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Celgene, Connect Biopharma, Daiichi Sankyo, DBV Technologies, Dermira, Eli Lilly, EMD Serono, Evidera, Galderma, Glenmark, GlaxoSmithKline, Ichnos Sciences, Incyte, Janssen Biotech, Kiniksa Pharmaceuticals, Kyowa Kirin, Leo Pharma, Menlo Therapeutics, Novartis, Pandion Therapeutics, Pfizer, RAPT Therapeutics, Realm Therapeutics, Regeneron Pharmaceuticals, Sanofi, Sato Pharmaceutical, Siolta Therapeutics, Target Pharma, UCB, and Ventyx Biosciences. E. Simpson reported personal fees from AbbVie, Amgen, Arena Pharmaceuticals, ASLAN, Benevolent AI Bio Ltd, BiomX Ltd, Bluefin Biomedicine, Boehringer Ingelheim, Boston Consulting Group, Collective Acumen, LLC (CA), Connect Biopharma, Coronado, Dermira, Eli Lilly, Evidera, ExcerptaMedica, Galderma, GlaxoSmithKline, Forte Bio RX, Incyte Dermatologics, Janssen, Kyowa Kirin Pharmaceutical Development, Leo Pharma, Medscape LLC, Merck, Novartis, Ortho Galderma, Pfizer, Physicians World LLC, Pierre Fabre Dermo Cosmetique, Regeneron Pharmaceuticals, Roivant, Sanofi-Genzyme, SPARC India, Trevi Therapeutics, WebMD, and Valeant; received grants from AbbVie, Amgen, Arcutis, ASLAN, Castle Biosciences, Celegene, CorEvitas, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Kymab, Kyowa Hakko Kirin, Leo Pharma, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi, and TARGET-DERM, outside the submitted work. P. Li, M. Longphre, J. Song, J. Guo, J. Yun, B. Williams, W. Pan, S. Ho, R. Collazo, and Z. Wei are either current or former employees or shareholders of Connect Biopharma. S. Ho is now an employee of Medigene AG.

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Clinical implications: This phase 2 trial supports the use of the IL-4Rα antagonist rademikibart (CBP-201), a convenient and efficacious option at 2- and 4-week dosing regimens, for adults with moderate to severe AD.

REFERENCES

1. Eichenfield LF, Tom WL, Chamlin SL, Feldman SR, Hanifin JM, Simpson EL, et al. Guidelines of care for the management of atopic dermatitis. J Am Acad Dermatol 2014;70:338-51.
2. Chovatiya R, Silverberg JI. Pathophysiology of atopic dermatitis and psoriasis: implications for management in children. Children (Basel) 2019;6:108.
3. Mathiesen SM, Thomsen SF. The prevalence of atopic dermatitis in adults: systematic review on population studies. Dermatol Online J 2019;25:13030.
4. Boguniewicz M, Alexis AF, Beck LA, Block J, Eichenfield LF, Fonacier L, et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: a multidisciplinary consensus addressing current and emerging therapies. J Allergy Clin Immunol Pract 2017;5:1519-31.
5. Chiesa Fuxench ZC, Block JK, Boguniewicz M, Boyle J, Fonacier L, Gelfand JM, et al. Atopic dermatitis in America Study: a cross-sectional study examining the prevalence and disease burden of atopic dermatitis in the US adult population. J Invest Dermatol 2019;139:583-90.
6. Dalgard FJ, Gieler U, Tomas-Aragones L, Lien L, Poot F, Jemec GBE, et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatological out-patients in 13 European countries. J Invest Dermatol 2015;135:984-91.
7. Schonmann Y, Mansfield KE, Hayes JF, Abuabara K, Roberts A, Smeeth L, et al. Atopic eczema in adulthood and risk of depression and anxiety: a population-based cohort study. J Allergy Clin Immunol Pract 2020;8:248-57.e16.
8. Silverberg JI, Gelfand JM, Margolis DJ, Boguniewicz M, Fonacier L, Grayson MH, et al. Symptoms and diagnosis of anxiety and depression in atopic dermatitis in U.S. adults. Br J Dermatol 2019;181:554-65.
9. Xie QW, Dai X, Tang X, Chan CHY, Chan CLW. Risk of mental disorders in children and adolescents with atopic dermatitis: a systematic review and meta-analysis. Front Psychol 2019;10:1773.
10. Freitas E, Gooderham M, Torres T. New topical therapies in development for atopic dermatitis. Drugs 2022;82:843-53.
11. Simpson EL, Bruin-Weller M, Flohr C, Ardern-Jones MR, Barbarot S, Deleuran M, et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. J Am Acad Dermatol 2017;77:623-33.
12. Borlu M, Guler E. Current concept in the treatment of atopic dermatitis. Recent Pat Inflamm Allergy Drug Discov 2007;1:133-41.
13. Butala S, Paller AS. Optimizing topical management of atopic dermatitis. Ann Allergy Asthma Immunol 2022;128:488-504.
14. Mayba JN, Gooderham MJ. Review of atopic dermatitis and topical therapies. J Cutan Med Surg 2017;21:227-36.
15. Kritsanaviparkporn C, Sangaphunchai P, Treesirichod A. Efficacy of moisturizers in paediatric atopic dermatitis: a systematic review and meta-analysis of randomised controlled trials. Indian J Dermatol Venereol Leprol 2021;88:22-31.
16. Miyano K, Tsunemi Y. Current treatments for atopic dermatitis in Japan. J Dermatol 2021;48:140-51.
17. Patel NU, D'Ambra V, Feldman SR. Increasing adherence with topical agents for atopic dermatitis. Am J Clin Dermatol 2017;18:323-32.
18. Fleischmann R. Recent issues in JAK inhibitor safety: perspective for the clinician. Expert Rev Clin Immunol 2022;18:295-307.
19. Svoboda SA, Johnson N, Phillips M. Dermatologic applications and safety considerations of Janus kinase inhibitors. Skin Ther Lett 2020;25:6-11.
20. Wood H, Chandler A, Nezamololama N, Papp K, Gooderham MJ. Safety of Janus kinase (JAK) inhibitors in the short-term treatment of atopic dermatitis. Int J Dermatol 2022;61:746-54.
21. Singh R, Heron CE, Ghamrawi RI, Strowd LC, Feldman SR. Emerging role of Janus kinase inhibitors for the treatment of atopic dermatitis. ImmunoTargets Ther 2020;9:255-72.
22. Akinlade B, Guttman-Yassky E, Bruin-Weller M, Simpson EL, Blauvelt A, Cork MJ, et al. Conjunctivitis in dupilumab clinical trials. Br J Dermatol 2019;181:459-73.
23. Thaçi D, Simpson EL, Beck LA, Bieber T, Blauvelt A, Papp K, et al. Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomised, placebo-controlled, dose-ranging phase 2b trial. Lancet 2016;387:40-52.
24. Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. N Engl J Med 2016;375:2335-48.
25. Tofte SJ, Papp K, Sadick N, Bohnert K, Simpson E, Thaçi D, et al. Efficacy and safety of dupilumab for the treatment of moderate-to-severe atopic dermatitis in adults: a pooled analysis of two phase 2 clinical trials. J Am Assoc Nurse Pract 2018;30:529-41.
26. Thaçi D, Simpson EL, Deleuran M, Kataoka Y, Chen Z, Gadkari A, et al. Efficacy and safety of dupilumab monotherapy in adults with moderate-to-severe atopic dermatitis: a pooled analysis of two phase 3 randomized trials (LIBERTY AD SOLO 1 and LIBERTY AD SOLO 2). J Dermatol Sci 2019;94:266-75.

27. Zhao Y, Wu L, Lu Q, Gao X, Zhu X, Yao X, et al. The efficacy and safety of dupilumab in Chinese patients with moderate-to-severe atopic dermatitis: a randomized, double-blind, placebo-controlled study. Br J Dermatol 2022;186:633-41.
28. Wollenberg A, Howell MD, Guttman-Yassky E, Silverberg JI, Kell C, Ranade K, et al. Treatment of atopic dermatitis with tralokinumab, an anti–IL-13 mAb. J Allergy Clin Immunol 2019;143:135-41.
29. Wollenberg A, Blauvelt A, Guttman-Yassky E, Worm M, Lynde C, Lacour J-P, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol 2021;184:437-49.
30. Guttman-Yassky E, Blauvelt A, Eichenfield LF, Paller AS, Armstrong AW, Drew J, et al. Efficacy and safety of lebrikizumab, a high-affinity interleukin 13 inhibitor, in adults with moderate to severe atopic dermatitis: a phase 2b randomized clinical trial. JAMA Dermatol 2020;156:411.
31. Werfel T, Layton G, Yeadon M, Whitlock L, Osterloh I, Jimenez P, et al. Efficacy and safety of the histamine H4 receptor antagonist ZPL-3893787 in patients with atopic dermatitis. J Allergy Clin Immunol 2019;143:1830-7.e4.
32. Yamamura K, Nakahara T. The dawn of a new era in atopic dermatitis treatment. J Clin Med 2022;11:6145.
33. Elmariah SB, Smith JS, Merola JF. JAK in the [black] box: a dermatology perspective on systemic JAK inhibitor safety. Am J Clin Dermatol 2022;23:427-31.
34. Tofacitinib FDA label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/203214s028,208246s013,213082s003lbl.pdf. Accessed December 16, 2022.
35. Dupilumab FDA label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s046lbl.pdf. Accessed October 12, 2022.
36. Tralokinumab EMA summary of product characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/adtralza-epar-product-information_en.pdf. Accessed December 16, 2022.
37. Tralokinumab FDA label. Available at: https://www.accessdata.fda.gov/spl/data/b8446805-b24c-4d26-97e0-44a8518e3404/b8446805-b24c-4d26-97e0-44a8518e3404.xml#S2.2. Accessed December 20, 2022.
38. Worm M, Simpson EL, Thaçi D, Bissonnette R, Lacour JP, Beissert S, et al. Efficacy and safety of multiple dupilumab dose regimens after initial successful treatment in patients with atopic dermatitis: a randomized clinical trial. JAMA Dermatol 2020;156:131.
39. Zhang L, Ding Y, Wang Q, Pan W, Wei Z, Smith PA, et al. Preclinical immunological characterization of rademikibart (CBP-201), a next-generation human monoclonal antibody targeting IL-4Rα, for the treatment of Th2 inflammatory diseases. Sci Rep 2023;13:12411.
40. Wang J, White J, Sansone KJ, Spelman L, Sinclair R, Yang X, et al. Rademikibart (CBP-201), a next-generation monoclonal antibody targeting human IL-4Rα: results from two phase 1 randomized trials, in healthy individuals and patients with atopic dermatitis. Clin Transl Sci 2023;16:2614-27.
41. Silverberg JI, Simpson EL, Armstrong AW, de Bruin-Weller MS, Irvine AD, Reich K. Expert perspectives on key parameters that impact interpretation of randomized clinical trials in moderate-to-severe atopic dermatitis. Am J Clin Dermatol 2022;23:1-11.
42. Silverberg J, Ho S, Collazo R. A mini review of the impact of baseline disease severity on clinical outcomes: should we compare atopic dermatitis clinical trials? Dermatol Ther (Heidelb) 2023;13:3019-29.
43. Lee HH, Patel KR, Rastogi S, Singam V, Vakharia PP, Chopra R, et al. Placebo responses in randomized controlled trials for systemic therapy in atopic dermatitis: a systematic review and meta-analysis. J Am Acad Dermatol 2020;82:62-71.
44. Offidani A, Stingeni L, Neri I, Cipriani F, Chen Z, Rossi AB, et al. Dupilumab treatment induced similar improvements in signs, symptoms, and quality of life in adults with moderate-to-severe atopic dermatitis with baseline Eczema Area and Severity Index score <24 or ≥24. Ital J Dermatol Venereol 2022;157:39-46.
45. Simpson EL, Forman S, Silverberg JI, Zirwas M, Maverakis E, Han G, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis: results from a randomized monotherapy phase 3 trial in the United States and Canada (BREEZE-AD5). J Am Acad Dermatol 2021;85:62-70.
46. Simpson EL, Lacour J-P, Spelman L, Galimberti R, Eichenfield LF, Bissonnette R, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: results from two randomized monotherapy phase III trials. Br J Dermatol 2020;183:242-55.
47. Alexis AF, Rendon M, Silverberg JI, Pariser DM, Lockshin B, Griffiths CEM, et al. Efficacy of dupilumab in different racial subgroups of adults with moderate-to-severe atopic dermatitis in three randomized, placebo-controlled phase 3 trials. J Drugs Dermatol 2019;18:804-13.
48. Ou Z, Chen C, Chen A, Yang Y, Zhou W. Adverse events of dupilumab in adults with moderate-to-severe atopic dermatitis: a meta-analysis. Int Immunopharmacol 2018;54:303-10.
49. Wu S, Wang H. Efficacy and safety of dupilumab in the treatment of moderate-to-severe atopic dermatitis: a meta-analysis of randomized controlled trials. Adv Dermatol Allergol 2022;39:601-10.

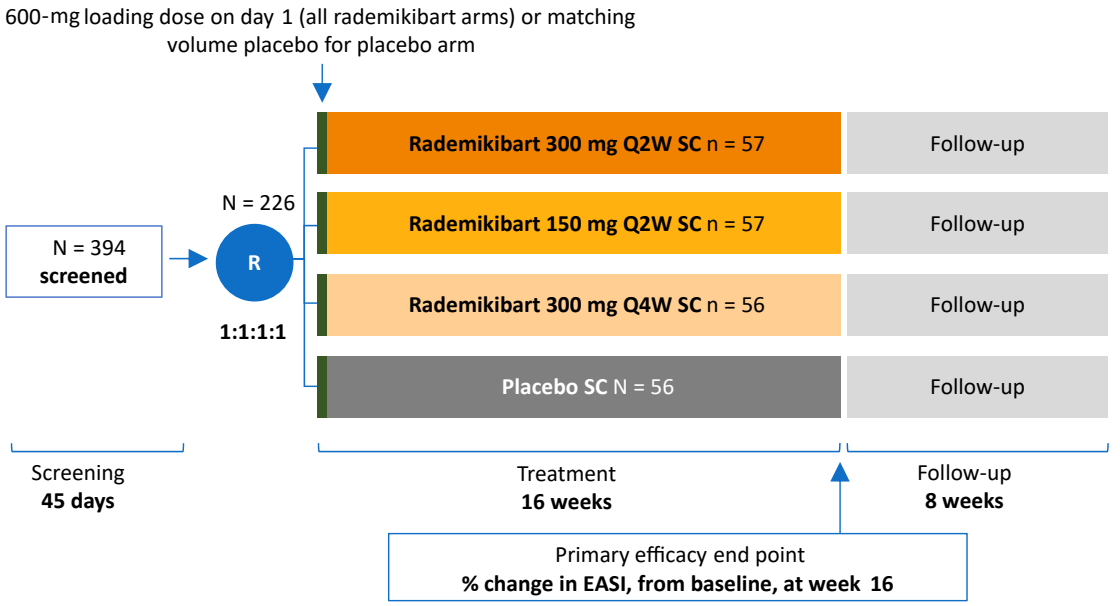

FIG E1. Design of CBP-201-WW001 phase 2 trial. The PP-NRS daily itch diary, which was assessed at weekly visits, commenced at least 7 days before the baseline visit and continued throughout the study. All other efficacy outcomes were assessed during screening, and predose during the treatment period (on day 1 and at weeks 2, 4, 8, 12, and 16). *R*, Randomization.

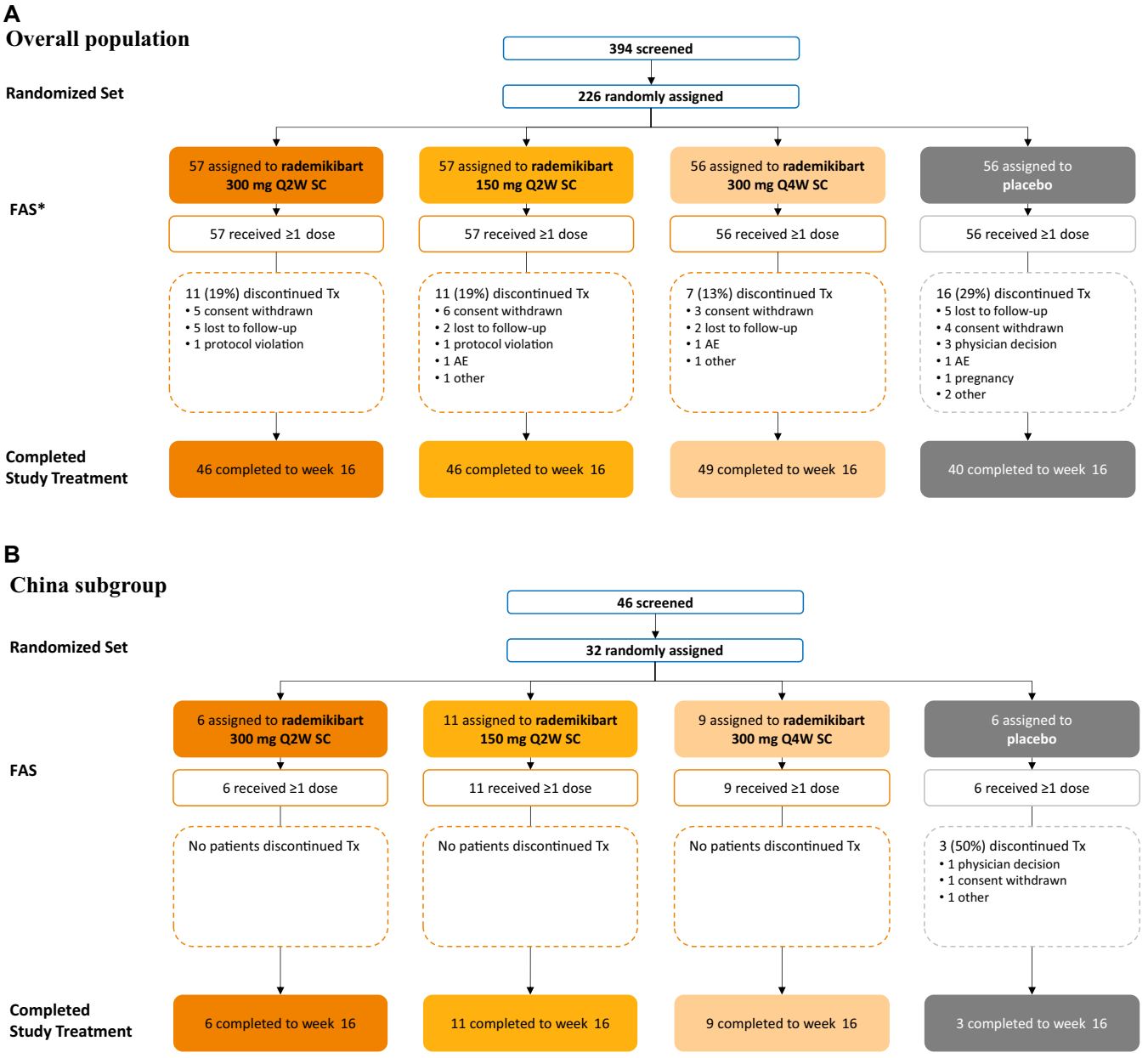

FIG E2. Patient disposition. *AE*, Adverse event; *Tx*, Treatment. *The PPS comprised all patients from the FAS without major protocol deviations (rademikibart 300 mg Q2W, n = 46; rademikibart 150 mg Q2W, n = 46; rademikibart 300 mg Q4W, n = 48; placebo, n = 38).

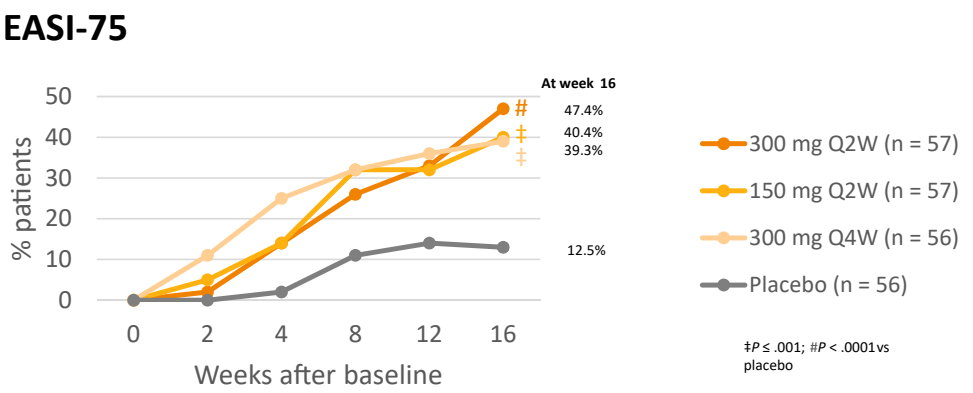

FIG E3. EASI-75 responder rates across 16 weeks in the overall population (FAS; NRI analysis). No statistical comparisons of EASI-75 were planned or conducted at time points before week 16. *NRI,* Nonresponder imputation.

TABLE E1. Inclusion and exclusion criteria

Inclusion criteria

Subjects must meet all of the following criteria to be considered eligible to participate in the study:

1. Be an adult 18 y or older and 75 y or younger at the screening visit (screening) with AD (according to the American Academy of Dermatology Consensus Criteria)
   (a) present for at least 1 y before the baseline visit (baseline) with an inadequate response, in the judgment of the investigator, to AD treatment with a topical regimen of corticosteroids, phosphodiesterase inhibitors, or calcineurin inhibitors, or for whom topical treatments are otherwise medically inadvisable (eg, because of important side effects or safety risks);
   (b) per investigator assessment have the following at screening and baseline for AD involvement: (i) IGA score ≥ 3 (according to the vIGA-AD scale, on the 0-4 vIGA-AD scale, in which 3 is moderate and 4 is severe); (ii) EASI score ≥ 16, and; (iii) BSA for total AD involvement ≥10%
2. Able and willing to apply a stable dose of a bland emollient twice a day to affected areas for at least 7 d before baseline and to continue for the duration of the study
3. Females of child-bearing potential must abstain from heterosexual activities or agree to use effective contraception. Women who are postmenopausal, as documented by measurement of follicle-stimulating hormone, or with documented evidence of surgical sterilization before screening (ie, tubal ligation or hysterectomy) are not considered as females of child-bearing potential. Men who have not undergone a vasectomy must abstain from heterosexual activities or agree to use effective contraception. All participants must be willing to use effective contraception throughout the entire study period if necessary.
   (a) Effective contraception options for participating subjects include (i) abstinence from sexual intercourse; (ii) using a condom, and a diaphragm or cervical cap, as well as use of a spermicidal (where available); (iii) oral contraceptives (the "pill") for at least 1 mo before baseline; and (iv) Depo-Provera or injectable birth control or implantable contraception (eg, Implanon).
4. Able to read and understand, and willing to sign the informed consent form
5. Willing and able to comply with clinic visits and study-related procedures

Exclusion criteria

Subjects will not be eligible to participate in this study if any of the following exclusion criteria is met:

1. Have any of the following laboratory abnormalities at screening:
   (a) Hemoglobin ≤ 90% of the lower limit of normal range (LLN)
   (b) White blood cell below the LLN
   (c) Neutrophil count below the LLN
   (d) Platelet count below the LLN
2. Have undergone treatment with any of the following:
   (a) Topical agents such as corticosteroids, phosphodiesterase inhibitors, Janus kinase inhibitors, tacrolimus or pimecrolimus within 1 wk before baseline. Note that low to medium topical corticosteroids are permitted after randomization to treat AD flares.
   (b) Previous treatment with dupilumab or any antibody against IL-4Rα or IL-13
   (c) Systemic treatment for AD or other condition with steroids or other immunosuppressive/immunomodulating substances (eg, cyclosporine, mycophenolate-mofetil, azathioprine, methotrexate, or oral Janus kinase inhibitors) within 4 wk before baseline. Use of steroid inhalers and nasal corticosteroids is allowed.
   (d) Cell-depleting agents (eg, rituximab) within 6 mo of baseline or treatment with other biologics within 5 half-lives (if known) or 3 mo before baseline visit, whichever is longer
   (e) Phototherapy (narrow-band ultraviolet B, ultraviolet B, ultraviolet A1, and psoralen + ultraviolet A), tanning beds, or any other light-emitting device within 4 wk of baseline)
   (f) ≥2 bleach baths within 2 wk of baseline
   (g) Prescription emollient to treat AD (eg, Atopiclair, MimyX, and Epicerum) within 2 wk of baseline
   (h) Any investigational drug within 30 d or within 5 half-lives, whichever is longer, before baseline
   (i) Live (attenuated) vaccine within 8 wk of baseline
   (j) Treatment with systemic traditional Chinese medicine or herbal medications within 4 wk before baseline visit or treatment with topical traditional Chinese medicine or herbal medications within 1 wk before baseline
3. Have any of the following:
   (a) Infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 4 wk before baseline, or superficial skin infection, such as impetigo, within 2 wk before baseline (subject may be rescreened after infection has resolved)
   (b) A history of parasitic infection (eg, helminth) within 6 mo of baseline
   (c) Per investigator judgment, known or suspected history of immunosuppression within 6 mo of baseline, including a history of invasive opportunistic infections, such as aspergillosis, coccidioidomycosis, histoplasmosis, HIV, listeriosis, pneumocystosis, or tuberculosis, despite infection resolution, or unusually frequent, recurrent, or prolonged infections
   (d) Any history of vernal keratoconjunctivitis and atopic keratoconjunctivitis
   (e) A history of malignancy with the following exceptions: completely treated carcinoma *in situ* of cervix or nonmetastatic squamous or basal cell carcinoma of the skin
   (f) Positive results at screening for hepatitis B surface antigen, hepatitis B core antibody, or hepatitis C antibody with positive hepatitis B virus RNA PCR; positive HIV serology at screening
   (g) An allergy to L-histidine, trehalose, or Tween (polysorbate) 80
   (h) Plans to undergo a major surgical procedure during the study
   (i) Alcohol or drug abuse within 2 y before screening
   (j) Any medical or psychiatric condition, laboratory parameters, or electrocardiograms which, in the opinion of the investigator or the sponsor's medical monitor, would place the subject at risk, interfere with participation in the study, or interfere with the interpretation of study results
4. Women must not be pregnant, planning to become pregnant, or breastfeed during the study

TABLE E2. Patient demographic and disease characteristics at baseline in the China subgroup (FAS)

Characteristics*	300 mg Q2W (n = 6)	150 mg Q2W (n = 11)	300 mg Q4W (n = 9)	All rademikibart (N = 26)	Placebo (N = 6)	Total (N = 32)
Age (y)	30.5 (23, 70)	28.0 (21, 41)	31.0 (23, 59)	28.5 (21, 70)	28.0 (24, 66)	28.0 (21, 70)
Sex: female, n (%)	1 (17)	2 (18)	4 (44)	7 (27)	3 (50)	10 (31)
Asian, n (%)	6 (100)	11 (100)	9 (100)	26 (100)	6 (100)	32 (100)
BMI (kg/m^2)	25.25 (23.6, 31.5)	25.00 (20.7, 44.3)	26.60 (18.3, 31.0)	25.65 (18.3, 44.3)	25.55 (20.0, 29.5)	25.55 (18.3, 44.3)
AD duration (y)	6.0 (1, 11)	3.0 (2, 21)	10.0 (1, 15)	4.5 (1, 21)	5.5 (2, 23)	4.5 (1, 23)
vIGA-AD, n (%)						
3 (moderate)	4 (67)	7 (64)	6 (67)	17 (65)	3 (50)	20 (63)
4 (severe)	2 (33)	4 (36)	3 (33)	9 (35)	3 (50)	12 (38)
EASI score	26.60 (16.5, 38.5)	26.60 (16.0, 54.0)	25.90 (16.3, 45.5)	26.35 (16.0, 54.0)	32.90 (17.2, 55.2)	26.90 (16.0, 55.2)
EASI score, mean ± SD	26.73 ± 9.6	26.73 ± 10.6	26.08 ± 10.2	26.50 ± 9.8	32.88 ± 13.3	27.70 ± 10.6
% BSA involvement	48.50 (18.0, 77.0)	41.00 (14.0, 94.0)	40.00 (18.0, 75.0)	41.00 (14.0, 94.0)	56.00 (23.0, 87.0)	42.50 (14.0, 94.0)

BMI, Body mass index.
*Median values (min, max) unless otherwise stated.

TABLE E3. Medical history of allergic conditions by preferred term (≥5% of patients in any treatment arm; FAS)*

Patients, n (%)	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	All rademikibart (N = 170)	Placebo (N = 56)
Asthma	13 (22.8)	19 (33.3)	11 (19.6)	41 (24.1)	12 (21.4)
Rhinitis allergic	3 (5.3)	5 (8.8)	9 (16.1)	17 (10.0)	6 (10.7)
Seasonal allergy	8 (14.0)	5 (8.8)	4 (7.1)	17 (10.0)	7 (12.5)
Anaphylactic reaction	3 (5.3)	2 (3.5)	2 (3.6)	7 (4.1)	5 (8.9)
Drug hypersensitivity	3 (5.3)	1 (1.8)	3 (5.4)	7 (4.1)	4 (7.1)
Food allergy	2 (3.5)	4 (7.0)	1 (1.8)	7 (4.1)	3 (5.4)

*All patients had moderate to severe AD at baseline.

TABLE E4. Baseline scores and week 16* efficacy outcomes in the overall population and China subgroup (FAS; LOCF analysis, except NRI for vIGA-AD responses)

	300 mg Q2W		150 mg Q2W		300 mg Q4W		Placebo	
	Overall (N = 57)	China (n = 6)	Overall (N = 57)	China (n = 11)	Overall (N = 56)	China (n = 9)	Overall (N = 56)	China (n = 6)
EASI score								
Baseline								
Mean ± SD	27.6 ± 11.8	26.7 ± 9.6	24.6 ± 10.5	26.7 ± 10.6	23.1 ± 8.2	26.1 ± 10.2	25.2 ± 9.0	32.9 ± 13.3
Median (min, max)	20.8 (16.0, 53.8)	26.6 (16.5, 38.5)	21.2 (16.0, 68.4)	26.6 (16.0, 54.0)	20.1 (16.0, 48.5)	25.9 (16.3, 45.5)	22.1 (16.3, 55.2)	32.9 (17.2, 55.2)
Week 16								
Mean ± SD	9.6 ± 10.1	3.4 ± 2.6	10.2 ± 9.5	11.1 ± 12.4	8.0 ± 7.2	5.9 ± 6.5	15.4 ± 11.3	23.9 ± 19.4
Median (min, max)	4.2 (0.0, 39.0)	3.3 (0.4, 6.5)	6.9 (0.0, 40.8)	4.5 (0.1, 37.7)	5.6 (0.0, 31.2)	2.8 (0.0, 18.2)	13.0 (0.0, 59.1)	18.9 (5.0, 59.1)
LS mean % change (SE)	−63.0 (5.0)	−81.9 (5.0)	−57.6 (4.6)	−59.3 (10.8)	−63.5 (4.7)	−75.1 (12.0)	−39.7 (4.6)	−33.9 (15.1)
% difference vs placebo (SE)	−23.4 (6.8)	−48.0 (23.9)	−17.9 (6.5)	−25.4 (18.6)	−23.8 (6.6)	−41.1 (19.4)	—	—
95% CI	−36.8 to −10.0	−97.4 to 1.5	−30.8 to −5.0	−63.9 to 13.1	−36.8 to −10.9	−81.2 to 1.1	—	—
P value vs placebo	.0007	.0566	.0067	.1857	.0004	.0445	—	—
SCORAD score								
Baseline								
Mean ± SD	65.9 ± 12.1	63.2 ± 12.6	62.8 ± 12.5	66.8 ± 13.5	61.8 ± 9.7	62.0 ± 12.8	67.5 ± 11.6	76.3 ± 9.0
Median (min, max)	67.1 (37.0, 89.1)	58.7 (52.0, 86.6)	62.7 (40.4, 100.8)	66.5 (41.4, 91.3)	63.4 (45.4, 91.2)	62.9 (46.7, 84.5)	68.2 (44.5, 92.5)	75.4 (65.0, 92.5)
Week 16								
Mean ± SD	30.2 ± 20.2	19.3 ± 8.7	33.6 ± 16.7	34.9 ± 19.7	31.7 ± 17.9	23.7 ± 16.4	46.5 ± 18.6	58.5 ± 24.8
Median (min, max)	26.9 (0.0, 86.2)	20.7 (7.4, 28.2)	32.5 (0.0, 74.0)	36.1 (3.7, 74.0)	30.5 (0.0, 82.4)	21.1 (2.0, 54.2)	48.3 (0.0, 90.2)	59.1 (25.6, 90.2)
LS mean % change (SE)	−52.9 (4.1)	−61.8 (14.7)	−46.9 (3.8)	−49.2 (8.4)	−49.3 (3.9)	−59.9 (9.4)	−27.8 (3.9)	−28.3 (12.4)
% difference vs placebo (SE)	−25.1 (5.6)	−33.5 (20.5)	−19.1 (5.4)	−20.9 (14.8)	−21.5 (5.5)	−31.6 (16.3)	—	—
95% CI	−36.1 to −14.0	−75.9 to 8.8	−29.8 to −8.4	−51.4 to 9.6	−32.4 to −10.6	−65.1 to 2.0	—	—
P value vs placebo	<.0001	.1150	.0005	.1699	.0001	.0643	—	—
Percent BSA with AD involvement								
Baseline								
Mean ± SD	43.1 ± 20.7	45.3 ± 22.3	39.9 ± 19.1	46.1 ± 22.5	37.3 ± 19.5	43.0 ± 19.2	37.7 ± 18.3	53.0 ± 24.7
Median (min, max)	37.0 (14.9, 85.0)	48.5 (18.0, 77.0)	36.1 (12.0, 94.0)	41.0 (14.0, 94.0)	32.5 (11.0, 89.5)	40.0 (18.0, 75.0)	35.1 (11.5, 87.0)	56.0 (23.0, 87.0)
Week 16								
Mean ± SD	20.2 ± 18.6	6.8 ± 5.2	20.7 ± 18.3	23.6 ± 28.3	16.8 ± 14.7	11.0 ± 12.0	27.5 ± 18.1	42.7 ± 30.4
Median (min, max)	15.0 (0.0, 65.0)	6.5 (2.0, 12.0)	17.0 (0.0, 79.0)	8.0 (1.0, 69.0)	13.0 (0.0, 66.0)	8.0 (0.0, 33.0)	25.0 (0.0, 89.0)	33.0 (9.0, 89.0)
LS mean % change (SE)	−51.5 (5.4)	−78.7 (21.2)	−45.3 (5.0)	−53.1 (12.7)	−50.7 (5.1)	−71.0 (14.0)	−26.2 (5.1)	−22.0 (17.3)
% difference vs placebo (SE)	−25.3 (7.4)	−56.7 (27.5)	−19.1 (7.2)	−31.1 (21.4)	−24.4 (7.2)	−49.0 (22.4)	—	—
95% CI	−40.0 to −10.6	−113.5 to 0.0	−33.2 to −5.0	−75.4 to 13.1	−38.6 to −10.3	−95.3 to −2.8	—	—
P value vs placebo	.0008	.0502	.0084	.1592	.0008	.0385	—	—
PP-NRS score								
Baseline								
Mean ± SD	6.9 ± 2.0	6.6 ± 1.2	6.8 ± 1.8	7.1 ± 1.7	6.4 ± 2.1	5.8 ± 2.1	7.1 ± 1.3	7.8 ± 0.9
Median (min, max)	7.1 (2.3, 10.0)	6.7 (5.0, 8.0)	6.9 (1.9, 10.0)	7.0 (4.9, 10.0)	6.7 (0.7, 10.0)	6.0 (1.7, 8.7)	7.0 (3.9, 10.0)	8.1 (6.4, 8.6)
Week 16								
Mean ± SD	3.4 ± 2.6	4.0 ± 3.7	4.1 ± 2.2	4.9 ± 2.9	3.5 ± 2.5	2.6 ± 1.7	4.6 ± 2.5	6.5 ± 2.1
Median (min, max)	3.1 (0.0, 10.0)	4.1 (0.0, 8.6)	3.8 (0.0, 9.6)	5.4 (0.0, 9.0)	3.0 (0.0, 9.0)	2.4 (0.7, 6.0)	4.6 (0.0, 9.1)	6.3 (4.0, 9.0)
LS mean % change (SE)	−51.3 (5.6)	−47.7 (17.0)	−34.2 (5.5)	−28.7 (12.6)	−40.8 (5.3)	−48.9 (14.6)	−32.0 (5.5)	−13.6 (17.6)
% difference vs placebo (SE)	−19.2 (7.9)	−34.1 (24.6)	−2.2 (7.8)	−15.1 (21.3)	−8.7 (7.7)	−35.3 (23.8)	—	—
95% CI	−34.8 to −3.7	−84.6 to 16.4	−17.5 to 13.1	−58.8 to 28.7	−23.9 to 6.4	−84.2 to 13.6	—	—

(Continued)

TABLE E4. *(Continued)*

	300 mg Q2W		150 mg Q2W		300 mg Q4W		Placebo	
	Overall (N = 57)	China (n = 6)	Overall (N = 57)	China (n = 11)	Overall (N = 56)	China (n = 9)	Overall (N = 56)	China (n = 6)
P value vs placebo	.0156	.1767	.7762	.4858	.2572	.1498	—	—
vIGA-AD response rate†								
No. of responders (%)	16 (28)	2 (33)	9 (16)	2 (18)	11 (20)	2 (22)	5 (9)	0
95% CI	17 to 42	4 to 78	7 to 28	2 to 52	10 to 32	3 to 60	3 to 20	0 to 46
Response rate difference vs placebo (%)	19	33	7	18	11	22	—	—
P value vs placebo	.0089	.1213	.2684	.2662	.1052	.2148	—	—
AD flares								
Baseline to week 16, n (%)	6 (11)	3 (50)	6 (11)	1 (9)	10 (18)	4 (44)	9 (16)	1 (17)
Baseline to week 8, n (%)	5 (9)	3 (50)	3 (5)	1 (9)	4 (7)	2 (22)	6 (11)	1 (17)
Week 8 to week 16, n (%)	3 (5)	0	3 (5)	0	7 (13)	3 (33)	2 (4)	0
No. of flares								
Mean ± SD	1.8 ± 0.8	1.7 ± 0.6	1.3 ± 0.8	1.0	1.7 ± 1.3	2.3 ± 1.9	1.3 ± 0.5	1.0
Median (min, max)	2.0 (1, 3)	2.0 (1, 2)	1.0 (1, 3)	1.0 (1, 1)	1.0 (1, 5)	1.5 (1, 5)	1.0 (1, 2)	1.0 (1, 1)
No. of days with flares								
Mean ± SD	20.5 ± 13.0	28.7 ± 13	51.0 ± 32.6	29.0	50.6 ± 102	106 ± 151	41.0 ± 42	126
Median (min, max)	16.5 (4, 42)	28.0 (16, 42)	42.0 (29, 108)	29.0 (29, 29)	12.0 (1, 281)	27.0 (11, 281)	15.0 (8, 126)	126 (126, 126)
POEM score								
Baseline								
Mean ± SD	20.1 ± 6.6	23.2 ± 5.2	17.9 ± 6.4	21.0 ± 5.9	17.6 ± 6.6	18.6 ± 8.6	20.0 ± 5.5	25.3 ± 2.7
Median (min, max)	21.0 (5.0, 28.0)	25.0 (13.0, 28.0)	18.0 (2.0, 28.0)	22.0 (9.0, 28.0)	18.5 (3.0, 28.0)	14.0 (9.0, 28.0)	20.5 (3.0, 28.0)	26.5 (21.0, 28.0)
Week 16								
Mean ± SD	8.5 ± 6.6	7.3 ± 6.2	9.3 ± 6.7	13.2 ± 7.5	9.2 ± 6.0	10.1 ± 4.5	14.4 ± 8.1	21.0 ± 4.9
Median (min, max)	7.0 (0.0, 28.0)	7.0 (1.0, 14.0)	8.5 (0.0, 28.0)	15.0 (0.0, 25.0)	8.0 (0.0, 23.0)	11.0 (2.0, 16.0)	15.0 (0.0, 28.0)	19.0 (17.0, 28.0)
LS mean % change (SE)	−52.9 (8.5)	−65.7 (17.6)	−44.9 (7.9)	−37.4 (10.6)	−33.2 (8.0)	−37.3 (12.1)	−22.9 (8.0)	−7.6 (14.9)
% difference vs placebo (SE)	−30.1 (11.6)	−58.1 (22.8)	−22.1 (11.3)	−29.8 (18.4)	−10.3 (11.3)	−29.7 (19.9)	—	—
95% CI	−53.0 to −7.1	−105.5 to −11.0	−44.3 to 0.2	−67.7 to 8.1	−32.7 to 12.1	−70.7 to 11.3	—	—
P value vs placebo	.0105	.0178	.0516	.1179	.3654	.1481	—	—
DLQI score								
Baseline								
Mean ± SD	13.6 ± 7.8	14.2 ± 5.3	12.1 ± 6.1	16.3 ± 5.8	13.5 ± 7.9	16.7 ± 8.7	13.9 ± 6.2	16.2 ± 4.0
Median (min, max)	12.0 (2.0, 30.0)	14.0 (7.0, 21.0)	11.0 (3.0, 26.0)	16.0 (7.0, 25.0)	11.5 (1.0, 30.0)	15.0 (4.0, 28.0)	13.0 (3.0, 28.0)	15.5 (12.0, 21.0)
Week 16								
Mean ± SD	5.3 ± 6.2	3.0 ± 2.7	6.1 ± 5.8	9.7 ± 7.8	6.2 ± 5.7	8.2 ± 4.1	9.3 ± 7.3	12.2 ± 3.5
Median (min, max)	3.0 (0.0, 30.0)	2.0 (1.0, 7.0)	5.0 (0.0, 26.0)	12.0 (0.0, 26.0)	4.0 (0.0, 29.0)	10.0 (1.0, 13.0)	8.0 (0.0, 30.0)	13.5 (6.0, 15.0)
LS mean % change (SE)	−56.0 (6.2)	−71.8 (20.2)	−48.4 (5.7)	−41.3 (11.6)	−47.4 (5.8)	−43.0 (12.9)	−28.9 (5.8)	−18.1 (15.7)
% difference vs placebo (SE)	−27.1 (8.5)	−53.7 (25.5)	−19.5 (8.2)	−23.2 (19.6)	−18.5 (8.2)	−24.9 (20.4)	—	—
95% CI	−43.8 to −10.4	−106.3 to −1.0	−35.6 to −3.4	−63.7 to 17.2	−34.6 to −2.4	−67.1 to 17.3	—	—
P value vs placebo	.0016	.0459	.0179	.2480	.0243	.2354	—	—

*Change from baseline to week 16, unless stated otherwise.
†vIGA-AD response defined as vIGA-AD score of 0 (clear) or 1 (almost clear) and a ≥2-point reduction from baseline.

TABLE E5. Percent change in EASI score at week 16 in the overall population, analyzed with various methodologies for missing postbaseline scores

Analysis	Statistics	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	Placebo (N = 56)
LOCF, FAS	LS mean % change (SE)	−63.0 (5.0)	−57.6 (4.6)	−63.5 (4.6)	−39.7 (4.6)
	Median % change (min, max)	−79.3 (+29.0, −100.0)	−64.7 (+18.7, −100.0)	−70.0 (+25.8, −100.0)	−41.0 (+39.9, −100.0)
	No. of patients	49	56	55	55
	P value vs placebo	.0007	.0067	.0004	
WOCF, FAS	LS mean % change (SE)	−62.7 (5.1)	−54.4 (4.7)	−59.2 (4.8)	−35.7 (4.8)
	Median % change (min, max)	−79.3 (+29.0, −100.0)	−62.0 (+18.7, −100.0)	−67.3 (+25.8, −100.0)	−36.1 (+39.0, −100.0)
	No. of patients	49	56	55	55
	P value vs placebo	.0001	.0055	.0006	
MI, FAS	LS mean % change (SE)	−63.5 (4.9)	−62.5 (4.7)	−68.3 (4.7)	−47.2 (5.0)
	No. of patients	57	57	56	56
	P value vs placebo	.0170	.0206	.0018	
OC, FAS	LS mean % change (SE)	−66.2 (4.7)	−62.8 (4.6)	−70.1 (4.5)	−50.0 (5.1)
	Median % change (min, max)	−84.9 (+29.0, −100.0)	−79.3 (+18.7, −100.0)	−69.3 (+25.8, −100.0)	−52.1 (+39.9, −100.0)
	No. of patients	48	48	50	40
	P value vs placebo	.0207	.0618	.0033	
OC, PPS	LS mean % change (SE)	−67.9 (4.7)	−63.5 (4.7)	−72.2 (4.6)	−50.2 (5.1)
	Median % change (min, max)	−85.8 (+29.0, −100.0)	−73.3 (+18.7, −100.0)	−82.3 (+25.8, −100.0)	−53.0 (+39.9, −100.0)
	No. of patients	46	46	48	38
	P value vs placebo	.0123	.0553	.0015	

ANCOVA models with treatment group, baseline score, and baseline vIGA-AD (moderate, severe). With LOCF methodology, the last observed postbaseline EASI score was imputed for a missing score at week 16, with assessments after the first use of rescue medication (either permitted or prohibited) set to missing. With WOCF methodology, the worst observed postbaseline EASI score was imputed for a missing score at week 16, with assessments after the first use of rescue medication (either permitted or prohibited) set to missing. MI of missing data using the Markov-chain Monte-Carlo method, with intermittent missing EASI scores through week 16 imputed separately for each treatment group; missing values at scheduled visits (weeks 2, 4, 8, 12, and 16) were imputed using a monotone regression model including treatment, baseline IGA score (moderate, severe), baseline EASI score, and EASI scores at the previous scheduled visits. The FAS OC analysis includes actual values after the first use of rescue medication (either permitted or prohibited). In the PPS OC analysis, patients who used permitted rescue medications were included, with assessments after the initiation of rescue medication set to missing.
ANCOVA, Analysis of covariance; *MI*, multiple imputation; *OC*, observed cases; *WOCF*, worst observation carried forward.

TABLE E6. vIGA-AD and EASI-75 responder rates at weeks 16, 20, and 24 in the overall population (FAS; NRI analysis)*

	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	Placebo (N = 56)
vIGA-AD response, n (%)				
Week 16	16 (28.1)	9 (15.7)	11 (19.6)	5 (8.9)
Week 20	16 (28.1)	12 (21.1)	14 (25.0)	7 (12.5)
Week 24	18 (31.6)	12 (21.1)	17 (30.4)	7 (12.5)
EASI-75 response, n (%)				
Week 16	27 (47.4)	23 (40.4)	22 (39.3)	7 (12.5)
Week 20	23 (40.4)	23 (40.4)	24 (42.9)	12 (21.4)
Week 24	24 (42.1)	19 (33.3)	23 (41.1)	10 (17.9)

NRI, Nonresponder imputation.
*The final dose of rademikibart or placebo was administered at week 16. vIGA-AD response defined as vIGA-AD score of 0 (clear) or 1 (almost clear) and a ≥2-point reduction from baseline.

TABLE E7. Serious TEAEs by preferred term in the overall population (FAS)

Patients, n (%)	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	All rademikibart (N = 170)	Placebo (N = 56)
Any serious TEAE	0	1 (1.8)	2 (3.6)	3 (1.8)	2 (3.6)
Angina pectoris	0	0	1 (1.8)	1 (0.6)	0
Cardiac arrest	0	0	1 (1.8)	1 (0.6)	0
Cholelithiasis	0	0	0	0	1 (1.8)
Headache	0	1 (1.8)	0	1 (0.6)	0
Nausea	0	1 (1.8)	0	1 (0.6)	0
Pneumonia	0	0	0	0	1 (1.8)
Rib fracture	0	0	1 (1.8)	1 (0.6)	0
Vomiting	0	1 (1.8)	0	1 (0.6)	0

TABLE E8. TEAEs by preferred term and system organ class in the overall population (≥5% of patients in any treatment arm; FAS)

Patients, n (%)	300 mg Q2W (n = 57)	150 mg Q2W (n = 57)	300 mg Q4W (n = 56)	All rademikibart (N = 170)	Placebo (N = 56)
Any TEAE	26 (45.6)	24 (42.1)	32 (57.1)	82 (48.2)	30 (53.6)
Skin and subcutaneous tissue disorders	8 (14.0)	11 (19.3)	18 (32.1)	37 (21.8)	12 (21.4)
AD	5 (8.8)	7 (12.3)	14 (25.0)	26 (15.3)	8 (14.3)
Infections and infestations	10 (17.5)	13 (22.8)	9 (16.1)	32 (18.8)	15 (26.8)
COVID-19	2 (3.5)	4 (7.0)	1 (1.8)	7 (4.1)	4 (7.1)
Nasopharyngitis	3 (5.3)	1 (1.8)	2 (3.6)	6 (3.5)	4 (7.1)
Upper respiratory tract infection	1 (1.8)	1 (1.8)	3 (5.4)	5 (2.9)	1 (1.8)
Urinary tract infection	1 (1.8)	4 (7.0)	0	5 (2.9)	1 (1.8)
Skin infection	0	0	1 (1.8)	1 (0.6)	3 (5.4)
Gastrointestinal disorders	4 (7.0)	3 (5.3)	6 (10.7)	13 (7.6)	3 (5.4)
Nausea	2 (3.5)	1 (1.8)	3 (5.4)	6 (3.5)	0
Investigations	3 (5.3)	2 (3.5)	4 (7.1)	9 (5.3)	2 (3.5)
Nervous system disorders	2 (3.5)	4 (7.0)	5 (8.9)	11 (6.5)	0
Headache	2 (3.5)	3 (5.3)	4 (7.1)	9 (5.3)	0
Eye disorders	2 (3.5)	2 (3.5)	2 (3.6)	6 (3.5)	4 (7.1)
General disorders and administration-site conditions	3 (5.3)	1 (1.8)	4 (7.1)	8 (4.7)	2 (3.6)
Injury, poisoning, and procedural complications	2 (3.5)	3 (5.3)	4 (7.1)	9 (5.3)	1 (1.8)
Respiratory, thoracic, and mediastinal disorders	2 (3.5)	1 (1.8)	4 (7.1)	7 (4.1)	1 (1.8)
Musculoskeletal and connective tissue disorders	1 (1.8)	0	3 (5.4)	4 (2.4)	3 (5.4)
Renal and urinary disorders	0	0	3 (5.4)	3 (1.8)	1 (1.8)