# MG-K10, a Long-Acting Anti-IL-4 Receptor Alpha Monoclonal Antibody in Adult Patients with Moderate-to-Severe Atopic Dermatitis

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***Abstract:*** ***Background:*** **There remains unmet need for therapies for atopic dermatitis (AD) with favorable symptom control but less frequent dosing.**

***Objective:*** **To evaluate the benefits and safety of MG-K10, a humanized interleukin-4 receptor alpha-targeting antibody, in moderate-to-severe AD.**

***Methods:*** **In this multi-center, double-blind, randomized, phase II trial, 163 moderate-to-severe AD patients were randomized to receive 16-week treatment with MG-K10 150 mg every 4 weeks (Q4W), 300 mg every 2 weeks (Q2W) (n = 41), 300 mg Q4W (n = 41), or placebo (n = 40). Primary endpoint was the change in Eczema Area and Severity Index (EASI) scores from baseline to week 16.**

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*The authors confirm that the data supporting the findings of this study are available within the article and its Supplementary Data.*

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***Results:*** **The mean differences in EASI score at week 16 for the 300 mg Q4W, 300 mg Q2W, and 150 mg Q4W groups were −38.83% (95% confidence interval [CI]: −56.47% to −21.20%, *P* < 0.001), −27.06% (95% CI: −44.73% to −9.38%, *P* = 0.003), and −16.00% (95% CI: −33.66% to 1.67%, *P* = 0.076) compared with placebo group. The proportion of participants achieving EASI-75 at week 16 was 79.5%, 66.7%, 53.8%, and 28.9% in the 300 mg Q4W, 300 mg Q2W, 150 mg Q4W, and placebo groups. The incidence of adverse events was comparable across groups.**

***Conclusion:*** **MG-K10 demonstrates potential as a long-acting therapeutic option for managing symptoms of moderate-to-severe AD, with favorable safety profile. The preliminary efficacy and safety supported further validation of 300 mg Q4W in phase III trial.**

## Capsule Summary

- MG-K10, a humanized monoclonal antibody targeting interleukin-4 receptor alpha (IL-4Rα), showed improvements in EASI scores, significant alleviation symptoms, and enhanced patient-reported quality of life in patients with moderate-to-severe AD compared with placebo in this phase II trial, with a favorable safety profile.
- MG-K10 is the most promising IL-4Rα monoclonal antibody for a prolonged injection interval of every 4 weeks (Q4W) among those currently available for the treatment of moderate to severe atopic dermatitis (AD) patients.

## INTRODUCTION

Atopic dermatitis (AD) is a widely prevalent chronic inflammatory skin disease.[1,2] It varies in severity, with moderate to severe AD causing extensive skin damage over large body areas,[3] significantly disrupting patients' work and daily activities.[4,5]

The standard treatments for AD include emollients, topical corticosteroids, topical immunomodulatory agents, systemic immunosuppressants, and targeted biological therapies.[6] While systemic therapies become essential for moderate-to-severe cases,[7] the side effects may contribute to reduced patient adherence and increased disease flare-ups, poses challenges.[8,9] Recently, the introduction of dupilumab, an anti-interleukin-4 receptor alpha (IL-4Rα) antibody, has significantly advanced moderate-to-severe AD treatment by offering improved symptom control with favorable safety profile.[10] However, its biweekly administration schedule can lead to nonadherence and increased health care utilization.[11,12] Along with the frequent dosing, the high cost of monoclonal antibodies like dupilumab makes access difficult for many patients,[13] underlining the continuous need for novel antibody-based therapies suited to them.

MG-K10 is a humanized monoclonal antibody that blocks the interaction of interleukin-4 (IL-4) and interleukin-13 (IL-13) with IL-4Rα. In order to prolong the injection interval, the fragment crystallizable (Fc) region of MG-K10 has been mutated to enhance the binding affinity to neonatal fragment crystallizable receptor (FcRn) on the cell surface. The Biacore assays revealed that the affinity (KD) of MG-K10 for human FcRn is 4.7 nM, compared with the non-mutated antibody at 45.8 nM and dupilumab at 31.3 nM, showing nearly a 10-fold increase in binding affinity. The phase Ib clinical trial of MG-K10 has shown MG-K10 reduced the level of Th2 biomarkers significantly, hinting at its ability to influence the inflammatory mechanisms of AD positively; meanwhile, the clinical data preliminarily revealed the potential for long-acting therapeutic option. These findings highlight the potential of MG-K10 in the management of AD, especially for a longer dosing interval to improve patient compliance and ease cost concerns.

Therefore, this study seeks to evaluate the efficacy and safety of MG-K10 across various dosages and dosing schedules in patients with moderate-to-severe AD, alongside its pharmacokinetics (PK), and pharmacodynamics (PD), and to gain a thorough insight into the therapeutic potential of MG-K10, aiming to minimize dosing frequency and refine AD treatment approaches.

## METHODS

### Study Design and Participants

This multicenter, double-blind, randomized, placebo-controlled, phase II trial adhered to the principles outlined in the Declaration of Helsinki and complied with Good Clinical Practice guidelines and was conducted in accordance with ethical standards and regulations governing clinical trials. The protocol was reviewed and approved by independent ethics committees of our Hospital (No. 2022-019), approval date: 8/2/2022. All participants provided written, informed consent prior to participation.

Eligible participants were individuals aged 18–70 years with moderate-to-severe AD, with an eczema area and severity index (EASI) score ≥16, an investigator global assessment (IGA) score ≥3, and ≥10% of body surface area affected by AD.[14] A minimum AD or eczema history of 6 months was required, along with inadequate control with at least 4 weeks of high-potency or 2 weeks of superpotent topical glucocorticoids or topical calcineurin inhibitors. Patients with recent use of biologics (within 12 weeks or 5 half-lives prior to randomization), systemic glucocorticoids, immunosuppressants, phosphodiesterase-4 inhibitors, targeted therapies (e.g., Janus kinase inhibitors), ultraviolet light therapy, systemic or topical herbal treatments for AD

within 4 weeks prior to randomization, and use of topical treatments for AD (such as topical glucocorticoids) within 1 week prior to randomization. A comprehensive list of inclusion and exclusion criteria is detailed in Supplementary Table S1.

## Procedure

Eligible participants were randomly allocated (1:1:1:1) to receive subcutaneous injections of MG-K10 at the dose of 150 mg every 4 weeks (Q4W), 300 mg biweekly (Q2W), 300 mg Q4W, and placebo. Randomization was stratified by baseline IGA scores (either 3 or 4 points).

Participants assigned to 150 mg Q4W group started with an initial 300 mg dose of MG-K10 (2 mL) subcutaneously, followed by 150 mg (1 mL) Q4W, while the starting dose was 600 mg in the 300 mg Q4W and 300 mg Q2W groups. Participants assigned to placebo received biweekly subcutaneous injections, initially at 4 mL, followed by 2 mL. To maintain blinding, participants in the MG-K10 Q4W group received matched placebo doses at specific intervals. Each participant received the final dose administered at week 14. Any modification to the prespecified dosing schedule was strictly prohibited. If necessary, rescue medications for AD were permitted at the discretion of the investigators. But if the rescue treatment was systemic, study treatment was discontinued. Participants were instructed to consistently apply emollients twice daily, starting at least 1 week prior to enrollment and throughout the study, barring any safety concerns.

Participants underwent comprehensive efficacy and safety assessments at baseline and weeks 2, 4, 6, 8, 10, 12, 14, and 16 during the treatment period. PD blood samples were collected at baseline and weeks 2, 4, 8, 12, 14, and 16. The follow-up period included two additional assessments of efficacy, safety, and PD (weeks 20 and 24). PD responses of biomarkers total immunoglobulin E (IgE) and thymus and activation-regulated chemokine (TARC) in serum were assessed with commercial enzyme-linked immunosorbent assay kit.

## Endpoints

The primary endpoint was the rate of improvement in the EASI score from baseline at week 16. Secondary endpoints included: the proportion of subjects achieving EASI-75 (defined as a 75% decrease in EASI score from baseline) at week 16; percentage changes in EASI score from baseline and proportions of subjects reaching EASI-75 at weeks 2, 4, 8, 12, 20, and 24; proportions of subjects with an IGA score of 0/1 with a decrease of ≥2 points from baseline at weeks 2, 4, 8, 12, 16, 20, and 24; proportions of subjects with IGA score with a decrease of ≥2 points from baseline; proportions of subjects with IGA score with a decrease of ≥3 points from baseline; peak weekly mean and percent changes in pruritus using the numerical rating scale (NRS) from baseline; proportions of subjects achieving EASI-50 (50% reduction from baseline) and EASI-90 (90% reduction); absolute changes in EASI score, BSA score, patient-oriented eczema measure (POEM) score, and dermatology life quality index (DLQI) score from baseline.

Safety assessments were conducted using laboratory test values and 12-lead electrocardiogram parameters, with adverse events (AEs) evaluated per the NCI Common Terminology for Adverse Events Version 5.0. The study also assessed the PD and PK of MG-K10.

## Statistical Analysis

Due to the exploratory nature, we aimed to enroll 160 patients in this study without statistical power considerations.

The full analysis set (FAS) included all subjects who received at least 1 dose of MG-K10 or placebo post-enrollment and excluded subjects with no efficacy evaluation records posttreatment. The per-protocol set (PPS) included subjects from the FAS without major protocol deviations potentially affecting the judgment of the primary efficacy endpoint. The safety analysis set included all subjects who received at least 1 dose of MG-K10 or placebo and had safety assessment.

Statistical analyses were conducted using SAS software, version 9.4. Continuous variables, including both primary and secondary endpoints, were analyzed using an Analysis of Covariance (ANCOVA) model. Least-squares (LS) means, which represent the group means adjusted for the covariates used in the model, were calculated for all treatment groups. This analysis was carried out without imputation for missing data. For sensitivity analyses, mixed effects models for repeated measures (MMRM) were applied to further evaluate the consistency of the primary endpoint results, with assumptions that any missing data were missing at random. Multiple imputation methods were used to address any missing data. Categorical variables were analyzed using CIs calculated via the Clopper-Pearson method, while CIs for intergroup differences were computed using the stratified Miettinen-Nurminen method. Intergroup comparisons were analyzed using the Cochran–Mantel–Haenszel method, with a significance level set at 0.05.

We conducted post hoc subgroup analyses of the percentage change from baseline in EASI score using ANCOVA. The change in average value of eosinophils and percentage change of lactate dehydrogenase (LDH) from baseline to week 16 were performed using MMRM. Kaplan–Meier curves were also plotted for time to first rescue therapy.

# RESULTS

## Demographic and Baseline Characteristics

From August 23, 2022, to February 8, 2023, 163 patients were enrolled across 28 study centers in China. In the FAS, patients were stratified into four treatment arms: 41 to the MG-K10

150 mg Q4W group, 41 to the 300 mg Q2W group, 41 to the 300 mg Q4W group, and 40 to the placebo group (Fig. 1).

The mean age of all participants was 45.07 years, with a slight male predominance at 67.5%. In terms of disease severity, 64.4% had an IGA score of 3, while 35.6% scored 4. The mean EASI score was 23.83, with a mean BSA of 40.32%. Peak weekly pruritus NRS scores had a mean score of 6.48. Baseline demographic and disease characteristics were well balanced across the groups, ensuring comparability (Table 1).

## Primary Endpoints

At week 16, patients in the 150 mg Q4W group displayed a mean improvement difference versus placebo of −16.00% (95% CI: −33.66% to 1.67%, $P = 0.076$), while those in the 300 mg Q2W group exhibited a mean difference of −27.06% (95% CI: −44.73% to −9.38%, $P = 0.003$). The 300 mg Q4W group achieved a mean difference of −38.83% (95% CI: −56.47% to −21.20%, $P < 0.001$) (Table 2).

The sensitivity analyses reinforced these results. In the analysis of FAS using MMRM, mean differences in EASI score improvements versus the placebo were −12.37% (95% CI: −30.29% to 5.56%, $P = 0.175$) for the 150 mg Q4W group, −27.23% (95% CI: −45.20% to −9.26%, $P = 0.003$) for the 300 mg Q2W group, and −38.49% (95% CI: −56.44% to −20.54%, $P < 0.001$) for the 300 mg Q4W group. In the analysis of PPS using ANCOVA, the mean differences were −16.03% (95% CI: −33.39% to 1.33%, $P = 0.070$), −29.37% (95% CI: −46.81% to −11.93%, $P = 0.001$), and −37.70% (95% CI: −55.04% to −20.37%, $P < 0.001$) across the respective MG-K10 groups versus placebo. The FAS using an ANCOVA model with multiple imputation for missing data further confirmed the robustness of these findings, with mean differences of −12.72% (95% CI: −31.20% to 5.76%, $P = 0.177$), −26.44% (95% CI: −44.92% to −7.97%, $P = 0.005$), and −38.74% (95% CI: −57.00% to −20.47%, $P < 0.001$) when compared with placebo.

## Secondary Endpoints

At week 16, the efficacy of MG-K10 was further demonstrated by the proportion of patients achieving EASI-75. Compared with the 28.9% with placebo, the MG-K10 treatment arms showed higher responses: 53.8% in the 150 mg Q4W group (a difference of 25.09%, 95% CI: 3.07% to 43.95%, $P = 0.027$), 66.7% in the 300 mg Q2W group (a difference of 37.86%, 95% CI: 15.58% to 55.44%, $P < 0.001$), and 79.5% in the 300 mg Q4W group (a difference of 50.36%, 95% CI: 28.50% to 65.97%, $P < 0.001$) achieved EASI-75. Besides, 53.8% of patients in the 300 mg Q4W group attained EASI-90, compared with the 15.8% in the placebo group ($P < 0.001$) (Table 2). The rate of improvement in EASI scores from baseline at each visit is shown in Supplementary Figure S1A. Further analysis revealed that the EASI-90 and EASI-75 were significantly higher in the MG-K10 300 mg groups when compared with placebo starting from week 8. These effects were persisted for 8 weeks after treatment cessation (Fig. 2 A and Supplementary Fig. S1B and C).

The improvement in IGA scores also mirrored this trend, with the proportion of patients achieving an IGA score of 0 or 1 and a reduction of ≥2 points from baseline rising gradually from week 4 to week 16 across all MG-K10 treatment arms. The 300 mg Q4W group achieved a 51.3% response rate at week 16 (a difference of 35.66%, 95% CI: 14.20% to 52.72%, $P = 0.001$), while 46.2% in the 150 mg Q4W group (a difference of 30.82%, 95% CI: 9.60% to 48.25%, $P = 0.003$), and 46.2% in the 300 mg

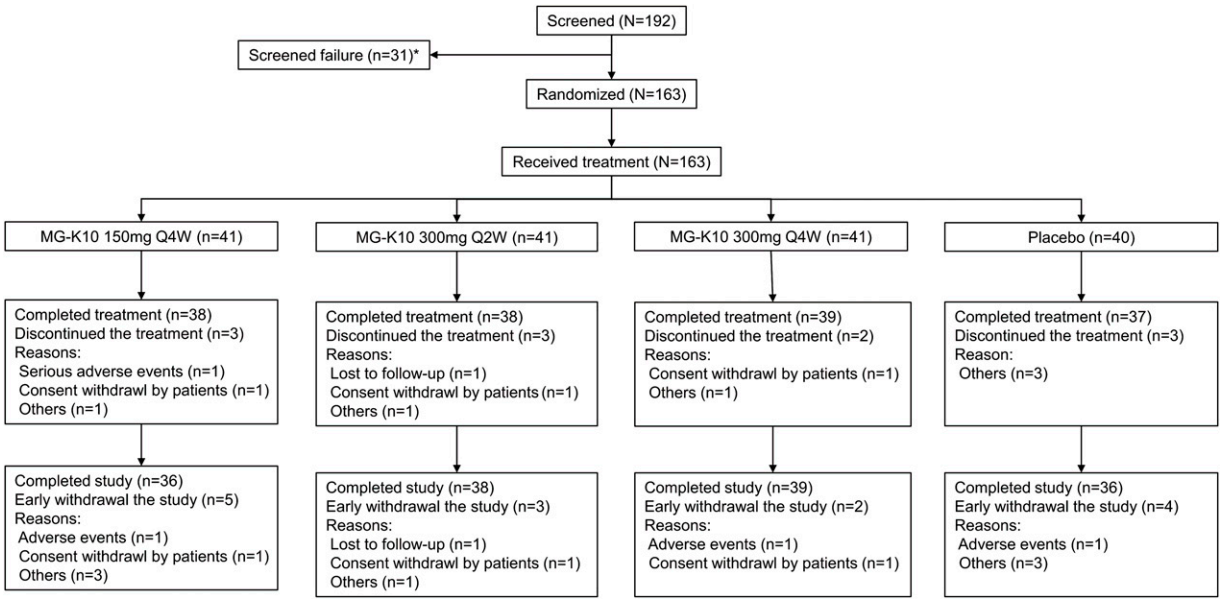


**Figure 1.** Patient flowchart.

**TABLE 1. Baseline Characteristics**

| Characteristics | MG-K10 150 mg Q4W (n = 41) | MG-K10 300 mg Q2W (n = 41) | MG-K10 300 mg Q4W (n = 41) | Placebo Q2W (n = 40) | Total (N = 163) |
|---|---|---|---|---|---|
| Age, mean ± SD, (year) | 45.76 ± 17.257 | 47.37 ± 16.266 | 42.24 ± 15.965 | 44.90 ± 15.369 | 45.07 ± 16.191 |
| Sex (male), n (%) | 28 (68.3) | 34 (82.9) | 26 (63.4) | 22 (55.0) | 110 (67.5) |
| Weight, mean ± SD (kg) | 69.50 ± 14.947 | 70.38 ± 11.877 | 68.61 ± 12.899 | 68.18 ± 13.815 | 69.17 ± 13.332 |
| BMI, mean ± SD (kg/m$^2$) | 24.66 ± 4.285 | 24.10 ± 3.106 | 23.34 ± 2.729 | 24.74 ± 3.796 | 24.21 ± 3.541 |
| IGA score | | | | | |
| 3, n (%) | 26 (63.4) | 27 (65.9) | 26 (63.4) | 26 (65.0) | 105 (64.4) |
| 4, n (%) | 15 (36.6) | 14 (34.1) | 15 (36.6) | 14 (35.0) | 58 (35.6) |
| EASI score, mean ± SD | 24.33 ± 9.585 | 24.18 ± 7.984 | 24.03 ± 8.784 | 22.77 ± 7.666 | 23.83 ± 8.485 |
| BSA score, mean ± SD | 42.55 ± 20.683 | 39.40 ± 17.616 | 41.04 ± 15.830 | 38.25 ± 19.717 | 40.32 ± 18.449 |
| Peak weekly pruritus NRS scores, mean ± SD[a] | 6.49 ± 2.121 | 6.77 ± 2.198 | 6.61 ± 1.951 | 6.02 ± 1.634 | 6.48 ± 1.993 |
| DLQI score, mean ± SD | 13.56 ± 6.874 | 12.37 ± 7.303 | 14.39 ± 6.910 | 12.60 ± 6.126 | 13.23 ± 6.806 |
| POEM score, mean ± SD | 18.71 ± 6.182 | 17.88 ± 6.439 | 18.32 ± 5.755 | 18.53 ± 6.148 | 18.36 ± 6.086 |
| TARC, mean, (pg/mL)[b] | 441.34 | 457.52 | 853.89 | 692.11 | / |
| IgE, mean, (ng/mL)[b] | 2971.67 | 2280.33 | 4073.47 | 4908.11 | / |
| Prior immunosuppressants treatment | 4 (9.8) | 12 (29.3) | 6 (14.6) | 3 (7.5) | 25 (15.3) |
| Tripterygium wilfordii Hook extract | 3 (7.3) | 9 (22.0) | 3 (7.3) | 1 (2.5) | 16 (9.8) |
| Thalidomide | 0 | 2 (4.9) | 1 (2.4) | 1 (2.5) | 4 (2.5) |
| Upadacitinib | 1 (2.4) | 1 (2.4) | 0 | 0 | 2 (1.2) |
| Tofacitinib | 0 | 1 (2.4) | 1 (2.4) | 0 | 2 (1.2) |
| Methotrexate | 0 | 1 (2.4) | 0 | 1 (2.4) | 2 (1.2) |
| Baricitinib | 0 | 1 (2.4) | 0 | 0 | 1 (0.6) |
| Hydroxychloroquine | 0 | 1 (2.4) | 0 | 0 | 1 (0.6) |
| Prior Dupilumab treatment | 2 (4.9) | 0 | 3 (7.3) | 1 (2.5) | 6 (3.7) |

[a]*The NRS baseline reflects the mean value calculated from day −6 to day 1. A minimum of 4 daily scores out of the 7 days is required to calculate the baseline average score.*

[b]*The sample sizes for TARC and IgE levels were 40 (150 mg Q4W), 41 (300 mg Q2W), 40 (300 mg Q4W), and 40 (Placebo), respectively.*

*BSA, body surface area; BMI, body mass index; DLQI, dermatology life quality index; EASI, eczema area and severity index; IgE, immunoglobulin E; IGA, investigator's global assessment; NRS, numerical rating scale; POEM, patient-oriented eczema measure; Q4W, every 4 weeks; Q2W, every 2 weeks; SD, standard deviation; TARC, thymus and activation-regulated chemokine.*

Q2W group (a difference of 30.33%, 95% CI: 9.18% to 47.81%, $P = 0.005$) (Fig. 2B and Table 2). The proportion of patients achieving IGA score with a reduction of ≥3 points from baseline rising gradually from week 4 to week 16 across all MG-K10 treatment arms (Supplementary Fig. S1D and E and Table 2). These effects were also persisted for 8 weeks after treatment cessation.

In the evaluation of BSA at week 16, patients treated with MG-K10 exhibited a greater reduction rate from baseline compared with the placebo group (Supplementary Fig. S2A and Table 2). In addition, the rate of improvement in peak weekly pruritus NRS scores at week 16 was better in the MG-K10 300 mg groups than in the placebo group (Fig. 2C, Supplementary Fig. S2B, and Table 2). POEM scores and DLQI scores improved in both MG-K10 300 mg groups compared with placebo (Supplementary Fig. S2C and D and Table 2). In addition, among the 4 groups, the incidence of rescue therapy during the 16-week treatment period was lowest in the 300 mg Q4W group. In the post hoc analysis, the time to first rescue therapy over time was later in the MG-K10 300 mg groups. During the 16-week treatment period, the 300 mg Q4W group seemed to have the latest trend in the time to first rescue therapy (Supplementary Fig. S3).

## Safety

Throughout the study period, the overall incidence of AEs was in alignment across both MG-K10 and placebo groups. As in Table 3, AEs were reported by 146 participants (89.6%), with a similar distribution among the four groups. The most common AE was coronavirus disease 2019 (COVID-19), affecting 19.6% of patients. The majority of AEs were grades 1 to 2, while only 6/163 (3.7%) subjects had grade ≥3 AEs, all unrelated to MG-K10. Treatment-related adverse events (TRAEs) were reported in 22.0% of the 150 mg Q4W group, 34.1% of the 300 mg Q2W group, 36.6% of the 300 mg Q4W group, and 25.0% of the placebo group. Serious AEs (SAEs) occurred in 2 out of 123 patients across all MG-K10 groups and in 1 out of 40 patients in the placebo group. There was one case of infectious pneumonia, lower limb fracture, and cerebral infarction, respectively, but none were deemed related to

**TABLE 2. Efficacy Outcomes at Week 16**

| Variables | MG-K10 150 mg Q4W (n = 41) | MG-K10 300 mg Q2W (n = 41) | MG-K10 300 mg Q4W (n = 41) | Placebo Q2W (n = 40) |
|---|---|---|---|---|
| EASI scores | | | | |
| Improvement rate from baseline, %, LS mean ± SE (Primary endpoints) | −58.72 ± 6.353 | −69.77 ± 6.380 | −81.55 ± 6.331 | −42.72 ± 6.392 |
| Difference of means versus placebo, (95% CI) | −16.00 (−33.66, 1.67), $P = 0.076$ | −27.06 (−44.73, −9.38), $P = 0.003$** | −38.83 (−56.47, −21.20), $P < 0.001$*** | / |
| EASI-75 | | | | |
| Responders, n (%) | 21 (53.8) | 26 (66.7) | 31 (79.5) | 11 (28.9) |
| Difference versus placebo, %, (95% CI) | 25.09 (3.07, 43.95), $P = 0.027$* | 37.86 (15.58, 55.44), $P < 0.001$*** | 50.36 (28.50, 65.97), $P < 0.001$*** | / |
| EASI-50 | | | | |
| Responders, n (%) | 29 (74.4) | 30 (76.9) | 34 (87.2) | 21 (55.3) |
| Difference versus placebo, %, (95% CI) | 19.27 (−1.97, 38.36), $P = 0.079$ | 21.69 (0.57, 40.49), $P = 0.047$* | 31.81 (11.06, 49.01), $P = 0.002$** | / |
| EASI-90 | | | | |
| Responders, n (%) | 15 (38.5) | 17 (43.6) | 21 (53.8) | 6 (15.8) |
| Difference versus placebo, %, (95% CI) | 22.76 (2.77, 40.50), $P = 0.027$* | 27.78 (7.32, 45.35), $P = 0.009$** | 37.99 (16.84, 54.84), $P < 0.001$*** | / |
| IGA | | | | |
| Decline ≥2 from baseline, and IGA score = 0 or 1, n (%) | 18 (46.2) | 18 (46.2) | 20 (51.3) | 6 (15.8) |
| Difference versus placebo, %, (95% CI) | 30.82 (9.60, 48.25), $P = 0.003$** | 30.33 (9.18, 47.81), $P = 0.005$** | 35.66 (14.20, 52.72), $P = 0.001$** | / |
| ≥2, n (%) | 20 (51.3) | 22 (56.4) | 26 (66.7) | 10 (26.3) |
| Difference versus placebo, %, (95% CI) | 25.09 (3.29, 43.78), $P = 0.026$* | 30.33 (8.28, 48.75), $P = 0.006$** | 39.96 (17.77, 57.32), $P < 0.001$*** | / |
| ≥3, n (%) | 7 (17.9) | 12 (30.8) | 16 (41.0) | 1 (2.6) |
| Difference versus placebo, %, (95% CI) | 15.23 (−0.48, 30.05), $P = 0.030$* | 28.31 (10.40, 44.08), $P < 0.001$*** | 38.26 (19.27, 53.99), $P < 0.001$*** | / |
| BSA | | | | |
| Improvement from baseline, %, LS mean ± SE | −21.38 ± 3.039 | −26.20 ± 3.020 | −31.87 ± 3.015 | −18.04 ± 3.052 |
| Difference of means versus placebo, (95% CI) | −3.35 (−11.81, 5.12), $P = 0.436$ | −8.17 (−16.58, 0.24), $P = 0.057$ | −13.83 (−22.25, −5.41), $P = 0.001$** | / |
| Improvement rate from baseline, %, LS mean ± SE | −50.93 ± 7.129 | −65.99 ± 7.085 | −77.78 ± 7.073 | −35.75 ± 7.160 |
| Difference of means versus placebo, (95% CI) | −15.18 (−35.03, 4.67), $P = 0.133$ | −30.24 (−49.96, −10.51), $P = 0.003$** | −42.03 (−61.78, −22.28), $P < 0.001$*** | / |

(*continued*)

**TABLE 2. (Continued)**

| Variables | MG-K10 150 mg Q4W (n = 41) | MG-K10 300 mg Q2W (n = 41) | MG-K10 300 mg Q4W (n = 41) | Placebo Q2W (n = 40) |
|---|---|---|---|---|
| NRS | | | | |
| Improvement from baseline, LS mean ± SE | −2.65 ± 0.413 | −3.82 ± 0.423 | −3.89 ± 0.424 | −2.23 ± 0.431 |
| Difference of means versus placebo, (95% CI) | −0.43 (−1.60, 0.74), $P = 0.472$ | −1.59 (−2.78, −0.40), $P = 0.009$** | −1.67 (−2.85, −0.48), $P = 0.006$** | / |
| Improvement rate from baseline, %, LS mean ± SE | −34.29 ± 7.809 | −54.15 ± 7.992 | −60.41 ± 8.026 | −30.38 ± 8.161 |
| Difference of means versus placebo, (95% CI) | −3.92 (−26.05, 18.21), $P = 0.727$ | −23.77 (−46.22, −1.33), $P = 0.038$* | −30.03 (−52.48, −7.59), $P = 0.009$** | / |
| Decline ≥4 from baseline, n (%) | 17 (47.2) | 23 (63.9) | 20 (55.6) | 10 (29.4) |
| Difference versus placebo, (95% CI) | 18.82 (−4.05, 39.02), $P = 0.108$ | 34.37 (10.98, 53.02), $P = 0.004$** | 26.08 (2.93, 45.61), $P = 0.029$* | |
| POEM | | | | |
| Improvement from baseline, LS mean ± SE | −6.79 ± 1.211 | −8.72 ± 1.212 | −11.01 ± 1.209 | −3.60 ± 1.227 |
| Difference of means versus placebo, (95% CI) | −3.19 (−6.56, 0.19), $P = 0.064$ | −5.12 (−8.50, −1.75), $P = 0.003$** | −7.41 (−10.79, −4.04), $P < 0.001$*** | / |
| DLQI | | | | |
| Improvement from baseline, LS mean ± SE | −4.50 ± 0.992 | −6.63 ± 0.995 | −7.99 ± 0.997 | −2.81 ± 1.005 |
| Difference of means versus placebo, (95% CI) | −1.69 (−4.46, 1.08), $P = 0.229$ | −3.82 (−6.59, −1.05), $P = 0.007$** | −5.18 (−7.96, −2.41), $P < 0.001$*** | / |

*BSA, body surface area; CI, confidence interval; DLQI, dermatology life quality index; EASI, eczema area and severity index; EASI-50, 50% reduction from baseline in EASI score; EASI-90, 90% reduction from baseline in EASI score; LS mean, least-squares mean; SE, standard error; EASI-75, 75% reduction from baseline in EASI score; IGA, investigator's global assessment; NRS, numerical rating scale; POEM, patient-oriented eczema measure.*

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

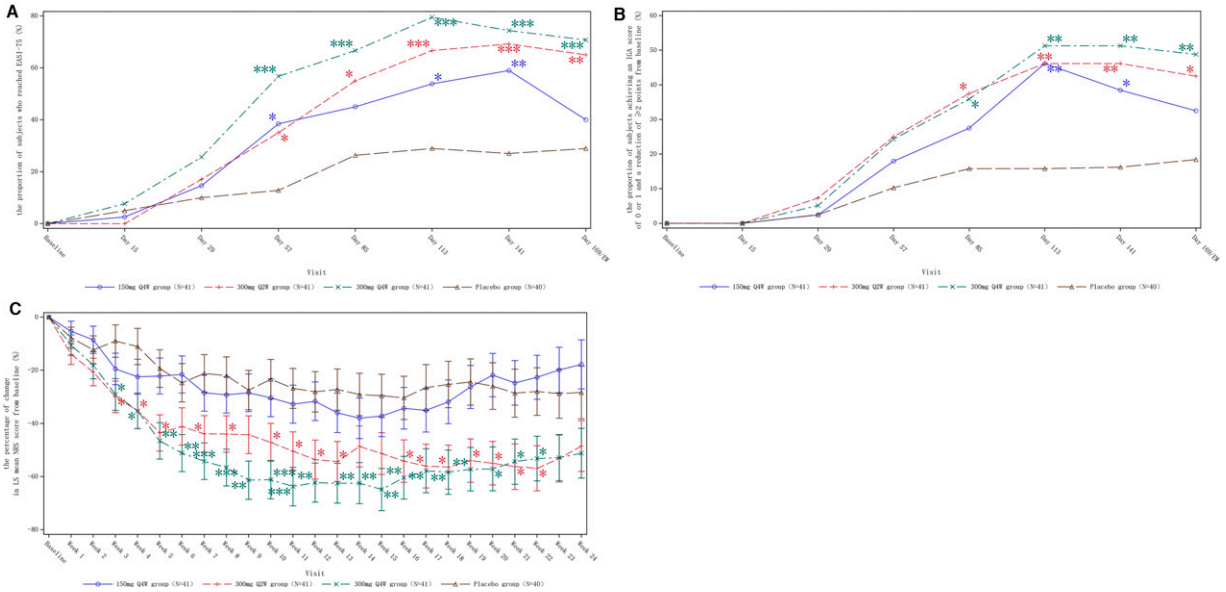


**Figure 2.** Trends in secondary endpoints over time. (A) the proportion of subjects who reached a 75% reduction in the eczema area and severity index (EASI-75); (B) the proportion of subjects achieving an investigator's global assessment (IGA) score of 0 or 1, representing clear or almost clear skin, with an improvement of ≥2 points from baseline. (C) the rate of improvement in the weekly average of daily Peak Pruritus numerical rating scale (NRS) over the course of the study, relative to baseline values. The improvement value is calculated as the score at each visit subtracted from the baseline score, and the improvement rate is the ratio of this value to the baseline score. *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$.

the treatment. AEs of special interest, such as increased eosinophil counts leading to symptoms, were infrequent, with one case in the 300 mg Q2W group (Table 3).

## Pharmacokinetics, Pharmacodynamics, and Biomarker Analysis

After multiple subcutaneous injections of MG-K10, the serum concentration increases with the administration of loading and maintenance doses. Notably, in the 300 mg Q4W group, blood concentrations of MG-K10 achieved steady-state by week 4. In terms of PD, there was a notable and rapid decline in the levels of TARC across all MG-K10 dosing groups, commencing as early as 2 weeks after the first dose and persisting throughout the study (Supplementary Fig. S4). Similarly, IgE levels showed a consistent decrease from the onset of dosing in all MG-K10 groups, in contrast to the placebo group, which exhibited a more gradual reduction (Supplementary Fig. S5). The post hoc analysis revealed that the eosinophils and LDH were decreased over time in all four groups (Supplementary Figs. S6 and Figs. S7), while the percentage change in LDH was higher over time in both MG-K10 300 mg groups than the placebo group, especially in 300 mg Q4W group (Supplementary Fig. S7).

## Subgroup Analysis

In the post hoc analysis of percentage change in EASI from baseline to week 16, patients aged 65 and older showed significant improvements in the 300 mg Q4W group (LS mean difference: −52.65, 95% CI: −95.69, −9.61). Patients with higher disease severity, as indicated by an IGA score of 4, also responded well, particularly in the 300 mg Q2W group (LS mean difference: −44.00, 95% CI: −73.83, −14.18) and the 300 mg Q4W group (LS mean difference: −55.45, 95% CI: −84.80, −26.11). In addition, those with a baseline NRS score of 7 or higher (300 mg Q4W: LS mean difference: −52.58, 95% CI: −76.49, −28.67), a BSA of 10–30% (300 mg Q4W: LS mean difference: −56.25, 95% CI: −94.29, −18.20), and patients who had not previously received immunosuppressive therapy (300 mg Q4W: LS mean difference: −44.48, 95% CI: −62.43, −26.53) exhibited greater EASI score improvements.

# DISCUSSION

The engineered Fc mutation in MG-K10, designed to extend its half-life, suggests its suitability for potentially less frequent administration than existing anti-IL-4Rα monoclonal antibodies.[11,12] Our findings indicate that MG-K10 was associated with improvements in EASI scores, reflected MG-K10's capability to meaningfully reduce AD symptoms. Enhancements in patient-reported quality of life supported its beneficial impact. The safety profile of MG-K10 appeared favorable. Overall, the two dose groups of 300 mg MG-K10 were more effective than the 150 mg dose group, especially in 300 mg Q4W group. Collectively, these findings suggest that MG-K10, with its extended half-life and reduced administration frequency, offers a potential long-acting therapeutic

**TABLE 3. Adverse Events**

| Events, n (%) | MG-K10 150 mg Q4W (n = 41) | MG-K10 300 mg Q2W (n = 41) | MG-K10 300 mg Q4W (n = 41) | Placebo Q2W (n = 40) | Total (N = 163) |
|---|---|---|---|---|---|
| Any AE | 37 (90.2) | 36 (87.8) | 37 (90.2) | 36 (90.0) | 146 (89.6) |
| TRAEs | 9 (22.0) | 14 (34.1) | 15 (36.6) | 10 (25.0) | 48 (29.4) |
| SAEs | 1 (2.4) | 0 | 1 (2.4) | 1 (2.5) | 3 (1.8) |
| Treatment-related SAEs | 0 | 0 | 0 | 0 | 0 |
| AEs ≥3 grade | 2 (4.9) | 1 (2.4) | 1 (2.4) | 2 (5.0) | 6 (3.7) |
| TRAEs ≥3 grade | 0 | 0 | 0 | 0 | 0 |
| AEs leading to withdraw from study | 1 (2.4) | 0 | 1 (2.4) | 1 (2.5) | 3 (1.8) |
| Death | 0 | 0 | 0 | 0 | 0 |
| The most common AE (≥5%) | | | | | |
| COVID-19 | 4 (9.8) | 7 (17.1) | 11 (26.8) | 10 (25.0) | 32 (19.6) |
| Fever | 7 (17.1) | 7 (17.1) | 7 (17.1) | 3 (7.5) | 24 (14.7) |
| Upper respiratory tract infections | 6 (14.6) | 4 (9.8) | 2 (4.9) | 6 (15.0) | 18 (11.0) |
| Suspected COVID-19 infection | 4 (9.8) | 4 (9.8) | 3 (7.3) | 1 (2.5) | 12 (7.4) |
| Urinary tract infection | 0 | 4 (9.8) | 1 (2.4) | 6 (15.0) | 11 (6.7) |
| Hyperuricemia | 3 (7.3) | 0 | 7 (17.1) | 1 (2.5) | 11 (6.7) |
| Hyperlipidemia | 3 (7.3) | 2 (4.9) | 3 (7.3) | 3 (7.5) | 11 (6.7) |
| Sinus arrhythmia | 0 | 2 (4.9) | 3 (7.3) | 5 (12.5) | 10 (6.1) |
| Cough | 2 (4.9) | 3 (7.3) | 3 (7.3) | 2 (5.0) | 10 (6.1) |

*AE, adverse event; COVID-19, coronavirus disease 2019; SAE, serious adverse event; TRAE, treatment-related adverse event.*

option in AD, emphasizing the need for additional studies to confirm its long-term efficacy and safety.

In this study, MG-K10 demonstrated significant efficacy in treating moderate-to-severe AD, particularly at the 300 mg Q4W dosing regimen, with meaningful reductions in EASI scores and pruritus. A phase IIb study of dupilumab reported LS mean percentage changes in EASI scores from baseline to week 16 of −45.4% and −50.1% for 300 mg Q4W and 300 mg Q2W regimens, respectively.[15] Similarly, CM310, another IL-4Rα-targeting monoclonal antibody, showed reductions of −19.2% and −30.7% for 150 mg Q2W and 300 mg Q2W doses, respectively.[11] In comparison, MG-K10 achieved reductions of −38.83% for the 300 mg Q4W dose and −27.06% for the 300 mg Q2W dose at week 16, indicating that its efficacy is in line with these established treatments. Moreover, MG-K10 exhibited a rapid onset of efficacy, with a decrease in EASI scores observed as early as week 2, and these improvements were sustained through week 24 after treatment cessation. The extended dosing interval of MG-K10 (Q4W) presents a significant advantage for patient adherence compared with more frequent dosing schedules like those of dupilumab. As literature has noted, one of the barriers to treatment continuation with dupilumab is economic, with discontinuation often resulting from high co-pays or insurance denial.[16] MG-K10's longer dosing interval could help mitigate these barriers by reducing the frequency of clinic visits and associated health care costs, making it a more accessible treatment option for many patients. This aspect of convenience, coupled with efficacy comparable with dupilumab, positions MG-K10 as a potential alternative for the treatment of moderate-to-severe AD.

In our study, the difference of LS mean percent changes versus placebo in EASI scores at week 16 was −16.00% for the 150 mg Q4W group, −38.83% for the 300 mg Q4W group, and −27.06% for the 300 mg Q2W group. Although 300 mg Q4W outperformed 300 mg Q2W in absolute terms, this result does not follow the expected dose-dependent trend. The overlapping 95% CIs suggested no conclusive claim of a dose-dependent discrepancy could be made, though this study was not powered to detect the difference between these two dosing regimens. Furthermore, similar nonlinear dose–response relationships have been observed with other biologics. For example, higher numerical improvement in disease severity was reported in pediatric AD patients treated with dupilumab at 2 mg/kg QW versus 4 mg/kg QW despite saturation of the IL-4 receptor at both regimens.[17] In a study of omalizumab for chronic idiopathic urticaria, the 300 mg dose demonstrated greater efficacy than the higher 600 mg dose, suggesting that increased dosing does not always result in better or equal outcomes.[18] Similarly, in a phase IIb trial of nemolizumab in AD, the 30 mg Q4W dose was more effective than the 90 mg Q4W dose.[19] Though the pharmacokinetic-pharmacodynamic models were constructed to show that maximum nemolizumab effect was observed at serum concentrations close to the observed serum concentration for the 30-mg dose,[19] the underlying mechanism remains to be explored. In these cases, once a therapeutic threshold or maximum PD effect is reached, further dose increases do not enhance efficacy, which may explain the results seen in our trial. The unpublished data of MG-K10 in healthy volunteers demonstrated the IL-4Rα saturation was maintained to be nearly 100% by day 43 in subjects receiving single dose of 300 or 600 mg MG-K10. The analysis of PK, TARC, and IgE levels in this study showed that both the 300 mg Q2W and Q4W regimens achieved through concentrations sufficient to reach an efficacy plateau with a similar suppression trend of

TARC and IgE levels. Thus, increasing the dosing frequency did not provide additional clinical benefits. The 300 mg Q4W regimen is being further evaluated in a larger phase III trial for AD, and both the 300 mg Q2W and Q4W regimens are being studied for their efficacy in other indications.

Considering secondary endpoints like symptom scores and quality of life, the MG-K10 demonstrated improvements in IGA scores, with benefits becoming apparent early on and sustained throughout the study. These improvements indicated that MG-K10 might have a lasting effect on AD symptoms. However, the MG-K10 150 mg Q4W dosage did not exhibit statistically significant differences from the placebo in several key measures, including weekly peak pruritus NRS scores and BSA coverage. But both 300 mg dosages of MG-K10 showed enhanced outcomes. Furthermore, in post hoc analyses, eosinophils, LDH, and the time to first rescue therapy all demonstrated the potential efficacy of MG-K10, which can reduce the activity of AD, consistent with the efficacy trend of the primary endpoint. Especially, the 300 mg Q4W group demonstrated the best potential efficacy in LDH results and also showed a latest trend in the time to first rescue therapy during the 16-week treatment period. Besides, the blood concentrations of MG-K10 in 300 mg Q4W group achieved steady state by week 4 following the initial administration, while the patients with dupilumab in 300 mg Q4W group reached a steady state by week 16.[20] Besides, the study observed a rapid and sustained decline throughout the trial in the levels of TARC across all MG-K10 dose groups, which aligns with the therapeutic goal of modulating immune responses in AD. Similarly, a continuous decrease in serum IgE levels was observed with MG-K10.[21] The steady decline of Th2-related biomarker levels in our study signifies MG-K10's potential efficacy. Moreover, post hoc analyses indicate that the absolute majority of subgroups show a better response to MG-K10 treatment than placebo.

The safety profile of MG-K10 observed in this study appears favorable, with no significant reports of injection site reactions or conjunctivitis. This aligns with findings from other trials of IL-4Rα inhibitors.[11,12,15,22] For example, in a phase II clinical trial of dupilumab, injection site reactions and conjunctivitis were observed in 7% of patients.[15] A phase II study of CM310 reported injection site reactions in only 1.7% of patients, with no cases of conjunctivitis.[11] However, real-world data from a meta-analysis of dupilumab efficacy and AEs offer a broader perspective on safety. In the meta-analysis, conjunctivitis was the most frequently reported AE, affecting approximately 26.1% of patients across 14 studies, with higher rates in European (30.8%) and Asian (36.4%) populations compared with North American patients (11.2%). Although the conjunctivitis was generally treatable and did not typically lead to treatment discontinuation, it was associated with a history of allergic conjunctivitis in many cases. Blepharitis and keratitis were also observed in a smaller proportion of patients, indicating that ocular surface disease is a notable concern during long-term treatment with dupilumab.[23] In comparison, no cases of conjunctivitis or other ocular surface diseases were reported with MG-K10 in this trial, suggesting a potentially better safety profile regarding ocular events. However, the relatively small sample size of this study (163 patients) limits the ability to draw definitive conclusions about rare AEs. Given the favorable short-term safety results, MG-K10's tolerability will be further explored in larger randomized controlled trials, and future real-world evidence will be necessary to confirm its long-term safety profile.

The PK/PD data for MG-K10 demonstrate that steady-state concentrations are achieved by week 4, supporting the 4-week dosing interval for the 300 mg Q4W regimen, with a loading dose of 600 mg to achieve steady-state concentration more rapidly. This aligns with the efficacy results observed in our study, where the 300 mg Q4W group exhibited substantial improvements in EASI scores. Importantly, the safety data did not indicate any increased risks, with no evidence of heightened safety concerns compared with existing biologics like dupilumab. In fact, MG-K10 exhibited a favorable safety profile, with no new safety signals emerging over the 16-week study period. However, we acknowledge that long-term safety must be monitored further, as the chronic nature of AD necessitates extended observation. In addition, population pharmacokinetic analyses indicate that the accumulation ratio for the target dose of 300 mg Q4W with a 600 mg loading dose is less than 1, suggesting that MG-K10 does not accumulate significantly over time (unpublished data). This finding mitigates concerns about prolonged exposure to high drug concentrations and supports the continued investigation of MG-K10 as a long-term treatment for AD.

The post hoc subgroup analyses provided some insights into which patient populations might derive the greatest benefit from MG-K10 treatment. Notably, patients aged 65 and older, those with more severe disease (IGA score of 4), and individuals with a baseline NRS score of 7 or higher showed the most significant improvements. In addition, patients with a lower BSA (10–30%) and those who had not previously received immunosuppressive therapy responded better to the 300 mg Q4W regimen. However, it is important to interpret these results with caution, as they are derived from post hoc analyses without formal P-interaction testing. These findings suggest potential areas for further exploration in future studies but should be regarded as hypothesis-generating rather than definitive conclusions. Larger, prospectively designed studies will be necessary to confirm whether these subgroups consistently benefit from MG-K10 treatment in clinical practice.

This study has several limitations that must be considered when interpreting the results. First, as an exploratory phase II clinical trial, it was conducted with a relatively modest sample size (163 patients) and a short treatment duration of 16 weeks. These factors limit our ability to comprehensively assess the long-term efficacy and safety of MG-K10, particularly given the

chronic nature of AD. In addition, the lack of statistical power considerations means that while our findings are promising, they should be interpreted as preliminary. The limited patient population also restricts the generalizability of these results across a wider and more diverse demographic. Furthermore, the response rates of placebo were slightly high in this study, which might be attributed to the numerically low average baseline EASI scores and small proportion of patients with IGA score 4, and the effect of background treatment (eg, emollients). Though commonly observed in AD trials,[24] it warrants careful consideration and more studies. Acknowledging these limitations, MG-K10's efficacy and safety are being further evaluated in a larger, more definitive phase III trial. This trial will involve a 52-week treatment period with MG-K10, a longer follow-up period, and a broader patient cohort, aiming to provide more robust data on its long-term potential.

## CONCLUSION

MG-K10 shows promise in managing symptoms of moderate-to-severe AD, with an encouraging safety profile and the potential for less frequent dosing compared with existing therapies. However, due to the exploratory nature of this study, the findings should be interpreted cautiously. The observed efficacy and safety of the 300 mg Q4W dosing regimen warrant further validation in the ongoing phase III trial (NCT06026891), which will include a larger patient cohort and a prolonged treatment duration. This phase III trial is expected to provide more definitive data on MG-K10's role as a long-acting therapeutic option for AD, marking the first phase III investigation of an anti-IL-4Rα antibody with a 4-week dosing interval.

## SUPPLEMENTARY MATERIAL

Supplementary Data

## REFERENCES


1. Weidinger S, Novak N. Atopic dermatitis. *Lancet*. 2016;387(10023):1109–1122.
2. Bieber T. Atopic dermatitis: An expanding therapeutic pipeline for a complex disease. *Nat Rev Drug Discov*. 2022;21(1):21–40.
3. Pereyra-Rodriguez JJ, Baldrich ES, Ruiz-Villaverde R, et al. Clinical approach to patients with moderate-to-severe atopic dermatitis: A Spanish Delphi consensus. *Acta Derm Venereol*. 2023;103:adv12314.
4. Bacci ED, Correll JR, Pierce EJ, et al. Burden of adult atopic dermatitis and unmet needs with existing therapies. *J Dermatolog Treat*. 2023;34(1):2202288.
5. Misery L, Seneschal J, Corgibet F, et al. Impact of atopic dermatitis on patients and their partners. *Acta Derm Venereol*. 2023;103:adv5285.
6. Narla S, Silverberg JI. Dermatology for the internist: Optimal diagnosis and management of atopic dermatitis. *Ann Med*. 2021;53(1):2165–2177.
7. Vestergaard C, Wollenberg A, Thyssen JP. European Task Force on Atopic Dermatitis (ETFAD) Position Paper: Treatment of parental atopic dermatitis during preconception, pregnancy and lactation period. *J Eur Acad Dermatol Venereol*. 2020;34(2):426–427.
8. Daniele S, Bunick C. JAK inhibitor safety compared to traditional systemic immunosuppressive therapies. *J Drugs Dermatol*. 2022;21(12):1298–1303.
9. Atopic Dermatitis Working Group IG, Chinese Society of Dermatology. Guideline for diagnosis and treatment of atopic dermatitis in China (2020). *Chinese Journal of Dermatology*. 2020;53:81–88.
10. Beck LA, Thaci D, Hamilton JD, et al. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med*. 2014;371(2):130–139.
11. Zhao Y, Zhang J, Yang B, et al. Efficacy and safety of CM310 in moderate-to-severe atopic dermatitis: A multicenter, randomized, double-blind, placebo-controlled phase 2b trial. *Chin Med J (Engl)*. 2024;137(2):200–208.
12. Zhao Y, Wu L, Lu Q, 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(4):633–641.
13. Kang DH, Kwon SH, Lew BL. Four-year long-term drug survival of dupilumab analyzed by treatment period in patients with moderate to severe atopic dermatitis: A real-world retrospective study. *J Dermatol*. 2024;51(3):e63–e65.
14. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: Section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338–351.
15. Thaci D, Simpson EL, Beck LA, 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(10013):40–52.
16. Khosravi H, Zhang S, Anderson AM, et al. Dupilumab drug survival, treatment failures, and insurance approval at a tertiary care center in the United States. *J Am Acad Dermatol*. 2020;82(4):1023–1024.
17. Cork MJ, Thaci D, Eichenfield LF, et al. Dupilumab provides favourable long-term safety and efficacy in children aged >/= 6 to < 12 years with uncontrolled severe atopic dermatitis: Results from an open-label phase IIa study and subsequent phase III open-label extension study. *Br J Dermatol*. 2021;184(5):857–870.
18. Saini S, Rosen KE, Hsieh HJ, et al. A randomized, placebo-controlled, dose-ranging study of single-dose omalizumab in patients with H1-antihistamine-refractory chronic idiopathic urticaria. *J Allergy Clin Immunol*. 2011;128(3):567–573.e561.
19. Silverberg JI, Pinter A, Pulka G, et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus. *J Allergy Clin Immunol*. 2020;145(1):173–182.
20. Blauvelt A, Guttman-Yassky E, Paller AS, et al. Long-Term efficacy and safety of Dupilumab in adolescents with moderate-to-severe atopic dermatitis: Results through week 52 from a phase III Open-Label extension trial (LIBERTY AD PED-OLE). *Am J Clin Dermatol*. 2022;23(3):365–383.
21. Huang TH, Chen YC, Lin SY, et al. Treatment of atopic dermatitis with dupilumab in Taiwan: Dynamic changes of IgE levels as a potential response biomarker. *Eur J Dermatol*. 2019;29(6):658–659.
22. Simpson EL, Bieber T, Guttman-Yassky E, et al.; SOLO 1 and SOLO 2 Investigators. Two phase 3 trials of Dupilumab versus placebo in atopic dermatitis. *N Engl J Med*. 2016;375(24):2335–2348.
23. Halling AS, Loft N, Silverberg JI, et al. Real-world evidence of dupilumab efficacy and risk of adverse events: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2021;84(1):139–147.
24. Bieber T, Simpson EL, Silverberg JI, et al.; JADE COMPARE Investigators. Abrocitinib versus placebo or Dupilumab for atopic dermatitis. *N Engl J Med*. 2021;384(12):1101–1112.