EA DV CONGRESS
PARIS 17-20 SEPTEMBER 2025
EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 66

Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of AK120 in Participants with Moderate to Severe Atopic Dermatitis: Results from a Randomized, Double-blind, Placebo-controlled Phase II Clinical Trial

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Introduction & Objectives:

Interleukin-4 (IL-4) and interleukin-13 (IL-13) are two essential cytokines involved in the Th2-mediated inflammatory response of diseases, such as atopic dermatitis (AD). AK120 is a humanized immunoglobulin G subclass 4 (IgG4) monoclonal antibody (mAb) directed against the IL-4 receptor alpha (IL-4Rα) subunit shared by the IL-4 and IL-13 receptor complexes. The binding of AK120 to IL-4Rα results in inhibition of the signaling of the IL-4 and IL-13 cytokines. This trial was to evaluate the efficacy, pharmacokinetics (PK), pharmacodynamics (PD), and safety of AK120 following multiple subcutaneous (SC) administrations in AD participants.

Materials & Methods:

Participants (male and female) with age ≥ 18 and ≤ 75 years were enrolled. There were 4 parallel dose groups with 160 participants. Eligible participants were randomized in a 1:1:1:1 ratio to receive 1 of 3 dose levels of the active drug AK120 (N=120) or matching placebo (N=40). For group 1 to 3, participants received a SC injection of 150mg, 300mg or 450 mg AK120 every 2 weeks (Q2W); participants in group 4 received placebo Q2W from week 0 to 14, then were randomly assigned in a 1:1 ratio to group 4A (AK120 300mg Q2W) and group 4B (AK120 450mg Q2W) from week 16 (Figure 1).

Results:

Efficacy: The proportion of participants in AK120 treatment groups (150 mg, 300 mg, 450 mg) who achieved EASI75 at week 16 was higher than in the placebo group, with the percentages of 55.0% (22/40), 57.5% (23/40), 56.1% (23/41) and 28.2% (11/39) ($P<0.05$) (Figure 2). The IGA0/1 response rate of each AK120 group at week 16 was 32.5% (13/40), 27.5% (11/40), and 29.3% (12/41), respectively, which was higher than that of the placebo group (10.3%, 4/39). Following one year treatment, the EASI75 and IGA0/1 response rates can be effectively maintained and further improved.

PK&PD: Steady-state concentrations were achieved by Week 12 in each dose of groups. The mean ±SD steady-state trough concentrations at Week 16 were 14.7 μg/mL, 45.2 μg/mL, and 78.8 μg/mL in 150 mg Q2W (300 mg loading dose), 300 mg Q2W (600 mg loading dose), and 450 mg Q2W (Figure 3). Serum TARC/CCL17 can be almost maintained with an over 50 % decrease in all AK120 treatment groups (Figure 4). Serum Ig E decreased over 40% at week 16 in the AK120 300-450 mg Q2W groups (Figure 5).

Safety: A total of 141 (90.4%) participants received AK120 treatment and 27 (69.2%) participants who received the placebo experienced at least one treatment-emergent adverse event (TEAE). The majority of TEAEs were mild and moderate in severity. The incidence of TEAE in AK120 groups was 90.4% for the overall treatment and follow-up period. During the placebo control period, incidence of TEAE was similar between the AK120 groups and the placebo group (71.1% vs. 69.2%). The most common treatment-related adverse events (TRAE) that occurred in the AK120 groups were elevated hyperuricaemia (8.3%, 13/156), upper respiratory tract infections (5.8%, 9/156) and alanine aminotransferase (5.1%, 8/156). There were 9 serious adverse events (SAE) in the trial, and all had improved or recovered. The majority were judged as possibly unrelated to the investigational products by investigators. No death was reported in the trial.

Conclusion:

AK120 ranging from 150 mg to 450 mg administered via SC injection was safe and well tolerated, and showed prefound efficacy in AD participants, which provided sufficient basis for the dose selection in the phase 3 confirmative trial.

Figure 1 Overall Study Design

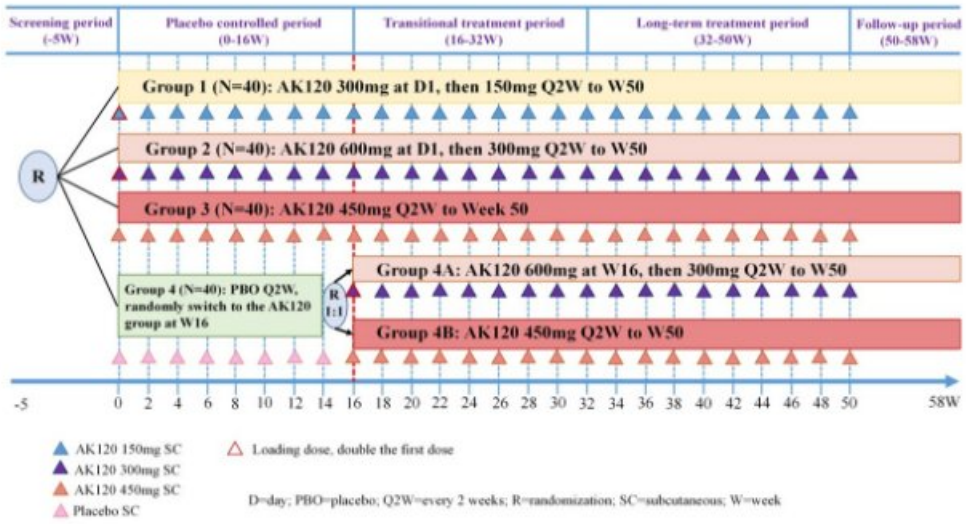


Figure 2 EASI 75 Response at Week 16

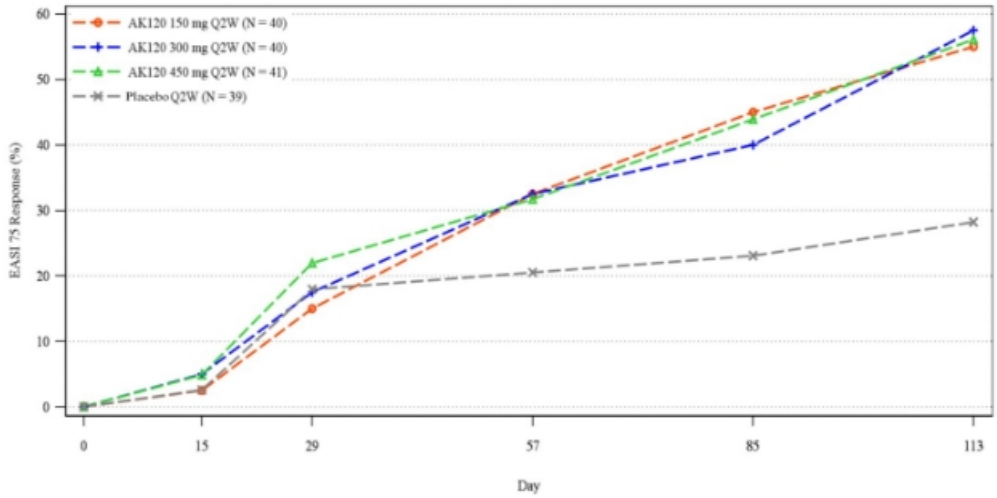
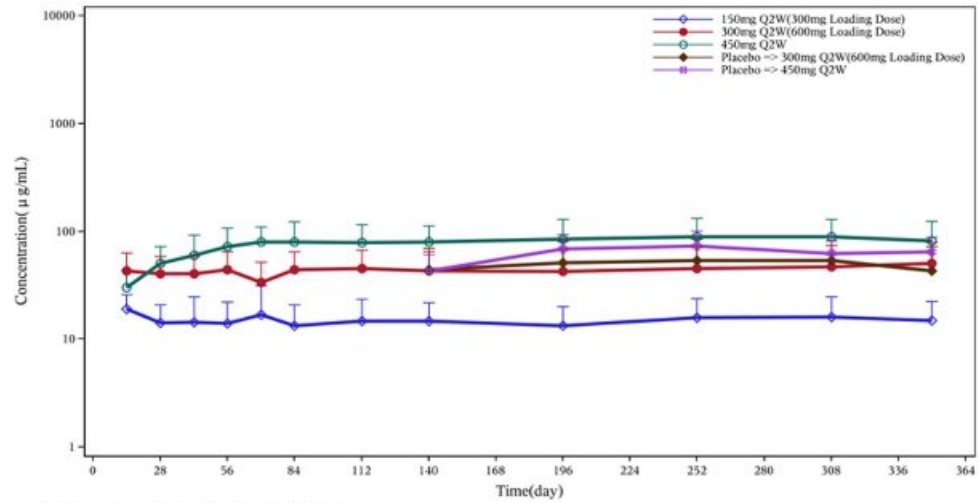
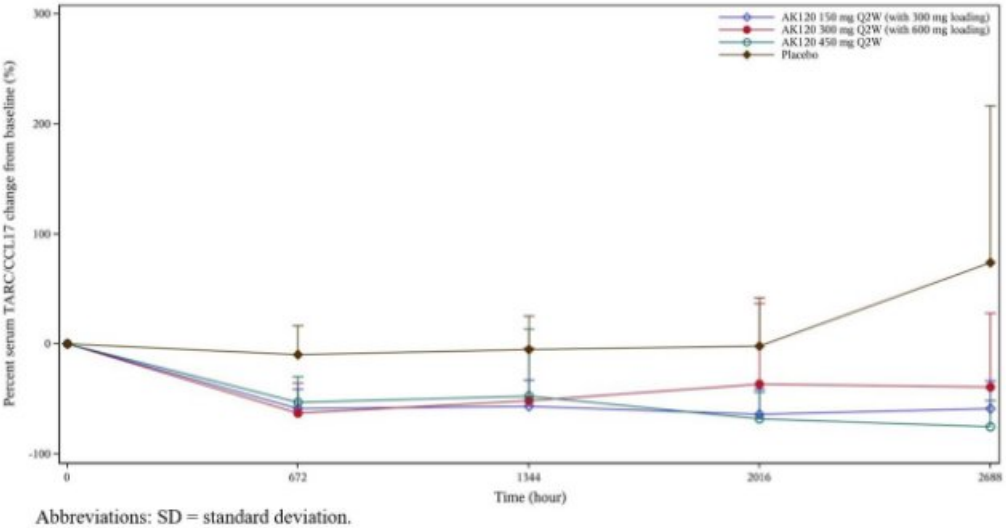


Figure 3 Mean (+SD) Serum Trough Concentration -Time Profiles in AD Patients



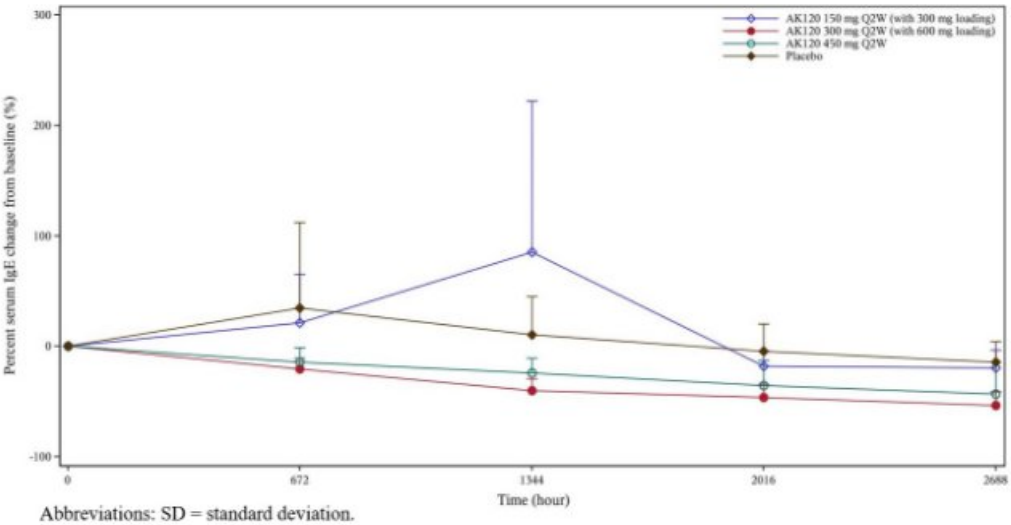
Abbreviations: SD = standard deviation.

Figure 4 Mean (+SD) Serum TARC -Time Profiles



Abbreviations: SD = standard deviation.

Figure 5 Mean (+SD) Serum Ig E -Time Profiles



Abbreviations: SD = standard deviation.