Durable Maintenance of EASI-90 With Amlitelimab in Adults With Moderate-to-Severe Atopic Dermatitis: 52-Week Results From The STREAM-AD Phase 2b Trial

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Key Conclusions

1. **High proportions of clinical responders *achieved EASI-90 responses* at Week 24**
2. **The majority *maintained* EASI-90 responses with *continued amlitelimab treatment* at Week 52**
3. **EASI-90 was also *maintained* at Week 52 after 28 weeks of *withdrawal from amlitelimab* by the majority of Week 24 EASI-90 responders**
4. **Targeting the OX40L/OX40 pathway via amlitelimab may lead to *sustained off-drug disease control* in patients with moderate-to-severe atopic dermatitis**
5. ***Ongoing OCEANA trials* will further evaluate the effect of continued amlitelimab treatment or withdrawal over longer observational period**
   - **Core Phase 3 trials (COAST-1, COAST-2, SHORE, AQUA)**
   - **Long-term studies (ATLANTIS, RIVER-AD, ESTUARY)**

Introduction

- **Amlitelimab** is a fully human, **nondepleting, anti-OX40L monoclonal antibody**[1,2]
- **Amlitelimab targets OX40 ligand** on APCs during early stages of T-cell activation and T-cell-mediated inflammation[3]
- Aims to **normalize the overactive immune system** and disease activity, restoring immune balance **without depleting T-cells**[4,5]
- Efficacy and safety of amlitelimab in patients with moderate-to-severe atopic dermatitis was evaluated in the Phase 2b STREAM-AD trial[6]
- The primary and key secondary end points **were met (Figure 2; Table 1)**
- **Durable responses were observed** on and off amlitelimab at Week 52 **(Figure 3)**

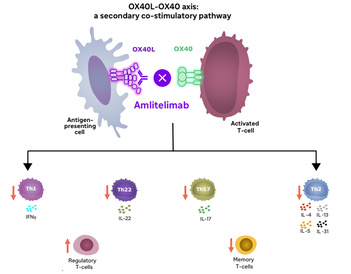
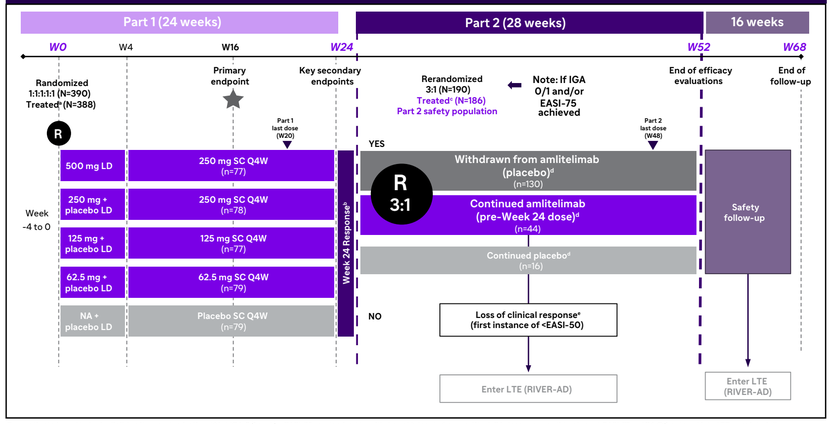


Figure adapted from Fu Y, et al. *Acta Pharm Sin B.* 2020;10(3):414–433 and Haddad EB, et al. *Dermatol Ther (Heidelb).* 2022;12(7):1501–1533.
IFNγ, interferon gamma; IL, interleukin; OX40L, OX40 Ligand; Th, helper T cell.

Figure 1: STREAM-AD Phase 2b trial design (NCT05131477)

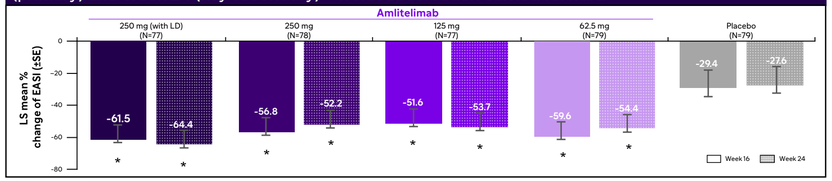


[a]Two patients found to be ineligible after randomization; [b]Met IGA 0/1 and/or EASI-75 randomized to withdrawal (placebo) or pre-Week 24 dose groups; did not meet EASI-75 or IGA 0/1 entered into LTE or safety follow-up; [c]Four patients were rerandomized but not treated; [d]Patients demonstrating loss of clinical response during Part 2 were entered into the LTE or safety follow-up; [e]Loss of clinical response was defined as the first instance of <EASI-50 during Part 2 in which rescue therapy was no longer permitted.
AD Atopic Dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; LD, loading dose; LTE, long-term extension; NA, not applicable; Q4W, every 4 weeks; R, randomization; SC, subcutaneous; W, week.

Objective

Evaluate **proportions of clinical responders** *(defined as patients who achieved IGA 0/1 and/or EASI-75 at Week 24 rerandomization)* **achieving EASI-90** at Week 24, and among those, proportions **maintaining EASI-90** at Week 52 while on or off amlitelimab in Part 2 of the STREAM-AD trial

Figure 2: STREAM-AD Part 1: Percentage point changes in EASI score from baseline at Week 16 (primary) and Week 24 (key secondary)—worst observation carried forward[1,a]



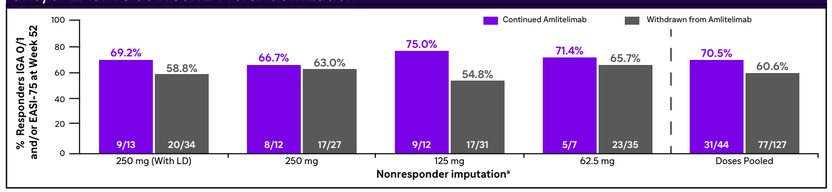
*P≤0.0002 compared with placebo.
[a]Any data on or after treatment discontinuation or use of rescue medication or prohibited medications and procedures affecting efficacy, whichever is earlier, are set to missing and imputed by worst observation carried forward.
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; LD, loading dose; LS, least squares; SE, standard error.

Table 1: STREAM-AD Part 1: Proportions of patients achieving EASI-75, IGA 0/1, and EASI-90 with amlitelimab at Week 24 vs placebo-*(NRI)*[1,a]

Proportion of Participants, n(%)	250 mg LD (N=77)	250 mg (N=78)	125 mg (N=77)	62.5 mg (N=79)	Placebo (N=79)
EASI-75	42 (54.5%)**	30 (38.5%)*	38 (49.4%)**	32 (40.5%)*	14 (17.7%)
IGA 0/1	35 (45.5%)**	26 (33.3%)**	31 (40.3%)**	23 (29.1%)*	9 (11.4%)
EASI-90	29 (37.7%)***	21 (26.9%)**	25 (32.5%)**	19 (24.1%)*	9 (11.4%)

*P<0.05; **P<0.01; ***P<0.001 (NRI).
[a]Data collected after early treatment discontinuation due to reasons other than lack of efficacy before endpoint time point are included. Data on or after rescue medication or prohibited medications and procedures affecting efficacy start date or after the date of treatment discontinuation due to lack of efficacy before endpoint time point, were considered as nonresponders. Any other unobserved values or other missing data are considered as nonresponders at Week 24.
EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; NRI, nonresponder imputation.

Figure 3: Durability of responses in clinical responders defined as patients who achieved IGA 0/1 and/or EASI-75 at Week 24 rerandomization[a]



[a]Participants who discontinued treatment due to lack of efficacy or received rescue medications or prohibited medications affecting efficacy on or before time point were considered nonresponders. At time of treatment discontinuation or rescue medicine, use is also imputed as nonresponder.
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; LD, loading dose.

Amlitelimab demonstrated a favorable safety profile[a]

- Most ***TEAEs were mild or moderate*** and considered ***not related*** to treatment
- ***Low incidence of SAEs and treatment discontinuation*** reported across all treatment arms with both 24 and 52 weeks of amlitelimab exposure
- No reports of parasitic infections, opportunistic infections[b], malignancy, chills/aphthous ulcers, or pyrexia/influenza-like illness within 72 hours of injection, or serious injection-site reactions; no deaths occurred

[a]Treatment with amlitelimab was given through Week 52 (last dose at Week 48) with safety follow-up through Week 68. Data cutoff was when the last participant reached Week 52; [b]As determined in standardized *Medical Dictionary for Regulatory Activities* queries, opportunistic infections [narrow].

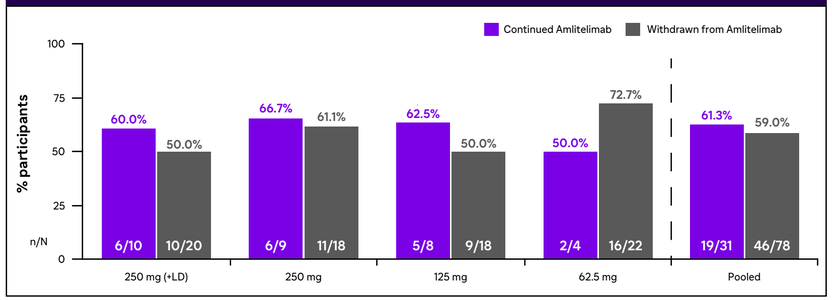
Results

Table 2: Week 24: EASI-90 responses among clinical responders *(NRI)*[a–c]

Proportion of Participants, n(%)	250 mg LD	250 mg	125 mg	62.5 mg	Pooled
EASI-90	30/47 (63.8%)	27/40 (67.5%)	26/45 (57.8%)	26/42 (61.9%)	109/174 (62.6%)

[a]Includes participants who received amlitelimab in Part 1 (excludes participants who received placebo in Part 1); [b]Percentage is based on the total number of responders and nonresponders, including imputed nonresponders; [c]Patients who discontinued treatment due to lack of efficacy or use of rescue medications or prohibited medications and procedures affecting efficacy on or after the rerandomization date or first-dose date and before the corresponding time point in Part 2 were considered as nonresponders. Patients who received rescue medications or prohibited medications and procedures affecting efficacy in Part 1 are not considered as nonresponders.
Patients with missing data were considered as nonresponders.
EASI, Eczema Area and Severity Index; LD, loading dose; NRI, nonresponder imputation.

Figure 4: Week 52: Maintenance of EASI-90 responses among Week 24 EASI-90 responders *(NRI)*[a–c]



[a]Includes participants who received amlitelimab in Part 1 (excludes participants who received placebo in Part 1); [b]Percentage is based on the total number of responders and nonresponders, including imputed nonresponders; [c]Patients who discontinued treatment due to lack of efficacy or use of rescue medications or prohibited medications and procedures affecting efficacy on or after the rerandomization date or first-dose date and before the corresponding time point in Part 2 were considered as nonresponders. Patients who received rescue medications or prohibited medications and procedures affecting efficacy in Part 1 are not considered as nonresponders.
Patients with missing data were considered as nonresponders.
EASI, Eczema Area and Severity Index; LD, loading dose; NRI, nonresponder imputation.

References: 1. Weidinger S, et al. *Br J Dermatol. 2023;189(5):531–539.* 2. Fu N, et al. *Front Immunol. 2021; 12:670637.* 3. Sadrolashrafi K, et al. *Cells. 2024;13(7):587.* 4. Elhai M, et al. *Proc Natl Acad Sci U S A. 2016;113(27):E3901–E3910.* 5. Krueger J, et al. *Poster presented at: EADV Congress; September 25–28, 2024; Amsterdam, Netherlands.* 6. Weidinger S, et al. *J Allergy Clin Immunol. 2025;155(4):1264–1275.* 7. Weidinger S, et al. *Nat Rev Dis Primers. 2018;4(1):1.*

Abbreviations: APC, antigen-presenting cell; EASI, Eczema Area and Severity Index; OX40L, OX40 ligand; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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