Long-term durability and stability of amlitelimab efficacy in adults with moderate-to-severe atopic dermatitis: 52-Week post hoc analysis of the STREAM-AD Phase 2b trial

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Key Conclusions

1. In the STREAM-AD study, participants who achieved clinical response at Week 24 maintained stable and durable IGA 0/1 responses with minimal fluctuations up to Week 52, regardless of whether they continued or were withdrawn from amlitelimab treatment
2. Stable and durable EASI-75 responses, with no or minimal fluctuations, were maintained up to Week 52 by STREAM-AD participants who achieved clinical response at Week 24, whether they continued or were withdrawn from amlitelimab treatment
3. These results indicate that amlitelimab may provide sustained effects, with clinical improvements persisting even after treatment withdrawal. This is especially meaningful for atopic dermatitis, where durable long-term disease control is a key goal

Introduction

- Amlitelimab (SAR445229, KY1005) is a fully human non-depleting anti-OX40 ligand (OX40L) monoclonal antibody[1,2]
- In the 2-part Phase 2b STREAM-AD clinical trial (NCT05131477) among participants with moderate-to-severe atopic dermatitis (AD)[2]:
  - The primary endpoint—percent change in EASI at Week 16—was met. Amlitelimab demonstrated sustained efficacy and a favorable safety profile through Week 24 (Part 1)
  - The durability of response in clinical responders (defined as those achieving EASI-75 and/or IGA 0/1) and safety on- and off-therapy was observed at Week 52 (Part 2)

Objective

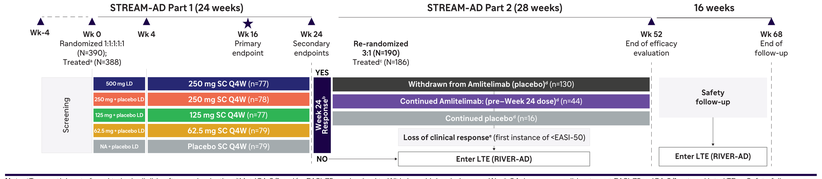
- To evaluate the stability and durability of response to amlitelimab on- and off-therapy during STREAM-AD Part 2 (Weeks 24-52) and to determine the proportions of participants with no or minimal efficacy fluctuations during this observation period of 28 weeks

Methods

Study Design

- STREAM-AD is a 2-part, randomized, double-blind, placebo-controlled, Phase 2b trial in adults (18 to <75 years) with moderate-to-severe AD (**Figure 1**)
  - **Part 1:** Participants (n=390) were randomized 1:1:1:1:1 to receive subcutaneous (SC) amlitelimab Q4W (250 mg with 500 mg loading dose [LD]; 250 mg without LD; 125 mg; or 62.5 mg) or placebo Q4W
  - **Part 2:** Of those who completed Part 1, 190 clinical responders (defined as participants achieving EASI-75 and/or IGA 0/1 at Week 24) were re-randomized 3:1 to amlitelimab withdrawal (switch to placebo) or continuation of their pre–Week 24 SC Q4W dose of amlitelimab
- For this post hoc analysis, response stability was defined as the proportion of participants achieving EASI-75 or IGA 0/1 for at least 80% of visits in Part 2 of STREAM-AD
- Individual participant trajectories of EASI were evaluated for those that achieved EASI-75 at Week 52

Figure 1. Study design of STREAM-AD (NCT05131477)

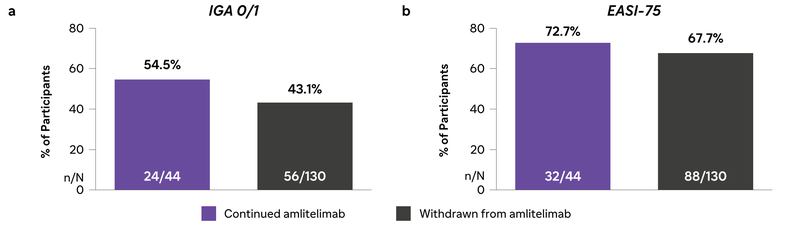


Note: [a]Two participants found to be ineligible after randomization; [b]Met IGA 0/1 and/or EASI-75 randomised to Withdrawal (placebo) or pre–Week 24 dose groups; did not meet EASI-75 or IGA 0/1 entered into LTE or Safety follow-up; [c]Four participants were re-randomised but not treated; [d]Participants 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 where rescue therapy was no longer permitted.

Results

- In Part 2 of STREAM-AD, amlitelimab demonstrated stable and durable efficacy among Week 24 clinical responders in both those who continued amlitelimab (N=44) and those who were withdrawn from amlitelimab (N=130)
  - By Week 52, IGA 0/1 was maintained for at least 80% of Part 2 visits in 24 (54.5%) participants who continued amlitelimab and 56 (43.1%) who were withdrawn from amlitelimab treatment (**Figure 2a**)
  - By Week 52, EASI-75 was maintained for at least 80% of STREAM-AD Part 2 visits in 32 (72.7%) participants who continued amlitelimab and 88 (67.7%) participants who were withdrawn from amlitelimab treatment (**Figure 2b**)

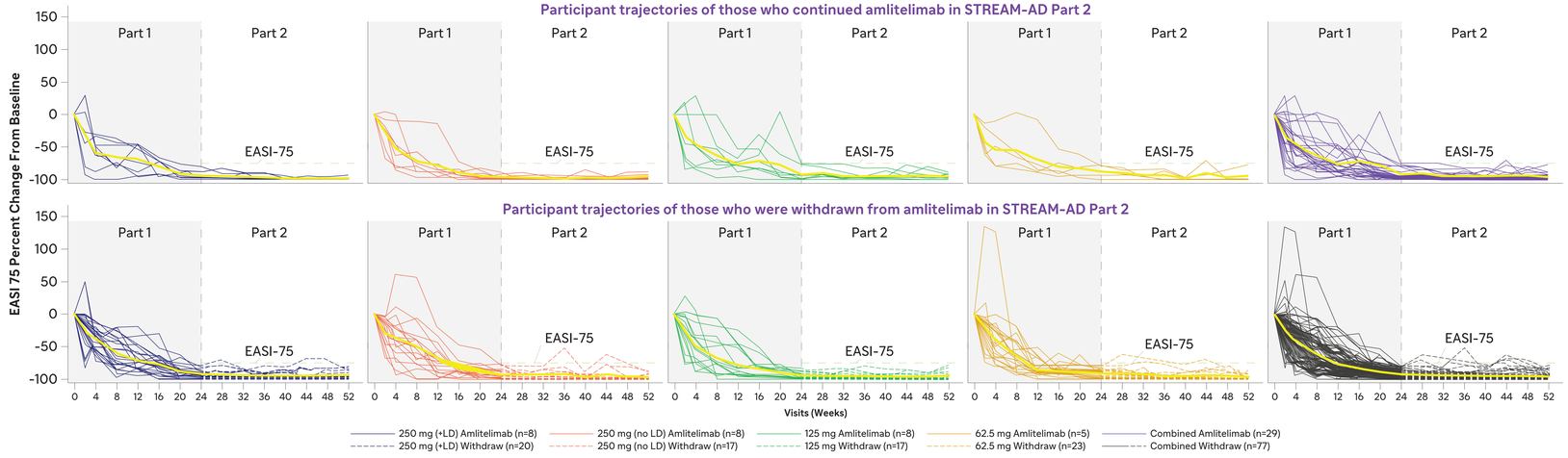
Figure 2. Clinical responders maintaining IGA 0/1 and EASI-75 for ≥80% of STREAM-AD Part 2 study visits in the pooled amlitelimab dose groups



Note: 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.

- The individual participant trajectories of Week 24 clinical responders who achieved EASI-75 at Week 52, demonstrate that participants exhibit no or minimal fluctuations in EASI-75 during Part 2, regardless of whether they continued or were withdrawn from amlitelimab (**Figure 3**)

Figure 3. Individual participant trajectories of EASI (baseline –Week 52) for Week 52 EASI-75 responders on- and off-therapy in STREAM-AD Part 2



Note: The mean slope for the patient trajectories is depicted by the yellow line. A dotted vertical blue line denotes Week 24, while a dotted horizontal green line signifies a 75% reduction from baseline. 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.

References

1. Weidinger S, et al. *Br J Dermatol*. 2023;189(5):531-539. 2. Weidinger S, et al. *J Allergy Clin Immunol Pract*. 2024; doi: 10.1016/j.jaci.2024.10.031. 3. ClinicalTrials.gov identifier: NCT05131477. Accessed August 26, 2024. clinicaltrials.gov/ct2/show/NCT05131477. 4. ClinicalTrials.gov identifier: NCT05492578. Accessed August 26, 2024. clinicaltrials.gov/ct2/show/NCT05492578.

Abbreviations

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA 0/1, Investigator's Global Assessment Score of 0 or 1; LTE, long-term extension; NRI, non-responder imputation; Q4W, every 4 weeks; SC, subcutaneous; Wk, week.

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Disclosures

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