Impact of amlitelimab (an anti-OX40 Ligand antibody) on clinical outcome assessments for atopic dermatitis: results from the 52-week STREAM-AD phase 2b study in adults with moderate-to-severe atopic dermatitis

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Introduction/Background: Atopic dermatitis (AD) is a chronic heterogeneous inflammatory disease characterized by recurrent eczematous lesions. Amlitelimab is a fully human, nondepleting, anti-OX40 Ligand (OX40L) monoclonal antibody that blocks upstream OX40L signaling. Here, clinical outcome assessments (COAs) from the 24-week treatment period (Part 1) and 28-week amlitelimab maintenance/withdrawal period (Part 2) of the phase 2b STREAM-AD trial in adults with moderate-to-severe AD are presented.

Objectives: Evaluate maintenance of COAs response, including SCORing of Atopic Dermatitis (SCORAD), Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), and Atopic Dermatitis Control Tool (ADCT), in participants achieving ≥75% improvement in EASI from baseline (EASI-75) and/or an Investigator Global Assessment (IGA) score of clear/almost clear (IGA 0/1) at Week 24 in STREAM-AD.

Methods: STREAM-AD (NCT05131477), a randomized, double-blind, placebo-controlled, phase 2b trial, included a 24-week treatment period (Part 1), a 28-week maintenance/withdrawal period (Part 2), and a 16-week safety follow-up. In Part 1, adult participants with moderate-to-severe AD were randomized 1:1:1:1:1 to subcutaneous amlitelimab every 4 weeks (Q4W; 250 mg with 500 mg loading dose [250 mg...
The primary endpoint was percent change in EASI from baseline at Week 16. Of 390 participants enrolled in Part 1, 190 entered Part 2. Participants on amlitelimab achieving EASI-75 and/or IGA 0/1 at Week 24 were rerandomized 3:1 to withdraw or continue their pre-Week 24 amlitelimab dose (250 mg +LD, n=34 [withdrawal]/n=13 [continuing]; 250 mg, n=28/n=12; 125 mg, n=33/n=12; 62.5 mg, n=35/n=7); participants achieving EASI-75 and/or IGA 0/1 on placebo continued placebo, (n=16). Participants were followed to Week 52 to evaluate maintenance of clinical responses. COAs, including SCORAD, POEM, DLQI, and ADCT, were recorded at various timepoints during the study period. ‘Responders’ for each of these COAs were defined as: SCORAD reduction from baseline ≥8.7 with baseline ≥8.7; POEM total score reduction from baseline ≥4 with baseline ≥4; DLQI reduction from baseline ≥4 with baseline ≥4; ADCT <7.

In this post hoc responder analysis, differences between continued and withdrawn amlitelimab groups were analyzed using the Cochran-Mantel-Haenszel test stratified by baseline region and disease severity (EASI ≤21, EASI >21). Data collected after early treatment discontinuation due to reasons other than lack of efficacy prior to Week 24 or 52 were included for those visits. Data collected after the use of rescue/prohibited medication or treatment discontinuation due to lack of efficacy were set to missing and imputed using a worst-observation-carried-forward (WOCF) approach. Patients who discontinued treatment due to lack of efficacy or received rescue/prohibited medications were considered as non-responders. Patients with missing data were considered as non-responders.

**Results:** Of the participants who achieved EASI-75 and/or IGA 0/1 at Week 24 and were rerandomized to continue amlitelimab in Part 2 (pooled, n=44), 93.2%, 81.8%, 86.4%, and 70.5% were SCORAD, POEM, DLQI, and ADCT responders at Week 24, respectively. Of these Week 24 responders who continued on amlitelimab, 82.9%, 83.3%, 86.8%, and 77.4% maintained responses at Week 52, respectively. Of the participants who met EASI-75 and/or IGA 0/1 at Week 24 and were rerandomized to withdraw from amlitelimab in Part 2 (pooled, n=130), 84.6%, 73.8%, 71.5%, and 53.8% were SCORAD, POEM, DLQI, and
ADCT responders at Week 24, respectively. Of these Week 24 responders who were withdrawn from amlitelimab, 79.1%, 71.9%, 68.8%, and 72.9% maintained responses at Week 52, respectively.

**Conclusions:** In the STREAM-AD trial, COA responses were achieved by the majority of participants who achieved EASI-75 and/or IGA 0/1 at Week 24 and were re-randomized in Part 2. High maintenance of durable responses was observed at Week 52 in patients continuing and withdrawn from amlitelimab.

**Keywords** (up to 5): amlitelimab, atopic dermatitis, SCORAD, POEM

**Acknowledgments and Funding Sources:** Medical writing assistance was provided by Sierra Swords, PhD, of IMPRINT Science, New York, NY, USA. Research was funded by Sanofi.

**Disclosures:**

AB- Served as a speaker (received honoraria) for Eli Lilly and Company and UCB, has served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Celldex, CTI BioPharma, Dermavant, EcoR1, Eli Lilly and Company, Escient, Evelo, Evommune, Forte, Galderma, HighlightII Pharma, Incyte, InnoventBio, Janssen, Landos, LEO, Lipidio, Microbion, Merck, Monte Rosa Therapeutics, Nektar, Novartis, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Ventyx, Vibliome, and Xencor, has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Allakos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Concert, Dermavant, DermBiont, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, LEO, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB Pharma, and Ventyx, and owns stock in Lipidio and Oruka.

RC- Advisor, consultant, speaker, and/or investigator for AbbVie, Amgen, Apogee Therapeutics, Arcutis, Argenx, ASLAN Pharmaceuticals, Beiersdorf, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, Eli Lilly and Company, FIDE, Formation Bio, Galderma, Genentech, GSK, Incyte, LEO Pharma, L’Oréal, Nektar Therapeutics, Novartis, Opsidio, Pfizer Inc., Regeneron, RAPT, Sanofi, Sitryx, and UCB.

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SW- Investigator, consultant, advisory board member, employee, and/or speaker for AbbVie, Almirall, AstraZeneca, Galderma, Janssen, Kymab Ltd (a Sanofi company), LEO Pharma, Lilly, Pfizer, Regeneron, Roche Posay, Sanofi

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