Safety of amlitelimab in a phase 2a clinical trial of patients with moderate-to-severe atopic dermatitis

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Introduction/Background: Amlitelimab (SAR445229), a fully human, non-depleting, non-cytotoxic, monoclonal antibody, binds to OX40Ligand (OX40L) on antigen-presenting cells to block OX40-OX40L interactions. Outcomes from a 36-week, double-blind, Phase 2a trial (NCT03754309) in patients with moderate-to-severe atopic dermatitis are described.

Objective: To assess the safety of OX40-OX40L signaling blockade with amlitelimab in patients with moderate-to-severe atopic dermatitis.

Methods: 89 patients were randomized to amlitelimab low-dose (LD; 200mg loading/100mg maintenance Q4W), high-dose (HD; 500mg/250mg Q4W), or placebo. The coprimary safety endpoint was treatment-emergent adverse event (TEAE) incidence to W16. Safety was assessed to W36.
**Results:** Amlitelimab was well tolerated. Related TEAE incidence was similar between amlitelimab (LD 35% [10/29]; HD 20% [6/30]) and placebo (31% [9/29]) to W16 and W36 (LD 10% [2/20]; HD 0 [0/22]; placebo 0 [0/17]).

TEAEs more common with amlitelimab versus placebo (≥5% difference) to W16 included: headache (LD 0; HD 3 [10%]; placebo 1 [3.4%]), upper respiratory tract infection (3 [10.3%]; 0; 1 [3.4%]), hyperhidrosis (0; 2 [6.7%]; 0), pyrexia (2 [6.9%]; 0; 0), aspartate aminotransferase increased (0; 2 [6.7%]; 0), and iron-deficiency anemia (2 [6.9%]; 0; 0); and to W36, Herpes simplex (0; 2 [9.1%]; 0).

Before W16, one severe adverse event (SAE) of infected dermal cyst was reported as possibly related; it resolved, and the patient completed the study. Post-W16, one unrelated SAE of sudden death occurred 87 days following the final amlitelimab dose.

No hypersensitivity or tolerability events, or clinically meaningful changes in laboratory values, vital signs, or electrocardiogram recordings were reported.

**Conclusions:** Amlitelimab was well tolerated in a Phase 2a trial of patients with moderate-to-severe atopic dermatitis, confirming the unremarkable safety profile observed in Phase 1.

**Keywords:** Monoclonal antibody, anti-OX40L, Phase 2a, biologic therapy, safety

**Acknowledgments**


The authors wish to thank all the site staff and patients who kindly agreed to participate in this proof-of-concept study. They also acknowledge Xiaodan Wei for statistical support.
Funding Sources

Medical writing assistance was funded by Sanofi, Paris, France, and provided by Erin Burns-Tidmore, PhD, and Renee Granger, PhD, of Elevate Scientific Solutions. Editorial assistance was provided by Callie Leuck, MA, of Fishawack Communications Ltd, part of Fishawack Health.

Research was funded by Kymab Ltd, Cambridge, United Kingdom, a Sanofi Company.

Disclosures

Stephan Weidinger – Abbvie – consultant and investigator; Almirall – consultant and investigator; Astra Zeneca – consultant; Galderma – consultant and investigator; Janssen – investigator; Kymab Ltd (a Sanofi company) – investigator; LEO Pharma – consultant and investigator; Lilly – consultant and investigator; Pfizer – consultant and investigator; Regeneron – investigator; Roche Posay – investigator; Sanofi – consultant and investigator.

Michael Cork – Boots – consultant; Eli Lilly – consultant; Hyphens Pharma – consultant and received research grants; Johnson & Johnson – consultant, author/speaker, and received research grants; Kymab Ltd (a Sanofi Company) – received research grants; L’Oréal – consultant, author/speaker, data safety monitoring/advisory board participant, and received research grants and travel support; LEO Pharma – consultant; Perrigo (ACO Nordic) – consultant and received research grants; Pfizer – consultant, author/speaker, data safety monitoring/advisory board participant, and received research grants and travel support; Procter & Gamble – consultant; Regeneron – consultant, author/speaker, data safety monitoring/advisory board participant, and received research grants and travel support; Sanofi Genzyme – consultant, author/speaker, data safety monitoring/advisory board participant, and received research grants and travel support; board member of the European Association for
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**Adam Reich** – AbbVie – consultant, speaker, and investigator; Bioderma – speaker; Celgene – speaker; Chema Elektromet – speaker; Drug Delivery Solutions Ltd – investigator; Eli Lilly – consultant, speaker, and investigator; Galderma – consultant, speaker, and investigator; Genentech – investigator; Janssen – consultant, speaker, and investigator; Kymab Ltd (a Sanofi company) – consultant and investigator; LEO Pharma – consultant, speaker, and investigator; Medac – speaker; Menlo Therapeutics – investigator; MetrioPharm – investigator; MSD – investigator; Novartis – consultant, speaker and investigator; Pfizer – investigator; Pierre-Fabre – speaker; Sandoz – consultant and speaker; Trevi – investigator.

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**Sally Gilbert** – Employee of Sanofi at the time the study was performed – holds stock in the company

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