Amlitelimab Reduces Serum IL-13 in a Phase 2a Clinical Trial in Atopic Dermatitis Without Impacting T-Cell Expansion in a T-Cell Recall Assay

Stephan Weidinger[1], Michael Cork[2], Adam Reich[3], Thomas Bieber[4], Davide Lucchesi[5], Natalie Rynkiewicz[6], Richard C A Sainson[7*], Ron Chen[7*], Francesca Prandi[5], Cassandra van Krinks[5], Marisa Stebegg[8], Ben Porter-Brown[5]

[1]Department of Dermatology and Allergy, University Hospital Schleswig-Holstein, Kiel, Germany; [2]Sheffield Dermatology Research, IICD, University of Sheffield, Sheffield, United Kingdom; [3]Department of Dermatology, University of Rzeszow, Rzeszow, Poland; [4]Department of Dermatology and Allergy, University Hospital of Bonn, Bonn, Germany; [5]Sanofi, Cambridge, United Kingdom; [6]Sanofi, Melbourne, Australia; [7]Kymab (a Sanofi Company), Cambridge, United Kingdom; [8]Sanofi, Frankfurt, Germany

*Formerly Kymab Ltd (a Sanofi Company)

Introduction/Background: Amlitelimab (SAR445229), a fully human non-depleting, non-cytotoxic, monoclonal antibody, binds to OX40Ligand (OX40L) on antigen-presenting cells (APC) to block OX40-OX40L interactions. In a 16-week, double-blind, Phase 2a trial (NCT03754309), amlitelimab induced clinically meaningful disease activity improvement in patients with moderate-to-severe atopic dermatitis (AD).

Objective: To assess effects of amlitelimab on interleukin (IL)-13 and T-cell recall responses.

Methods: In the trial, 89 patients were randomized to amlitelimab low dose (LD; 200 mg loading/100 mg maintenance every 4 weeks [Q4W]), high dose (HD; 500 mg loading/250 mg maintenance Q4W), or placebo. Serum IL-13 levels were assessed by single molecule immunoassay (259 samples).

Using human peripheral blood mononuclear cells from 5 healthy donors, a T-cell recall assay was performed.

Results: At baseline in the trial**,** IL-13 levels significantly correlated with disease severity (Eczema Area and Severity Index; r=0.4784, p<0.0001). Week 16 IL-13 levels were significantly reduced with amlitelimab versus baseline but not placebo (median fold change [95% confidence interval, CI] from baseline to Week 16 with p-values based on two-way Analysis of Variance [ANOVA] of log10-transformed fold change for patients with a complete dataset at Week 16: LD 0.345 [0.23–0.44], p<0.0001; HD 0.390 [0.30–0.63], p=0.0002; placebo 0.835 [0.34–1.12], p=0.1544).

In a T-cell recall assay, amlitelimab significantly reduced IL-13 protein levels at Days 3 and 6 without negatively impacting T-cell expansion, based on percentage of proliferating $CD4^+$ T-cells versus isotype control.

Conclusions: Amlitelimab decreased IL-13 levels in patients with AD and in a T-cell recall assay without negative effects on T-cell expansion, thus reducing inflammation without blocking T-cell proliferation during recall responses.

Keywords (up to 5): monoclonal antibody, biomarkers, anti-OX40L, Phase 2a, biologic therapy

Acknowledgments

Research first presented at ISAD 2022, Montreal, Canada, October 17, 2022.

The authors wish to thank all the site staff and patients who kindly agreed to participate in this proof-of-concept study. The authors also thank Manisha Brahmachary, PhD, for statistical review.

Medical writing assistance, supported financially by Sanofi, was provided by Erin Burns-Tidmore, PhD, and Renee Granger, PhD, of Elevate Scientific Solutions. Editorial support in restyling this abstract was provided by Sam Leeves and Callie Leuck, MA, of Fishawack Health.

This study was funded by Kymab Ltd, a Sanofi Company.

Disclosures

Stephan Weidinger – Consultant: AbbVie, Almirall, Astra Zeneca, Galderma, LEO Pharma, Lilly, Pfizer, Regeneron, Sanofi; Speaker: AbbVie, Almirall, LEO Pharma, Lilly, Pfizer, Regeneron, Sanofi; Investigator: AbbVie, Almirall, Galderma, Janssen, Kymab Ltd, LEO Pharma, Lilly, Pfizer, Regeneron, Roche Posay, Sanofi

Michael Cork – Consultant: Boots, Eli Lilly, Hyphens Pharma, Johnson & Johnson, Procter & Gamble, Regeneron, L'Oréal, Leo Pharma, Perrigo (ACO Nordic), Pfizer, Sanofi Genzyme; Author/Speaker: Johnson & Johnson, Regeneron, L'Oréal, Pfizer, Sanofi Genzyme; Data Safety Monitoring/Advisory Board Participant: Regeneron, L'Oréal, Pfizer, Sanofi Genzyme; Research grants: Hyphens Pharma, Johnson & Johnson, Kymab (a Sanofi Company), Pfizer, Sanofi Genzyme, L'Oréal, Leo Pharma, Perrigo (ACO Nordic), Regeneron; Travel support: Regeneron, L'Oréal, Pfizer, Sanofi Genzyme; Board member of the European Association for Dermatology and Venereology, voluntary adviser for the National Eczema Society (UK), editorial board member for JEADV Clinical Practice (JEACP)

Adam Reich – Consultant: AbbVie, Eli Lilly, Galderma, Janssen, Kymab Ltd, LEO Pharma, Novartis, Sandoz; Speaker: AbbVie, Bioderma, Celgene, Chema Elektromet, Eli Lilly, Galderma, Janssen, LEO

Pharma, Medac, Novartis, Pierre-Fabre, Sandoz; Investigator: AbbVie, Drug Delivery Solutions Ltd., Eli Lilly, Galderma, Genentech, Janssen, Kymab Ltd, LEO Pharma, Menlo Therapeutics, MetrioPharm, MSD, Novartis, Pfizer, Trevi

Thomas Bieber – Consultant: AbbVie, Allmiral, AnaptysBio, Arena, Asana Biosciences, ASLAN Pharma, Bayer Health, BioVerSys, Boehringer Ingelheim, Bristol Myers Squibb, Domain Therapeutics, Galapagos/MorphoSys, Galderma, Glenmark, GSK, Incyte, IQVIA, Janssen, Kirin, Kymab Ltd, LEO Pharma, LG Chem, Lilly, L'Oréal, MenloTx, Novartis, OM-Pharma, Pfizer, Pierre Fabre, Sanofi/Regeneron, UCB; Speaker: AbbVie, Allmiral, LEO Pharma, Lilly, Pfizer, Sanofi/Regeneron

Davide Lucchessi – Employee of Sanofi –may hold stock and/or stock options in the company

Natalie Rynkiewicz – Employee of Sanofi –may hold stock and/or stock options in the company

Richard C A Sainson – Employee of Kymab (a Sanofi Company) at the time the study was performed – may hold stock and/or stock options in the company

Ron Chen – Employee of Kymab (a Sanofi Company) at the time the study was performed – may hold stock and/or stock options in the company

Francesca Prandi – Employee of Sanofi – may hold stock and/or stock options in the company

Cassandra van Krinks – Employee of Sanofi – may hold stock and/or stock options in the company

Marisa Stebegg – Employee of Sanofi – may hold stock and/or stock options in the company

Ben Porter-Brown – Employee of Sanofi – may hold stock and/or stock options in the company