A Phase 2a study of amlitelimab, a novel non-depleting anti-OX40Ligand (OX40L) mAb in patients with moderate-to-severe AD

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INTRODUCTION

- In immune-mediated diseases, the OX40Ligand (OX40L), found on Antigen-Presenting Cells (APCs), promotes pro-inflammatory responses via binding with the OX40 on T cells.

Amlitelimab (SAR445229/KY1005)

- A fully human, non-depleting, non-cytotoxic anti-OX40Ligand IgG4 monoclonal antibody (mAb) that inhibits OX40-OX40L signaling by binding to the OX40L on APCs2,3

- In pre-clinical models, amlitelimab has been shown to re-establish immune homeostasis without depleting T cells by suppression of pro-inflammatory T-effector and maintenance of anti-inflammatory T-regulatory cells2

- OX40L blockade targets T-helper (Th) 2 and Th1/17/22 inflammation mechanisms in atopic dermatitis (AD)2

METHODS

Study design

- Phase 2a, randomized, double-blind, placebo-controlled, parallel group, multicenter study (NCT03754309)

- Intravenous administration every 4 weeks (Q4W) until Week 12 (loading dose at baseline; maintenance dose: 50% of loading dose), with the primary endpoint at Week 16

ENDPOINTS AND RESPONDENT DEFINITION

- Co-primary endpoints were safety and efficacy, assessed by the incidence of treatment-emergent adverse events (TEAEs) and the percentage change in EASI score from baseline to Day 113 (Week 16)

RESULTS

Patient disposition and baseline characteristics

- Eighty-nine patients were randomized, of which 81 patients were treated (amlitelimab low dose n=29; amlitelimab high dose n=30; placebo n=28)

- Fifty-nine patients completed the main study to Week 16

- Baseline characteristics were as expected for patients with moderate-to-severe AD (mean age, 33.6 years; 42.0% female, mean EASI 31.3) and were generally well balanced across groups

Key findings

- In this Phase 2a trial, amlitelimab (SAR445229/KY1005), a non-depleting, non-cytotoxic anti-OX40Ligand IgG4 mAb, given as a monotherapy once a month, was shown to be effective in the treatment of moderate-to-severe AD with an acceptable and unremarkable safety profile

- Amlitelimab provided sustained and clinically meaningful improvements at both low and high doses in treating moderate-to-severe AD

- Improvements in EASI scores (Figures 1, 3a, and 3b) and clear to almost clear skin (vIGA 0/1; Figure 2) were achieved across low- and high-dose amlitelimab treatment groups

- Amlitelimab was well tolerated with an unremarkable safety profile

- In patients who achieved ‘clear’ or ‘almost clear’ skin (vIGA 0/1) at Week 16, clinical improvements were sustained to Week 36, 24 weeks after the last dose of study treatment. The results of this trial demonstrate the value of targeting the OX40-OX40L axis as a novel approach to addressing the underlying pathology of AD, providing additional clinical benefit to patients with moderate-to-severe AD

- A Phase 2b study is now enrolling (STREAM-AD: NCT01513477)

- Among responders, 68% of amlitelimab patients sustained vIGA 0/1 to Week 36, 24 weeks following their final dose

Efficacy

- Clinically meaningful improvements in mean percentage change from baseline in EASI were seen with amlitelimab low dose (<80% vs placebo -49%; nominally statistically significant, p<0.001) and high dose (>70% vs placebo -49%; p<0.002) compared with placebo (Figure 1)

- Significant improvements were observed at all time points in patients receiving amlitelimab versus placebo in those patients achieving clear or almost clear skin (vIGA 0/1) from baseline to Week 16 (Figure 2)

- At Week 16, more patients in the amlitelimab groups achieved EASI-75 and EASI-90 compared with placebo (Figure 3a and 3b)

- Among patients defined as responders (vIGA 0/1) at Week 16, 24 patients completed the study extension (amlitelimab high dose n=10, low dose n=12; placebo n=2)

- Among responders, 68% of amlitelimab patients sustained vIGA 0/1 to Week 36, 24 weeks following their final dose

Key findings

Figure 1. Percentage change in EASI from baseline to Week 16

Figure 2. Percentage of patients defined as vIGA 0/1 responders over time by treatment regimen. Combination—Median—Quartile box (FAQ)

Figure 3a. Percentage of patients defined as EASI-75 responders over time by treatment regimen. Descriptive statistics (FAQ)

Figure 3b. Percentage of patients defined as EASI-90 responders over time by treatment regimen. Descriptive statistics (FAQ)

Figure 3c. Percentage of patients defined as EASI-90 responders over time by treatment regimen. Descriptive statistics (FAQ)

Figure 3d. Percentage of patients defined as EASI-90 responders over time by treatment regimen. Descriptive statistics (FAQ)

Efficacy

- Overall, amlitelimab was well tolerated in this Phase 2a trial, with an unremarkable safety profile

- No hyporeactivity or tolerability events were reported and no pattern in TEAEs was observed

- One related serious adverse event (SAE) reported prior to Week 16 (infected dental cyst) resolved and the patient completed the study

- In the post-Week 16 period there was one SAE: one sudden death on Day 173, 87 days following the final amlitelimab low dose, considered unrelated to amlitelimab by both the investigator and the independent data monitoring committee

- In the post-Week 16 period, there were no new deaths or SAEs

- Adverse events were generally consistent with the safety profile of amlitelimab previously reported

- The safety profile of amlitelimab was acceptable across all study groups

- There was no evidence of a relation between dose escalation and safety

- Changes in Laboratory Safety Parameters were consistent with the known safety profile of amlitelimab

RESULTS (cont.)

Safety

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ENDPOINTS AND RESPONDENT DEFINITION

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- Responders defined as vIGA 0/1 at Week 16

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