Efficacy Of Ligelizumab In Patients With Chronic Spontaneous Urticaria Inadequately Controlled With Omalizumab

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In relation to this presentation, I declare the following real or perceived conflicts of interest:

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Introduction

Ligelizumab, a next generation high-affinity humanized monoclonal anti-IgE antibody, has been shown to be effective in patients with chronic spontaneous urticaria (CSU) inadequately controlled by H₁-antihistamines during a Phase 2b core study (NCT02477332)¹, ²

A higher percentage of patients experienced a complete control of CSU symptoms (UAS7=0) with ligelizumab therapy of 72 mg or 240 mg, compared to patients treated with 300 mg omalizumab or placebo.

Here, in an exploratory analysis of the Phase 2b extension study (NCT02649218)³, we assess the response to ligelizumab 240 mg in patients who did not achieve complete Urticaria Activity Score (UAS7>0) with omalizumab in the core study.

Design of the core Phase 2b and open-label extension study

R = Randomisation  Wk 12 = Primary endpoint  ↓ = Treatment visit in the core study and extension study

n, number of patients; q4w, every 4 weeks; SD, single dose; UAS7, weekly Urticaria Activity Score; Wk, week. *The 120 mg single-dose (SD) arm was chosen to characterise the pharmacokinetics/pharmacodynamics. Data from this arm assesses the duration of the response and correlates this with the concentration of drug in the serum at the time when symptoms reappear. Patients who remained in the follow-up period for at least 12 weeks and had active disease (UAS7 ≥12), could enter the extension study from Week 32 onwards. Following the 52-week open-label period, patients entered a 48-week treatment free follow-up period to assess durability of treatment effect, including potential for disease modification.
Patient disposition in the core Phase 2b study

382 patients randomised

349 patients\(^a\) entered post-treatment follow-up

226 patients with UAS7≥12 entered the extension

44 patients discontinued the double-blind treatment period

29 patients discontinued the post-treatment follow-up period

UAS7, 7-day urticaria activity score; Wk, week

\(^a\)Patients who discontinued treatment during the double-blind period were encouraged to remain in the study for the safety analysis and enter the post-treatment follow-up
Patient disposition in the open-label extension study

- 226 patients with UAS7≥12 entered the extension
- 201 patients completed open-label treatment
- 25 patients discontinued the open-label treatment period

UAS7, 7-day urticaria activity score; Wk, week
Methods

- Urticaria was measured using the weekly UAS7, with complete urticaria symptom control defined as UAS7=0.
- The absolute mean change from baseline (CFB) ± standard deviation (SD) in UAS7 (CFB-UAS7) for all patients during the core study and ligelizumab 240 mg during the extension study were calculated and compared.
- Disease activity for all patients in the core and extension studies were evaluated for the duration of treatment.
- UAS7 scores were evaluated for patients who received omalizumab 300 mg in the core study, and who were re-treated with ligelizumab 240 mg in the extension study.
- In this exploratory analysis, UAS7 scores were evaluated for a sub-group of patients who did not achieve UAS7=0 at Week 12 in the core study after treatment with omalizumab 300 mg, and were re-treated with ligelizumab 240 mg (during the extension study).
In the core study, patients treated with ligelizumab showed a numerically greater reduction in UAS7 (change from baseline) vs. omalizumab.

UAS7 scores: absolute mean change from baseline values. Core study: placebo, 72, 240 mg ligelizumab and 300 mg omalizumab for 20 weeks. *Extension study: 240 mg ligelizumab for 52 weeks. Metz M., et al. EADV, 2020; Abstract 2778.
Patients re-treated with ligelizumab showed stable disease activity during long-term treatment in the extension study

![Graphs showing change from baseline in UAS7 score over weeks in core and extension studies](image)

Population comprises of re-treated omalizumab patients, including complete responders.

Change from baseline in UAS7 score = End of treatment in the core study (Week 20)

Change from baseline in UAS7 score = End of treatment in the extension study (Week 52)

9 EoT, end of treatment; UAS7, 7-day urticaria activity score; a Patients received omalizumab during core study (n=53); b Patients received omalizumab during core study and then ligelizumab in the extension study (n=53). Each coloured line represents an individual patient. Maurer M., et al. EAACI, June 2020; Oral Presentation.
All patients re-treated with ligelizumab in the extension study showed a numerically greater reduction in UAS7 (change from baseline) vs. omalizumab in the core study.

Population comprises of re-treated omalizumab patients, including complete responders.
Greater proportion of patients were completely-controlled (UAS7=0) after re-treatment with ligelizumab vs. omalizumab

Proportion (percentage) of patients with a complete urticaria disease response (UAS7=0) for patients who were not completely controlled (UAS7>0) by omalizumab 300 mg (n=37) at the primary endpoint, Week 12, in the core study and re-treated with ligelizumab 240 mg in the extension study (n=37), evaluated at primary endpoint, Week 12 (27.0%) and at the end of the treatment period, Week 52 (43.2%)

Population comprises of re-treated omalizumab patients, excluding complete responders
In the subset of omalizumab-treated patients not completely controlled (UAS7>0) in the core study, re-treatment with ligelizumab shows a numerically greater response (CFB-UAS7).

Population comprises of re-treated omalizumab patients, excluding complete responders.

UAS7 scores: absolute mean change from baseline values. Patients received 300 mg omalizumab for 20 weeks in the core study and then re-treated with 240 mg ligelizumab in the extension study for 52 weeks.
Conclusions

- Overall, at the end of both the Phase 2b core and extension studies, the CFB-UAS7 was higher for patients treated with ligelizumab than those treated with omalizumab.
- Changes in disease activity measured over time showed that patients were stable long-term under ligelizumab treatment.
- Ligelizumab re-treatment exhibited added benefit of better urticaria control vs. omalizumab, especially in those patients who did not achieve complete responses (UAS7=0) with omalizumab in the Phase 2b core study.
- Phase 3 studies and a Phase 3 extension study are ongoing to evaluate the long term efficacy and safety of ligelizumab and will determine the optimal dose to achieve sustained control of CSU symptoms in patients who are inadequately controlled with H₁-anti-histamines and/or omalizumab.