Efficacy of ligelizumab in chronic spontaneous urticaria patients inadequately controlled with omalizumab: sub-analysis of the Phase 2 program

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Disclosures

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Introduction

- **Ligelizumab**, a **next generation high-affinity** humanised 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)

- A **numerically higher percentage** of patients had **complete control of CSU symptoms** with ligelizumab therapy of 72 mg or 240 mg, than with 300 mg omalizumab or placebo

- Here, in the Phase 2b extension study (NCT02649218), we assess the response to ligelizumab 240 mg in patients who did not achieve complete urticaria activity control with omalizumab in the core study

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CSU, chronic spontaneous urticaria
3. ClinicalTrials.gov Identifier: NCT02649218.

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Methods

Study design and patients

- In the 20-week Phase 2b core study, adult patients with moderate to severe CSU (defined by a UAS7≥16) were randomised to receive ligelizumab 24, 72 or 240 mg, omalizumab 300 mg, ligelizumab 120 mg (single dose) or placebo every 4 weeks (q4w) for five injections.
- Following a 16-week wash-out period after last dose in the core study, eligible patients (UAS7≥12) entered a 52-week open-label, single-arm (ligelizumab 240 mg q4w) Phase 2b extension study.

Endpoints and assessments: UAS7

- In the Phase 2 studies, urticaria was measured using the UAS7, with complete urticaria activity control defined as UAS7=0.
- In this analysis, UAS7 was evaluated for all patients who received ligelizumab 72 or 240 mg, omalizumab 300 mg, or placebo in the core study and compared to the extension study.
- UAS7 was then evaluated for patients who did not achieve UAS7=0 at Week 12 in the core study after treatment with omalizumab 300 mg and re-treated with ligelizumab 240 mg in the extension study.
  - The proportion of patients who achieved UAS7=0 for omalizumab (during the core study) and ligelizumab 240 mg (during the extension study) were calculated and compared.

CSU, chronic spontaneous urticaria; UAS7, weekly Urticaria Activity Score
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Study design of the ligelizumab Phase 2b trial in patients with moderate to severe CSU inadequately controlled with H₁-antihistamines

Screening → Treatment
Week -2 → Week 12 → Week 20 → Week 32 → Week 44
Ligelizumab 240 mg q4w (n=85)
Ligelizumab 72 mg q4w (n=84)
Ligelizumab 24 mg q4w (n=43)*
Omalizumab 300 mg q4w (n=85)
Ligelizumab 120 mg SD
Placebo q4w (n=42)
Placebo (n=43)

Follow-up
Week 52 → Week 100
Ligelizumab 240 mg q4w

Eligible to enrol in the extension study from Week 32 onwards, if UAS7 ≥ 12

R = Randomisation
Week 12 = Primary endpoint
= Treatment visit in the core study or extension study

*The ligelizumab 24 and 120 mg SD arms are not presented further as they were not relevant to outcomes presented in this oral presentation

b 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 onward

Following the 52-week open-label period, patients entered a 52-week treatment free follow-up period to assess durability of treatment effect, including potential for disease modification. CSU, chronic spontaneous urticaria; n, number of patients; q4w, every 4 weeks; SD, single dose;

UAS7, weekly Urticaria Activity Score
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Patient disposition: From the core study population, 70.6% (226/320) of patients were eligible and willing to enter the extension study.

- In total, 88.9% of these patients (201/226) completed the extension study. A total of 53 patients were treated with omalizumab in the core study and were re-treated with ligelizumab in the extension study.
- Among these, 37 patients did not achieve complete control of urticaria (UAS7>0) at Week 12 of the core study.

**Diagram:**

- **Core Study**
  - 382 patients randomized
  - Wk -2: Screening
  - Wk 20: Double-blind treatment
  - Wk 32: Follow-up
  - Wk 44: End of Core Study
  - Wk 0: Open-label treatment

- **Extension Study**
  - 85 patients received omalizumab
  - 53 patients treated with omalizumab switched to extension study
  - Wk 52: Completed of open-label treatment
  - Wk 100: End of extension Study

- **Notes:**
  - 37 patients with UAS>0 at Week 12
  - 37 patients with UAS>0 used for sub-analysis

A = Randomization

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*A total of 37 of the 53 patients had UAS7>0 at Week 12 of the core study and included in a sub-analysis.
UAS7, weekly Urticaria Activity Score; Wk, week.
Overall, a numerically larger proportion of CSU patients treated with ligelizumab showed complete symptom control after 20 weeks vs. omalizumab

- A numerically greater proportion of patients achieved UAS7=0 when treated with ligelizumab 72 and 240 mg (39.3%, 95% CI [28.8, 50.5], 40.0% 95% CI [29.5, 51.2]) at Week 20 in the core study and with ligelizumab 240 mg (46.0%, 95% CI [39.4, 52.8]) at Week 20 in the extension study respectively, compared to omalizumab (30.6% 95% [21.0, 41.5]) at Week 20 in the core study.

UAS7=0, complete urticaria response. All patients included in the analysis.
CI, confidence interval; n, number of patients; UAS7, weekly Urticaria Activity Score

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At Week 52 of the extension study, more than 40% patients achieved complete response with ligelizumab 240 mg, who had previously received omalizumab 300 mg.

- Overall, re-treatment with ligelizumab 240 mg of the 37 patients initially treated with omalizumab resulted in 27% (95% CI [13.8%, 44.1%]) of patients reaching UAS7=0 at Week 12, increasing to 43.2% (95% CI [27.1%, 60.5%]) at the end of the extension study.

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%).

CI, confidence interval; n, number of patients; q4w, every 4 weeks; UAS7, weekly Urticaria Activity Score.

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Conclusions

- Overall, a **numerically larger proportion** of CSU patients treated with ligelizumab showed **complete symptom control** after 20 weeks vs. omalizumab

- CSU patients who had previously not reached a complete response after 12 weeks of treatment with omalizumab, achieved **numerically greater reductions in UAS7** when re-treated with ligelizumab vs. omalizumab

- **Ligelizumab** can be effective and may provide **added benefit of achieving complete control** of urticaria in patients with CSU