Treatment with ligelizumab achieves a higher complete response rate in chronic spontaneous urticaria patients originally treated with omalizumab

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Introduction

- **Chronic spontaneous urticaria** (CSU) is characterised by the occurrence of itchy wheals (hives), angioedema, or both for ≥6 weeks in the absence of specific external stimuli\(^1\), and has a significant negative impact on patients' quality of life\(^1,2\)

- **Ligelizumab** is a next generation, high affinity humanised monoclonal anti-IgE antibody, which has shown improved control of symptoms compared with omalizumab in the Phase 2b core study (NCT02477332)\(^3\)

- Here, we report levels of disease activity measured by weekly Urticaria Activity Score (UAS7) for patients who received omalizumab in the core study followed by ligelizumab in the extension study (NCT02649218)\(^4\)

- The proportion of patients with completely-controlled disease (UAS7=0) was also evaluated

CSU, chronic spontaneous urticaria; UAS7, weekly Urticaria Activity Score
3. ClinicalTrials.gov Identifier: NCT02477332; 4. ClinicalTrials.gov Identifier: NCT02649218
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Methods

Study design and patients

- Phase 2b core study has been reported previously
  - 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, the change from baseline in UAS7 for patients who received omalizumab 300 mg in the core study followed by ligelizumab 240 mg in the extension study was evaluated. UAS7 change from baseline as a function of time for each individual patient during the core and the extension study was also evaluated
- The proportions of patients achieving UAS7=0 for patients treated with omalizumab in the core study were calculated

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 0-2
  - Week 12
- **Follow-up**
  - Week 20
  - Week 32
  - Week 44
- **Treatment**
  - Week 52
  - Week 100

- **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)**

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

- **R** = Randomisation
- **Week 12** = Primary endpoint
- **Week 20, 32, 44** = Treatment visit in the core study or extension study
- **Week 52, 100** = End of 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**
- **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**


5 Business Use Only
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 onomalizumab switched to ligelizumab in the extension study.

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44 patients discontinued the double-blind treatment period.

29 patients discontinued the post-treatment follow-up period.

25 patients discontinued the open-label treatment period.

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6 Business Use Only
Re-treatment with ligelizumab 240 mg (n=53) showed a mean absolute change of -20.9±13.1 in UAS7 score, following 12 weeks of treatment in the extension study

- In the core study, mean±SD absolute change in UAS7 from baseline to Wk 12 and Wk 20 with omalizumab 300 mg (n=53) was -17.6±13.1 and -17.1±12.6 respectively
- Re-treatment with ligelizumab 240 mg showed a -21.3±13.3 change following 20 weeks of treatment in the extension study, and -22.8±11.8 at the end of the extension study (Week 52)

Patients presented were on 300 mg omalizumab (n=53) in the Phase 2b core study. All patients received ligelizumab 240 mg (n=53) q4w in the extension study SD, standard deviation; UAS7, weekly Urticaria Activity Score, Wk, week

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Retreatment of patients previously treated with omalizumab results in a more stable disease activity pattern.

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.

- Patients received omalizumab during core study (n=53);
- Patients received omalizumab during core study and then ligelizumab in the extension study (n=53), each coloured line represents an individual patient.

UAS7, weekly Urticaria Activity Score

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At Week 52 of the extension study, 56.6% achieved complete response with ligelizumab 240 mg in patients who had previously received omalizumab 300 mg

- In the core study, 30.2% (n=16; 95% CI [18.3%, 44.3%]) of patients treated with omalizumab 300 mg achieved UAS7=0 at Week 12, increasing to 43.4% (n=23; 95% CI [29.8%, 57.7%]) upon 12 week re-treatment with ligelizumab 240 mg in the extension study.

- At the end of the core study (Week 20), 32.1% (n=17; 95% CI [19.9%, 46.3%]) of patients treated with omalizumab 300 mg achieved UAS7=0, increasing to 47.2% (n=25; 95% CI [33.3%, 61.4%]) upon re-treatment with ligelizumab 240 mg (at Week 20), and then to 56.6% (n=30; 95% CI [42.3%, 70.2%]), at the end of the extension study (Week 52).

Patients presented were on 300 mg omalizumab (n=53) in the Phase 2b core study. All patients received ligelizumab 240 mg (n=53) q4w in the extension study. Error bars represent standard deviation.

CI, confidence interval; n, number of patients; UAS7, weekly Urticaria Activity Score; UAS7=0, complete urticaria response

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Conclusions

- This analysis showed that CSU patients who were first treated with omalizumab experienced a **numerically greater reduction** in disease activity **when re-treated with ligelizumab 240 mg**

- **Changes in disease activity** measured over time showed that patients are **more stable long-term** under ligelizumab

- Importantly, a **numerically higher proportion** of re-treated patients **achieved complete urticaria disease response**

- Phase 3 studies 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-antihistamines

CSU, chronic spontaneous urticaria;
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