Complete symptom control in chronic spontaneous urticaria patients leads to improved sleep and quality of life: results from the Phase 2b ligelizumab study

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Disclosures

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Introduction

- **Chronic spontaneous urticaria** (CSU) symptoms can **adversely affect daily activities, sleep** and **cause substantial health-related quality of life (HRQoL) impairment**\(^1\)

- Here, we analysed the **impact of urticaria activity** (weekly Urticaria Activity Score [UAS7]) on **Weekly Sleep Interference** (WSI, sleep interference scores summed over 7 days) and **Dermatology Life Quality Index (DLQI)**, during a 20-week Phase 2b core study (NCT02477332)\(^2\) and a 52-week open-label, single-arm Phase 2b extension study (NCT02649218)\(^3\)

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CSU, chronic spontaneous urticaria; DLQI, dermatology life quality index; UAS7, weekly Urticaria Activity Score; WSI, Weekly Sleep Interference

2. ClinicalTrials.gov Identifier: NCT02477332.
3. ClinicalTrials.gov Identifier: NCT02649218.


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Methods

Study design and patients

- In the Phase 2b 20-week core study\(^1\), adult patients with moderate to severe CSU (defined by [UAS7] ≥16) were randomised to receive ligelizumab 24 (out-of-scope for this analysis), 72 or 240 mg, omalizumab 300 mg, ligelizumab 120 mg (single dose, out-of-scope for this analysis) 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

- Patient-reported data from the core and extension studies were used to analyse WSI scores and DLQI scores.

- WSI and DLQI scores between adjacent UAS7 disease activity categories (UAS7=0 [urticaria-free]; UAS7=1–6 [well-controlled]; UAS7=7–15 [mild]; UAS7=16–27 [moderate]; UAS7=28–42 [severe]) were compared.

- In this analysis, data for patients across treatment arms and timepoints for the core study (ligelizumab 72 and 240 mg and omalizumab 300mg), and across time points for the extension study were pooled.

Statistical analysis

- The descriptive summary statistics are provided for the WSI scores and DLQI scores over time based on the observed data. Mixed models of repeated measures were performed to compare the WSI and DLQI mean scores in the adjacent disease category based on the UAS7 classification.

CSU, chronic spontaneous urticaria; DLQI, dermatology life quality index; UAS7, weekly Urticaria Activity Score; WSI, Weekly Sleep Interference


Study design: 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

"The ligelizumab 24 and 120 mg SD arms are not presented further as they were not relevant to outcomes presented here. 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.

n, number of patients; q4w, every 4 weeks; SD, single dose; UAS7, weekly Urticaria Activity Score


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For ligelizumab 240 mg, the absolute mean±SD change in WSI scores for patients at the end of the core study was -7.9±6.1

- The absolute mean±SD change in WSI scores for patients at the end of the core study was -8.5±5.9, -7.9±6.1, -7.0±6.0 and -5.7±6.3 for ligelizumab 72 mg, 240 mg, omalizumab 300 mg and placebo, respectively, and -7.5±6.4 at Week 20 and -7.6±6.7 at the end of the extension study.

- Blue dotted line indicates primary endpoint. Red dotted line indicates the end of the treatment period in the core study. 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.

- Blue dotted line indicates Week 20. Red dotted line indicates the end of the treatment period in the extension study.

- n, number of patients; SD, standard deviation; WSI, Weekly Sleep Interference


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For ligelizumab 240 mg, the absolute mean±SD change in DLQI scores for patients at the end of the core study was -9.8±8.4

- The absolute mean change±SD in DLQI scores for patients at the end of the core study was -9.5±7.9, -9.8±8.4, -7.8±8.0 and -6.2±6.1 for ligelizumab 72 mg, 240 mg, omalizumab 300 mg and placebo respectively and -9.4±7.5 at the end of the extension study.

<table>
<thead>
<tr>
<th>Core Weeks</th>
<th>Extension Weeks</th>
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<tr>
<td>Placebo (n=43)</td>
<td>ligelizumab 240 mg (n=226)</td>
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<tr>
<td>ligelizumab 240 mg (n=85)</td>
<td>ligelizumab 240 mg (n=85)</td>
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<td>omalizumab 300 mg (n=85)</td>
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</table>

Blue dotted line indicates primary endpoint. Red dotted line indicates the end of the treatment period in the core study. 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.

Red dotted line indicates the end of the treatment period in the extension study.

DLQI, dermatology life quality index; n, number of patients; SD, standard deviation


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WSI scores were highly correlated with disease activity; and reduced with decreased disease activity

- The comparison by UAS7 responder status demonstrated that urticaria-free patients had a significantly lower least square mean±SE WSI score vs. patients with well-controlled urticaria in both core (0.2±0.2 vs. 1.0±0.2) and extension (0.3±0.2 vs. 0.7±0.2) studies
- WSI scores reduction with decreased disease activity, shows significant differences between adjacent UAS7 disease activity categories

LS mean, least squares mean; SE, standard error; UAS7, weekly urticaria score; WSI, Weekly Sleep Interference


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DLQI scores were also highly correlated with disease activity; and were reduced with decreased disease activity

- The comparison by UAS7 responder status demonstrated that patients achieving UAS7=0 had better mean DLQI scores vs. patients with UAS7=1–6 in both core (0.8±0.4 vs. 2.3±0.4) and extension (0.6±0.3 vs. 2.0±0.4) studies.
- DLQI scores reduced with decreased disease activity, showing significant differences between adjacent UAS7 disease activity categories.

DLQI, dermatology life quality index; LS mean, least squares mean; SE, standard error; UAS7, weekly urticaria score


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Conclusions

- Improvement in urticaria activity is associated with improvement in sleep and dermatology-related QoL.

- Overall, effective treatments such as ligelizumab have benefits beyond urticaria symptoms, showing the importance of targeting complete urticaria control.

- Patients free of urticaria are more likely to achieve a low DLQI score (low impact on QoL) and low WSI score (low impact on sleep).