INTRODUCTION

• Chronic spontaneous urticaria (CSU) is characterized by the occurrence of itchy wheals (hives), angioedema, or both for 6 weeks or more in the absence of specific external stimuli and has a significant negative impact on quality of life.

• Ligelizumab, a next generation anti-IgE antibody, has demonstrated to improve symptom control in patients with CSU, who remain symptomatic despite the use of H-antihistamines, in a Phase 2b randomized clinical trial.

• Baseline characteristics that can predict treatment outcomes as well as sustainability of response during treatment free period can help identify patients that may benefit most from a particular therapy.

• Here, we explore possible predictors of response to ligelizumab using a multivariate analysis of the core Phase 2b data.

METHODS

Study Design

• The Phase 2b dose-finding multicentre, randomised, double-blind, active and placebo-controlled study was designed to establish a dose-response relationship of ligelizumab and to evaluate its efficacy and safety compared with placebo andomalizumab (Figure 1).

• Adult patients with moderate to severe CSU (Urticaria Activity Score [UAS7] ≥ 16) were enrolled.

• Patients were randomised to receive subcutaneous ligelizumab 24, 72, or 240 mg,omalizumab 300 mg, or placebo every 4 weeks (q4w) over 20 weeks (five injections), or a single dose of ligelizumab 120 mg (Figure 1).

RESULTS

• In the core Phase 2b study, CFB-UAS7 during the treatment period was impacted by patients' baseline UAS7.

• Treatment effect was assessed by change from baseline in UAS7 (CFB-UAS7) after treatment with ligelizumab 72 mg or 240 mg.

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Multivariate regression analysis

• A multivariate analysis using a stepwise regression method was performed on the Phase 2b study data.

• Several patient baseline characteristics were investigated for their impact on treatment response during the treatment period and post-treatment follow-up. These included:

  - urinary albumin-to-creatinine ratio
  - background medication, – chronic spontaneous urticaria [CSU] index
  - baseline total IgE
  - body mass index
  - duration of CSU
  - gender
  - baseline weekly angioedema activity score
  - Asian
  - non-Asian

• The multiple regression model (main effects only and no interaction terms used) was fitted to all 32 weeks of assessment time points in the core study (from week 0-20 of the treatment period, and week 21-32 of the post-treatment follow-up period).

• The treatment effect was assessed by change from baseline in UAS7 (CFB-UAS7) after treatment with ligelizumab 72 mg or 240 mg.

Table 1: Results from an exploratory stepwise regression modelling for each of the 32 time points in the Phase 2b study: association between baseline characteristics and CFB in UAS7 with ligelizumab (72 mg or 240 mg) treatment in CSU patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment period (Week 0–20)</th>
<th>Follow-up period (Week 21–32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>p=0.037; β=0.207</td>
<td>p=0.000; β=0.006</td>
</tr>
<tr>
<td>Asian</td>
<td>Week 1</td>
<td>Week 26 – 30</td>
</tr>
<tr>
<td>BMI</td>
<td>p=0.030; β=−0.703</td>
<td>p=0.030; β=−0.703</td>
</tr>
<tr>
<td>BL UAS7</td>
<td>Week 14 – 20</td>
<td>Week 21 – 32</td>
</tr>
<tr>
<td>CSU disease duration</td>
<td>β=−0.830 – −0.806</td>
<td>p=0.037; β=−0.345 – −0.345</td>
</tr>
<tr>
<td>Treatment</td>
<td>Week 26–30</td>
<td>Week 29 – 32</td>
</tr>
<tr>
<td>Ligelizumab 240 mg</td>
<td>p=0.04; β=−0.415</td>
<td>p=0.024; β=−0.207</td>
</tr>
</tbody>
</table>

Figure 1: Design of the ligelizumab Phase 2b trial in patients with moderate to severe CSU inadequately controlled with H-antihistamines

Figure 2: Results from an exploratory stepwise regression modelling for each of the 32 time points in the Phase 2b study (20 weeks of treatment and 12 weeks of treatment-free follow-up period): association between baseline characteristics and CFB in UAS7 with ligelizumab (72 mg or 240 mg) in patients with CSU.

CONCLUSIONS

• Disease severity at baseline likely affects the magnitude of CFB in UAS7 with ligelizumab treatment.

• This exploratory analysis from the Phase 2b study generates hypotheses that early treatment with ligelizumab may result in a better therapeutic response in patients with CSU, and patients with high BMI may show early relapse.

• The hypotheses generated from this analysis, as well as potential interactions among other factors, will be further explored with data from the ongoing Phase 3 studies (NCT03580365 and NCT03580396).

References


Disclosures

Pink line indicates that the information was obtained from the authors' website.