Ligelizumab Achieves Freedom From Disease Activity in Chronic Spontaneous Urticaria Regardless of Previous Hi-antihistamine Dose

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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.

• The international guidelines recommend treatment with approved and escalated doses (up to 4x) of 2nd generation Hi-antihistamines (Hi-AH) as the two-step first-line treatment for patients with CSU.

• Patients unresponsive to escalated doses of Hi-AH could be considered as a harder-to treat population.

• Anti-immunoglobulin (IgE) therapy is recommended for patients with uncontrolled CSU despite treatment with escalated doses of Hi-AH.

• Treatment with ligelizumab, a next generation high affinity monoclonal anti-IgE antibody, has demonstrated an improvement of symptom control in patients with CSU on locally-approved or escalated doses of Hi-AH.

METHODS

• The ligelizumab Phase 2b trial was a multicenter, randomized, double-blind, active, placebo-controlled study and included treatments with ligelizumab 72mg or 240mg, omalizumab 300mg q4w, or placebo every 4 weeks (q4w) for 20 weeks.

Study Population

• The proportion of patients stratified by previous medication: locally- approved or escalated doses of Hi-AH without hives and itch (weekly Ursiculoria Activity Score [UAAS]=0) was compared between ligelizumab and omalizumab within the two study arms of medication (locally- approved vs. escalated doses of Hi-AH).

Statistical Analysis

• The post-hoc analyses of logistic regression modeling was performed following the pre-specified analyses, in which the efficacy responses were adjusted for background medication type and chronic urticaria (CU) index.

• The logistic regression analyses model of the complete response on hives and itch (UAAS=0) was performed and adjusted for background medication type and CU index.

• Comparisons of each ligelizumab dose (72mg and 240mg q4w) vs. omalizumab 300mg q4w were summarized using odds ratio (OR) and 95% confidence interval (CI).

RESULTS

Baseline Demographics and Disease Characteristics

• At baseline, a total of 108 and 146 patients were on locally-approved Hi-AH and escalated doses of Hi-AH in the ligelizumab 72mg, 240mg and omalizumab 300mg q4w groups, respectively.

• The baseline meanstandard deviations (SD) UAAS for patients were balanced across treatment groups.

• Locally- approved doses of Hi-AH with 29.6±7.1 (N=35), 30.7±7.8 (N=39), and 30.1±6.7 (N=57) for ligelizumab 72mg, 240mg, and omalizumab 300mg q4w, respectively.

• Escalated doses of Hi-AH with 33.2±7.2 (N=49), 30.6±6.9 (N=49), and 28.6±8.7 (N=48) for ligelizumab 72mg, 240mg, and omalizumab 300mg q4w, respectively.

• Patients’ baseline demographics and disease characteristics are presented in Table 1.

Table 1. Patient demographics and baseline disease characteristics for each treatment group for patients who are on locally approved Hi-AH.

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>N</th>
<th>Age (years)</th>
<th>Gender, n (%)</th>
<th>Baseline Disease Activity (UAS7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligelizumab 72mg</td>
<td>35</td>
<td>41.4±13.0</td>
<td>Female, 24 (68.6%)</td>
<td>3.7±4.7</td>
</tr>
<tr>
<td>Ligelizumab 240mg</td>
<td>36</td>
<td>42.6±10.6</td>
<td>Female, 27 (75.0%)</td>
<td>2.7±2.8</td>
</tr>
<tr>
<td>Omalizumab 300mg q4w</td>
<td>37</td>
<td>46.4±11.6</td>
<td>Female, 37 (75.5%)</td>
<td>6.1±7.7</td>
</tr>
</tbody>
</table>

• At Week 12, the proportion of patients with UAS7=0 on ligelizumab was 51.4% and 38.9% vs. 27.0%, respectively (Figure 2A).

• For patients on escalated doses of Hi-AH, the proportions of patients with UAS7=0 were 38.8% and 40.8% vs. 25.0%, respectively (Figure 2B).

• The OR (95% CI) for UAS7=0 response at Week 12 (igelizumab vs. omalizumab) were 1.69 (0.65–4.25) for CSU patients on locally-approved or escalated doses of Hi-AH (Figure 3).

CONCLUSIONS

• A previous Hi-AH dose is unlikely to have an impact on response to anti-IgE treatment.

• Ligelizumab treatment may provide better CSU control vs. omalizumab, regardless of previous Hi-AH doses, including the harder-to-treat patients who are unresponsive to up to 4x doses of Hi-AH.

• This exploratory outcome will be further evaluated in larger, ongoing ligelizumab Phase 3 studies (PEARL 1 and PEARL 2).

References


Figure 1. The proportion of patients on (A) locally-approved Hi-AH and (B) escalated doses of Hi-AH as background medication showing complete response.

Figure 2. Change from baseline in UAS7 in patients on (A) locally-approved Hi-AH and (B) escalated doses of Hi-AH.

Figure 3. OR (igelizumab vs. omalizumab) for UAS7=0 response at Week 12 in CSU patients on locally-approved or escalated doses of Hi-AH.

CONFLICT OF INTEREST

All authors completed the development of the poster for presentation. The authors report roles as a Medical Advisor for Uriach Pharma, Sanofi and Genentech, reports roles as a Medical Advisor for Uriach Pharma, Sanofi and Genentech, has been an advisor and/or clinical investigator and/or received speaker’s honoraria and/or received consulting fees and/or grants from Amgen, Amgen, Celldex, Genentech and Sanofi Regeneron outside the submitted work.

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