**INTRODUCTION**

Chronic spontaneous urticaria (CSU) is characterized by recurrent wheals (urticaria) in patients for more than 6 weeks and can have a major impact on patients’ well-being. Remibrutinib is a novel, oral, highly selective Bruton’s tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU inadequately controlled by second-generation H1-receptor antagonists. Remibrutinib showed clinical efficacy and a favorable safety profile for up to 52 weeks in the Phase 2a and extension studies (NCT03920515 and NCT04034398) in patients with CSU inadequately controlled by H1-receptor antagonists. The Phase 2a study included remibrutinib 25 mg b.i.d. (n=20) and remibrutinib 35 mg q.d. (n=19) groups. The Phase 2a trial became available and all patients were included and treated according to the study protocol. The primary endpoint was the mean (standard deviation [SD]) duration of worsening episode across remibrutinib groups ranging from 9.8 (5.0) to 21.9 (9.1) days and placebo 22.0 (5.8) days (Figure 2).

**RESULTS**

Demographics and baseline disease characteristics in patients without any worsening episode and in patients with at least one worsening episode are presented in Table 1. During the treatment period, a higher proportion of patients were free of worsening episodes across remibrutinib groups (range: 50.0% to 68.2%) versus placebo (44.9%; Table 1). The median (95% confidence interval) time to first worsening episode was not reached across remibrutinib groups (except 10 mg b.i.d. 770 days). The placebo group (10 mg b.i.d.) was not applicable (P=0.005) due to clinical departure (Table 1).

The mean (SD) duration of worsening episode was shortest with remibrutinib 25 mg b.i.d. (≤12 weeks) versus placebo. The mean (SD) peak intensity of worsening episode during the treatment period was lower with remibrutinib (22.0/9.3) versus placebo 27.4/8.5 (Figure 2). The end of the worsening episode was defined as the day, when rUAS7 dropped back to ≤10 points above the baseline (Figure 2). A worsening episode was defined as a temporary increase of rolling weekly Urticaria Activity Score (rUAS7) ≥10.

**CONCLUSIONS**

This exploratory analysis from the Phase 2b study showed more patients free of urticaria in all remibrutinib treatment arms compared with placebo. The duration, intensity and peak intensity of worsening episode was decreased and time to first worsening episode was delayed with remibrutinib compared to placebo. The treatment response remained stable during the study indicating better disease control for patients on remibrutinib, which may have a favorable impact on patients’ lives.

**STUDY ASSESSMENTS**

The rates of side effects, duration of worsening episode, time to first worsening episode, and the intensity of worsening episode during the treatment period were assessed. A worsening episode was defined as a temporary increase of rolling weekly Urticaria Activity Score (rUAS7) ≥10 (based on minimal clinically important difference for UAS7) from the lowest rUAS7 achieved before the episode. The end of the worsening episode was defined as the day, when rUAS7 dropped back to ≤10 points above the initial rUAS7 achieved in the treatment period.

The rUAS7 was calculated as the UAS7 for every possible set of 7 consecutive days across the study treatment period. The number of days, including the first day, spent with a worsening episode was calculated at the duration of the worsening episode. Overall frequency was calculated based on the area under the curve (AUC) for rUAS7 when a patient experienced worsening episode, and peak intensity was defined as maximum rUAS7 when a patient experienced a worsening episode.

Patients captured their daily UAS in an e-diary. Data are presented as mean±SD, unless stated otherwise. b.i.d., twice daily; CSU, chronic spontaneous urticaria; CU, chronic urticaria; n, number of patients; N, total number of patients; q.d., once a day; SD, standard deviation; UAS7, rolling weekly Urticaria Activity Score. SD, standard deviation.

**Table 1. Patient demographics and baseline disease characteristics**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Placebo (n=23)</th>
<th>Remibrutinib 25 mg b.i.d. (n=21)</th>
<th>Remibrutinib 35 mg q.d. (n=19)</th>
<th>Remibrutinib 100 mg q.d. (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD</td>
<td>50.0±13.9</td>
<td>50.3±14.3</td>
<td>50.0±13.9</td>
<td>49.7±13.9</td>
</tr>
<tr>
<td>Range</td>
<td>35–70</td>
<td>29–69</td>
<td>35–70</td>
<td>35–70</td>
</tr>
<tr>
<td>Sex (n, %)</td>
<td>10 (43.5)</td>
<td>10 (47.6)</td>
<td>10 (52.6)</td>
<td>10 (50.0)</td>
</tr>
<tr>
<td>Race (n, %)</td>
<td>16 (70.0)</td>
<td>16 (76.2)</td>
<td>17 (85.0)</td>
<td>15 (75.0)</td>
</tr>
</tbody>
</table>

**Figure 1. Percentage of patients experiencing number of worsening episodes based on rUAS7 by treatment group, during 14-week daily treatment**

**Figure 2. Duration of worsening episode based on rUAS7**

**Figure 3. Intensity of worsening episode based on rUAS7**

**DISCLOSURES:** Jeffrey Tillinghast, Vijul Jain, Marcus Maurer, Ana M Giménez-Arnau, Adam Reich, Christine-Elke Ornstein, Pauline Wahl, Sibylle Haemmerli.

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