**Aims**

HES is a debilitating multisystem disorder characterized by hypereosinophilia leading to the dysfunction of a variety of organ systems. Many patients with HES experience disease flares (seemingly unrelated classic signs and symptoms resulting in the need for increased OCS or immunosuppressants), which are associated with significant morbidity and mortality.1,2

Mepolizumab, a humanized, monoclonal anti-IL-5 antibody, is approved for the treatment of patients with HES, based on the results of the Phase III 200622 study (KCT20062446). This study demonstrated that mepolizumab significantly reduced disease flares in patients with HES versus placebo.3,4

This post hoc analysis of the 200622 study aimed to characterize the symptoms of disease flares in patients from the Phase III 200622 study and to assess the impact of mepolizumab on flare duration.

**Methods**

Study design: 2×2, double-blind, randomized, parallel group study. Patients were randomized to treatment or placebo for the 32-week study period; here we present post hoc analyses of the 12-week up period. Up to 256 flares were evaluated during the up period, which was only for those patients who did not enter the subsequent open label extension period. Eligible patients were aged ≥12 years of age and met the following criteria: (1) history of ≥6 months previously ≥12 flares within the past 12 months; (2) ≥2 flares within the past 12 months; (3) baseline eosinophil count of ≥1500 cells/µL; (4) no OCS or cytotoxic/Immunosuppressant therapy for ≥6 months previously; (5) no corticosteroid treatment for ≥12 months previously. The primary endpoint of the study was the proportion of patients who experienced a flare during the 32-week study period. Flare symptoms were determined by GSK clinical review of verbatim flare narratives.

**Baseline demographics and characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=44)</th>
<th>Mepolizumab (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of flares</td>
<td>14 (26)</td>
<td>24 (44)</td>
</tr>
<tr>
<td>Number of OCS</td>
<td>10 (19)</td>
<td>14 (26)</td>
</tr>
<tr>
<td>OCS, n (%)</td>
<td>49 (91)</td>
<td>40 (74)</td>
</tr>
<tr>
<td>No OCS or cytostatic therapy</td>
<td>9 (17)</td>
<td>14 (26)</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>45 (18)</td>
<td>45 (18)</td>
</tr>
</tbody>
</table>

**Flare definition**

- Constitutional symptoms: Fatigue and pain (constitutional), rash and itch (skin), and breathing and dyspnea (respiratory)
- Other symptoms:
  - Chills or sweats
  - Nasal congestion
  - Ear congestion
  - Stool urgency or diarrhea
  - Abdominal pain
  - Vascular symptoms
  - Rash
  - Skin symptoms

**Flare duration**

- Up to 61 days
- Up to 26 days
- Up to 15 days
- Up to 10 days
- Up to 6 days
- Up to 3 days

**Constitutional symptoms**

- Chills or sweats
- Nasal congestion
- Ear congestion
- Stool urgency or diarrhea
- Abdominal pain
- Vascular symptoms
- Rash
- Skin symptoms

**Other symptoms**

- Pain
- Dyspnea
- Cough
- Rash
- Fatigue
- Sweats

**Conclusions**

- Irrespective of the treatment group, constitutional symptoms were the most frequently reported symptoms for flares. Nasal and respiratory symptoms were more frequently reported as flare symptoms in the mepolizumab group; whereas skin and vascular symptoms were most frequently reported in the placebo group.

- Pain and fever were the most common constitutional flare symptoms, rash and itch the most common skin flare symptoms, and breathing and dyspnea the most common respiratory flare symptoms.

- Mepolizumab treatment was associated with the occurrence of fewer flares and a reduced total flare duration versus placebo.

- Overall, these findings provide further insights into the multi-organ nature of flares and highlight the potential benefit of mepolizumab treatment in patients with HES.

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- The content is based on phase 3 data from the GSK Phase III 200622 study.