**Background and objectives**

- Aspirin-exacerbated respiratory disease (AERD) or Samter’s triad occurs in about 15% of patients with severe asthma, it is characterized by the presence of three conditions including asthma, nasal polyps and intolerance to aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs).
- The efficacy of mepolizumab has been shown to reduce the rate of clinically significant exacerbations, improve symptoms and reduce the need for polyp surgery in patients with severe eosinophilic asthma (SEA) and nasal polyps, compared with placebo.
- The objective of this analysis was to assess the efficacy of the licensed dose of mepolizumab (100 mg subcutaneously [SC] every 4 weeks) versus placebo in patients with SEA and co-existing nasal polyps and aspirin/NSAID intolerance (i.e., AERD).

**Methods**

- This was a post hoc meta-analysis (GSK ID: 208115) of data from the Phase III MENSIA (MEA115586/01CT16106151+) and MUSCA (00101422/02/2851/318) trials.
- The analysis presents data from patients who received 1 mg dose of mepolizumab 100 mg SC or placebo. Eligible patients were ≥12 years of age with SEA and a history of ≥5 exacerbations in the previous 12 months despite using high-dose inhaled corticosteroids and ≥1 additional controller.
- The primary endpoint for this meta-analysis was the annual rate of clinically significant exacerbations (asthma worsening requiring system corticosteroids and/or hospitalization and/or an emergency room [ER] visit).
- Three subgroups were analyzed according to presence/absence at screening of: 1) nasal polyps, 2) aspirin/NSAID intolerance, or 3) both (AERD). Diagnosis of nasal polyps or aspirin/NSAID intolerance were based on patient-reported medical history form. AERD was classified according to patients who reported both nasal polyps and aspirin/NSAID intolerance on the forms.
- Exacerbation rates were analyzed by subgroup in each study using a negative binomial regression model. The estimated end-of-study treatment differences for each subgroup were combined using an inverse variance weighted fixed-effects meta-analysis.

**Results**

- Of the 936 patients, 166 (18%) had nasal polyps, 87 (9%) had aspirin/NSAID intolerance, and 40 (4%) had AERD at screening (Figure 1).
- Patients with AERD versus those without had higher (versus St George’s Respiratory Questionnaire (SGRQ) and Asthma Control Questionnaire (ACQ)-5 scores), as well as higher eosinophilic count and oral corticosteroid (OCS) use, and lower forced expiratory volume in 1 second (FEV1) at baseline (Table 1). In addition, baseline blood eosinophil counts and OCS use were higher in patients with nasal polyps versus without.
- Mepolizumab reduced clinically significant exacerbations versus placebo in patients with and without each comorbidity (Figure 2); the greatest improvements were seen in patients with nasal polyps.

**Conclusions**

- This post hoc meta-analysis of the MENSIA and MUSCA trials shows that mepolizumab 100 mg SC significantly reduced the rate of clinically significant exacerbations versus placebo in patients with SEA, regardless of the presence of nasal polyps, self-reported aspirin/NSAID intolerance, or both (AERD).
- The effect was greatest in those patients with nasal polyps alone. However, caution should be taken interpreting the results due to smaller sample sizes in some subgroups. These initial data demonstrate that mepolizumab is likely to be of benefit for patients with SEA and concomitant AERD.

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**Table 1. Baseline demographics and clinical characteristics by presence of comorbidity**

<table>
<thead>
<tr>
<th>Presence of comorbidity at screening</th>
<th>Nasal polyps</th>
<th>Aspirin/NSAID intolerance</th>
<th>AERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>n=835 (89%)</td>
<td>n=166 (18%)</td>
<td>n=770 (92%)</td>
<td>n=89 (9%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>52 (64.9)</td>
<td>51 (66.4)</td>
<td>52 (58.5)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>30 (37.1)</td>
<td>26 (33.6)</td>
<td>37 (41.5)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>49.7±17</td>
<td>50.1±16</td>
<td>47±18</td>
</tr>
<tr>
<td>Asthma duration, years, mean (SD)</td>
<td>18.0±13</td>
<td>20.0±14</td>
<td>18.1±13</td>
</tr>
<tr>
<td>Exacerbations last year, mean (SD)</td>
<td>46.9±24</td>
<td>47.0±25</td>
<td>47.0±25</td>
</tr>
<tr>
<td>Maintenance OCS use, n (%)</td>
<td>32 (80.0)</td>
<td>37 (92.1)</td>
<td>37 (92.1)</td>
</tr>
<tr>
<td>Rate ratio (mepolizumab/placebo)</td>
<td>0.66 (0.24, 1.79)</td>
<td>0.51 (0.41, 0.64)</td>
<td>0.43 (0.35, 0.55)</td>
</tr>
</tbody>
</table>

**Figure 2. Rate ratio of clinically significant exacerbations requiring hospitalization/ER visit by presence of comorbidity**

- Current nasal polyps (n=166) 0.20 (0.11, 0.35)
- No nasal polyps (n=770) 0.51 (0.41, 0.64)
- Aspirin/NSAID intolerance (n=87) 0.66 (0.37, 1.18)
- No aspirin/NSAID intolerance (n=895) 0.43 (0.35, 0.55)
- AERD (n=40) 0.66 (0.24, 1.79)
- No AERD (n=892) 0.45 (0.36, 0.56)

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**References**