**Introduction**

Mepolizumab is a monoclonal antibody that by targeting a targeted blocking of interleukin-5 (IL-5) reduces eosinophil recruitment and survival. It is indicated for Maintenance therapy for patients with severe asthma aged 12 years or older with an eosinophilic phenotype.

Achieving asthma control is an important goal of asthma management. This can be measured through validated questionnaires like the Asthma Control Questionnaire (ACQ) - which addresses both symptoms (right symptoms, morning symptoms, activity limitation, shortness of breath and wheezing). The score ranges from 0 to 6, with higher scores indicating more active symptoms. ACQ 0.5 scores of 1.5 (or greater) indicate uncontrolled asthma, scores below 0.75 indicate Complete Asthma Control and scores between 0.75 and 1.5 Indicate Partial Asthma Control. The minimally important clinical difference (MICD) is an improvement of 0.5 in ACQ 0.5.

**Objectives**

- Identify patients that were uncontrolled at baseline in the MENSA and MUSCA studies, and who subsequently achieved complete or partial asthma control during the study period.
- Compare the proportions between treatment with Mepolizumab and Placebo over 24 weeks.

**Methods**

This post-hoc analysis used data from two phase III trials comparing the licensed dose of mepolizumab 100 mg SC to placebo. In total, 466 patients treated with mepolizumab and 468 patients treated with placebo were part of this analysis.

MENSA (NCT01691521) was a 32-week, randomized, double blind, placebo-controlled study in 576 patients with severe asthma (SA). Patients treated with Mepolizumab 100 mg SC (n=194) or 75 mg IV (n=191, not included in this analysis) or placebo (n=191). The primary endpoint was the annualized rate of exacerbations. The number of exacerbations was reduced by 53%, among those receiving subcutaneous Mepolizumab, as compared with those receiving placebo.

MUSCA (NCT02281538) was a 24-week, randomized, double blind, placebo-controlled study in 551 patients with SA, treated with Mepolizumab 100 mg SC (n=227) or placebo (n=224). The primary endpoint was the asthma change from baseline in the Saint George's Respiratory Questionnaire (SGRQ), assessing improvement in quality of life, with a treatment difference of -2.7 points compared to placebo (MDCi for SGRQ is -4 points; lower scores indicating greater improvement).

Both studies enrolled patients who were using high dose Inhaled Corticosteroids (ICS) plus a second controller and had at least 2 exacerbations in the previous year that required a minimum of 3 days of oral corticosteroids (OCS) treatment. They also required to have a blood eosinophil count of at least 150 cells/µL at screening or 300 cells/µL in the previous year.

The proportion of uncontrolled patients achieving different levels of asthma control over the treatment period of each study was summarized and compared between treatment groups using a logistic regression model.

**Results**

- At baseline 69% (n=464) of all subjects had uncontrolled asthma, 21% had partially controlled asthma and 9% were controlled at baseline.
- In this meta-analysis, following 32 weeks of treatment in MENSA and 24 weeks in MUSCA, of patients with uncontrolled asthma at baseline:
  - 25% (Mepolizumab) and 3.6% (Placebo) achieved partial or complete asthma control (OR 2.54, 95% CI 1.78,3.63).
  - Clinically significant and persistent improvement vs placebo in the proportion of patients achieving complete asthma control or partial asthma control was observed after 3 doses (at 12 weeks, Figures 1 and 2).

**Conclusions**

- Achieving and maintaining asthma control is an important goal of asthma management. Despite GINA step 4-5 recommended treatment with high dose ICS plus a second controller, 69% of the severe eosinophilic asthma patients in MENSA and MUSCA studies were uncontrolled on ACC-5 score at baseline.
- Among these patients Mepolizumab significantly increased the odds of achieving complete asthma control at the end of the treatment period compared to placebo.
- Additionally, of those patients almost half treated with Mepolizumab were controlled or partially controlled (49%) at the end of the study compared to just under a third (30%) in the Placebo group.
- These findings support a significant and meaningful benefit with Mepolizumab in achieving asthma control compared to placebo in this population.

**References**

- Nair PS et al. GSK Global Medical Affairs, 2017.

**Table 1. Baseline characteristics**

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>Mepolizumab 100 mg</th>
<th>Overall Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>50.9 (13.4)</td>
<td>50.4 (13.4)</td>
<td>50.6 (13.9)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>293 (50)</td>
<td>295 (57)</td>
<td>294 (56)</td>
</tr>
<tr>
<td>Exacerbations in last year, n (%)</td>
<td>3 (18)</td>
<td>23 (14)</td>
<td>22 (15)</td>
</tr>
<tr>
<td>Pre-bronchodilator FEV1% predicted, (SD)</td>
<td>88.7 (3.9)</td>
<td>88.7 (3.9)</td>
<td>88.7 (3.9)</td>
</tr>
<tr>
<td>Blood eosinophil count, cells/µL (SD)</td>
<td>465 (96)</td>
<td>466 (96)</td>
<td>466 (96)</td>
</tr>
<tr>
<td>ACQ 5 score, mean (SD)</td>
<td>2.23 (1.14)</td>
<td>2.15 (1.17)</td>
<td>2.23 (1.17)</td>
</tr>
<tr>
<td>SGRQ geometric mean (SD Logs)</td>
<td>314 (87)</td>
<td>334 (71)</td>
<td>329 (79)</td>
</tr>
</tbody>
</table>

**Table 2. Complete/Partial Asthma Control at end of study in patients uncontrolled at baseline**

<table>
<thead>
<tr>
<th>Patient Group – Placebo</th>
<th>Mepolizumab 100 mg</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncontrolled at baseline, n (%)</td>
<td>314 (87)</td>
<td>334 (71)</td>
</tr>
<tr>
<td>Patients uncontrolled at baseline – Complete or Partial Control</td>
<td>12%</td>
<td>25%</td>
</tr>
<tr>
<td>Patients uncontrolled at baseline – Partial Control</td>
<td>30%</td>
<td>49%</td>
</tr>
</tbody>
</table>

**Figure 1. Uncontrolled patients at baseline that achieve complete Asthma Control over first 24 weeks of each study**

**Figure 2. Uncontrolled patients at baseline that achieve partial or complete Asthma Control over first 24 weeks of each study**


**Meta-analysis of Asthma Control in Patients with Severe Eosinophilic Asthma Treated with Mepolizumab**

**Llanos JP1, Forshag M1, Carstens D2, Mayer B3, Albers FC4, Liu M5**

1 GSK US Medical Affairs, RTP, NC, USA; GSK US Medical Affairs, Philadelphia, PA, USA; GSK Stockley Park, Uxbridge, Middlesex, UK; 5 GSK Global Medical Affairs, RTP, USA; 4 Johns Hopkins Asthma and Allergy Center, Baltimore, MD, USA.