### Aims

Mepolizumab has been shown to reduce the rate of clinically significant exacerbations, as well as improve asthma control compared with placebo in patients with severe eosinophilic asthma. Previous studies have shown that baseline blood eosinophil count is predictive of response to mepolizumab. Separately, supervised cluster analysis of the DREAM study suggested that airway reversibility is a significant predictor of mepolizumab response in patients with severe eosinophilic asthma. Therefore, this post hoc analysis was performed to evaluate the efficacy of mepolizumab in patients with severe eosinophilic asthma who are non-reversible and to determine whether baseline eosinophil count and airway reversibility can be used to predict response to mepolizumab therapy.

### Methods

**Patients**

In the randomized controlled phase IIb/III DREAM study (NCT01000506), patients with severe eosinophilic asthma were randomized to receive either mepolizumab, 75 mg administered every 4 weeks, or placebo. The primary endpoint of this study was exacerbation reduction in patients based upon baseline eosinophil counts and FEV1 reversibility. Baseline characteristics are presented in Table 1. The primary analysis was performed as planned and was not modified based on safety or efficacy of the drug (as determined by the sponsor).

### Post hoc analysis

**Exacerbation Reduction in Patients Based Upon Baseline Eosinophil Counts and FEV1 Reversibility**

Separately, supervised cluster analysis of the DREAM study suggested that airway reversibility is a significant predictor of mepolizumab response in patients with severe eosinophilic asthma. Therefore, this post hoc analysis was performed to evaluate the efficacy of mepolizumab in patients with severe eosinophilic asthma who are non-reversible and to determine whether baseline eosinophil count and airway reversibility can be used to predict response to mepolizumab therapy.

**Main outcomes**

**FEV1% reversibility**

- **Non-reversible + <300 cells/µL**
- **Non-reversible + ≥300 cells/µL**
- **Reversible + <300 cells/µL**
- **Reversible + ≥300 cells/µL**

**Baseline blood eosinophil count:**

- **<150 cells/µL**
- **≥300 cells/µL**

**Exacerbation rate ratio:**

- **Placebo:**
  - **<150 cells/µL:** 3.91 (0.79, 19.40)
  - **≥300 cells/µL:** 0.26 (0.16, 0.42)

- **Mepolizumab:**
  - **<150 cells/µL:** 0.51 (0.38, 0.70)
  - **≥300 cells/µL:** 0.75 (0.46, 1.21)

**Reductions in the rate of clinically significant exacerbations over 52 weeks favored mepolizumab versus placebo in patients with severe eosinophilic asthma over a 52-week period according to baseline blood eosinophil count and forced expiratory volume in 1 second (FEV1) reversibility.**

### Conclusions

- Previous analyses have shown an association between exacerbation reduction with mepolizumab and higher baseline eosinophil counts.
- This exploratory analysis confirms that baseline blood eosinophil counts remain the most useful predictor of improved response to mepolizumab treatment in terms of exacerbations.
- Based on this analysis the role of airway reversibility in predicting response to mepolizumab treatment is still unclear and may not have additional impact, although the line number of patients requiring rescue in the placebo arm was lower compared with patients receiving mepolizumab.
- In cases where patients performed worse with mepolizumab compared with placebo, this was driven mainly by a relatively small number of patients with baseline blood eosinophil counts <150 cells/µL, which could explain the superior response in the placebo group.
- Furthermore, it is possible that some patients classified as non-reversible may also have had airflow variability or hyperresponsiveness.

### References