# Efficacy of Mepolizumab in Patients With Severe Eosinophilic Asthma and Concomitant Aspirin-Exacerbated Respiratory Disease: Meta-analysis of Two Phase III Trials

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Laidlaw T[1], Albers FC[2], Bratton DJ[3], Bradford ES[4], Smith SG[2], Llanos JP[5], Taillé C[6], Lugogo NL[7]

[1]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, USA; [2]Respiratory Medical Franchise, GSK, Research Triangle Park, NC, USA; [3]Clinical Statistics, GSK, Stockley Park, Uxbridge, Middlesex, UK; [4]GSK, Research Triangle Park, NC, USA; [5]GSK US Medical Affairs, Research Triangle Park, NC, USA; [6]Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Service de Pneumologie et Centre de Référence Constitutif des Maladies Pulmonaires Rares; UMR1152, Université Paris-Diderot, Paris, France; [7]Division of Pulmonary and Critical Care, University of Michigan, Ann Arbor, MI, USA


## Background and objective

- 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).[1,2]
- Mepolizumab has been shown to reduce the rate of clinically significant exacerbations, improve symptoms and reduce the need for nasal polyps surgery in patients with severe eosinophilic asthma (SEA) and nasal polyposis, compared with placebo.[3–8]
- The efficacy of mepolizumab in patients with SEA and AERD has not been reported.
- 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 (ie, AERD).

## Methods

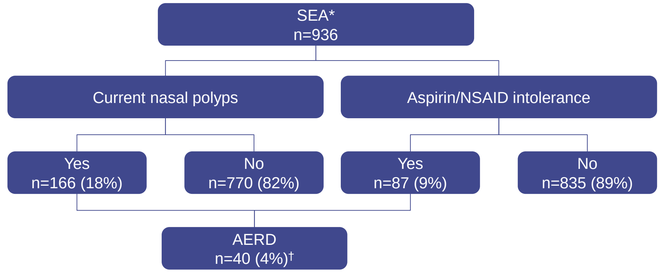
- This was a post hoc meta-analysis (GSK ID: 208115) of data from the Phase III MENSA (MEA115588/NCT01691521)[4] and MUSCA (200862/NCT02281318) trials.[6]
- This analysis presents data from patients who received ≥1 dose of mepolizumab 100 mg SC or placebo. Eligible patients were ≥12 years of age with SEA and a history of ≥2 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 systemic 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). Diagnoses 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 study 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 (worse) St George's Respiratory Questionnaire (SGRQ) and Asthma Control Questionnaire-5 (ACQ-5) scores, as well as higher blood eosinophil count and oral corticosteroid (OCS) use, and lower forced expiratory volume in 1 second ($FEV_1$) 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.

## Results

### Figure 1. Distribution of patients by comorbidity



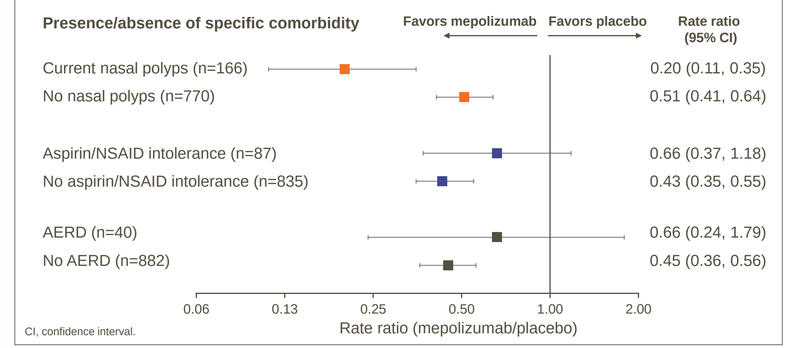

*Patients enrolled into MENSA and MUSCA; †based on N=922, as 14 patients did not have a Samter's Triad assessment at screening.

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

| | Nasal polyps | | Aspirin/NSAID intolerance | | AERD | |
|---|---|---|---|---|---|---|
| **Presence of comorbidity at screening** | **Yes n=166** | **No n=770** | **Yes n=87** | **No n=835** | **Yes n=40** | **No n=882** |
| **Age, years, mean (SD)** | 52.4 (12.1) | 50.2 (14.2) | 51.9 (12.4) | 50.5 (14.0) | 53.9 (13.5) | 50.5 (13.8) |
| **Female, n (%)** | 85 (51) | 463 (60) | 56 (64) | 484 (58) | 23 (58) | 517 (59) |
| **Asthma duration, years, mean (SD)** | 18.3 (13.0) | 20.0 (14.7) | 21.8 (13.4) | 19.5 (14.5) | 20.3 (13.2) | 19.7 (14.4) |
| **Exacerbations in last year, n (%)** | | | | | | |
| 2 | 94 (57) | 427 (55) | 46 (53) | 473 (57) | 22 (55) | 497 (56) |
| 3 | 34 (20) | 156 (20) | 20 (23) | 164 (20) | 8 (20) | 176 (20) |
| ≥4 | 38 (23) | 187 (24) | 21 (24) | 198 (24) | 10 (25) | 209 (24) |
| **Maintenance OCS use, n (%)** | **48 (29)** | **179 (23)** | **27 (31)** | **194 (23)** | **11 (28)** | **210 (24)** |
| **Pre-bronchodilator $FEV_1$, mL, mean (SD)** | 1896 (622) | 1810 (680) | **1705 (597)** | **1838 (674)** | **1790 (594)** | **1827 (672)** |
| **SGRQ total score** Mean (SD) | 47.9 (19.4) | 46.9 (18.8) | **53.5 (16.7)** | **46.4 (19.2)** | **53.3 (17.7)** | **46.8 (19.1)** |
| **ACQ-5 score** Mean (SD) | 2.26 (1.18) | 2.22 (1.17) | **2.51 (1.08)** | **2.20 (1.18)** | **2.54 (1.08)** | **2.22 (1.18)** |
| **Blood eosinophil count, cells/μL** Geometric mean (SD*) | **440 (0.938)** | **290 (1.010)** | **410 (0.853)** | **300 (1.025)** | **450 (0.782)** | **310 (1.020)** |

Items highlighted in bold suggest a difference between those with and those without the comorbidity
*SD of log-transformed eosinophil count. SD, standard deviation

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




CI, confidence interval.

## Conclusions

- This post hoc meta-analysis of the MUSCA and MENSA trials shows that mepolizumab 100 mg SC reduces 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.

## References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