## REDES Study: Mepolizumab Is Effective in Patients With Severe Asthma and Comorbid Nasal Polyps

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More than 90% of patients with the eosinophilic phenotype of severe asthma have comorbid diseases [1]. Of these, chronic rhinosinusitis with nasal polyps (CRSwNP) is among the most common, with up to 46.2% of patients impacted by upper airway inflammation [2]. Between 10% and 30% of patients with mild asthma also have CRSwNP, and this incidence increases to 70% to 90% in severe asthma [3].

Several biologics approved for severe asthma have proven beneficial in patients with comorbid nasal polyps in clinical trials, which revealed an enhanced response in this subgroup [4,5]. The REDES study was a real-world, observational, retrospective, multicenter study of the effectiveness and safety of mepolizumab 100 mg SC q4w in Spain over 12 months. The study population comprised 318 severe asthma patients, of whom 147 had comorbid CRSwNP. The principal inclusion criteria were a diagnosis of severe eosinophilic asthma in patients aged ≥18 years who had initiated mepolizumab at least 12 months prior to inclusion in the study and with at least 12 months of key clinical information available before initiation of treatment [2].

We conducted a post hoc analysis of the REDES study to evaluate the effectiveness of mepolizumab according to the presence or absence of comorbid CRSwNP. At 12 months, we analyzed changes in the annual number of exacerbations,

 

maintenance oral corticosteroid (OCS) use, lung function measured as prebronchodilator forced expiratory volume in 1 second ($FEV_1$), and blood eosinophil counts. We also assessed the improvement in asthma control as per the Asthma Control Test (ACT). Baseline demographic features were also compared between the groups. Two-tailed *t* tests were carried out to compare continuous variables within groups (paired) and between groups (unpaired).

The baseline characteristics were similar across both subgroups of patients (Table), with no significant differences other than the blood eosinophil counts at baseline, which were slightly higher: mean (SD) 798.78 (923.26)/μL in patients with CRSwNP vs 633.54 (748.50)/μL in those without CRSwNP (*P*=.04). After 12 months, eosinophils had returned to normal concentrations in both cohorts: 77.38 (58.18)/μL and 115.67 (314.32)/μL. The OCS maintenance dose was also different at baseline: 14.31 mg/d in those without CRSwNP and 9.48 mg/d in those with CRSwNP (*P*=.0163).

Exacerbations at 12 months decreased by 83.4% in patients with comorbid CRSwNP from a mean (SD) of 4.33 (3.55) to 0.73 (1.14) exacerbations per year, compared with a 73.0% reduction in those without CRSwNP, from 4.60 (3.49) to 1.24 (1.61) exacerbations per year after therapy with mepolizumab (intergroup *P*=.0017). Maintenance OCS were withdrawn at 12 months in 53.7% of patients with nasal polyps and in 42.9% of patients without nasal polyps. The ACT score increased in patients with CRSwNP from a mean (SD) of 14.63 (5.16) to 21.09 (3.72) after 12 months (*P*<.01), achieving ACT≥20 in 76.0% of cases, compared with 69.8% of patients without nasal polyps, whose mean ACT score also increased, from 13.57 (4.90) at baseline to 20.60 (3.98) (*P*<.01). Pre-BD $FEV_1$ improved in both cohorts by 0.18 L and 0.23 L, and z-scores changed from –2.04 and –2.11 to –1.54 and –1.61 with and without comorbid nasal polyps, respectively. The FEOS ($FEV_1$, Exacerbations, Oral corticosteroids, Symptoms) score was calculated where data were available, with slightly higher scores reported in patients with nasal polyps (Table S1) [6,7]. Recently published real-world studies show consistent results in terms of reduced exacerbations, OCS use, and overall response in patients with comorbid nasal polyps in real life compared with severe asthma patients without nasal polyps [8].

The concept of unified airway disease highlights the relationship between inflammatory mechanisms of upper airway disease (chronic rhinosinusitis with or without nasal

**Table.** Effectiveness of Mepolizumab According to the Presence or Absence of Nasal Polyposis.

| Demographic features | Valid no. | Severe asthma without NP (n=171) | | | Valid no. | Severe asthma with NP (n=147) | | |
|---|---|---|---|---|---|---|---|---|
| Mean (SD) age, y | 171 | 56.74 (13.43) | | | 147 | 56.33 (11.36) | | |
| Mean (SD)/median age at diagnosis, y | 159 | 34.69 (18.95)/37 | | | 142 | 33.37 (16.68)/32.5 | | |
| Female sex, No. (%) | 171 | 130 (76.0%) | | | 147 | 90 (61.2%) | | |
| Mean (SD) BMI, $kg/m^2$ | 170 | 29.37 (5.75) | | | 146 | 27.67 (5.05) | | |
| Nonsmoker, No. (%) | 171 | 116 (67.8%) | | | 147 | 82 (55.8%) | | |
| Exsmoker No. (%) | 171 | 48 (28.1%) | | | 147 | 58 (39.5%) | | |
| Atopic sensitization, No. (%) | 171 | 80 (46.78%) | | | 145 | 51 (35.17%) | | |
| Clinical outcomes | Valid n | Baseline | 12 months | *P* Value | Valid n | Baseline | 12 months | *P* Value |
| Blood eosinophil counts, mean (SD) | 171 | 633.54[a] (748.50) | 115.67 (314.32) | <.001 | 103 | 798.78a (923.26) | 77.38 (58.18) | <.001 |
| Annual exacerbations, mean (SD) | 171 | 4.60 (3.49) | 1.24 (1.61)[b,c] | <.001 | 147 | 4.33 (3.55) | 0.73 (1.14)[b,c] | <.001 |
| Mean (SD) prednisolone dose mg/d<br>Patients with prednisone 0 mg/d, No./No. (%) | 49 | 14.31 (9.86)[a] | 5.49 (7.47)<br>21/49 (42.9%) | .002 | 41 | 9.48 (9.56)[a]<br>- | 4.14 (6.12)<br>22/41 (53.7%) | <.001 |
| Mean (SD) ACT score<br>Patients with ACT score >20, % | 139 | 13.57 (4.90)<br>12.1% | 20.60 (3.98)<br>69.8% | <.001 | 121 | 14.63 (5.16)<br>18.5% | 21.09 (3.72)<br>76.0% | <.001 |
| Mean (SD) pre-BD $FEV_1$ L | 117 | 1.80 (0.72) | 1.99 (0.64) | <.001 | 94 | 1.99 (0.81) | 2.19 (0.87) | <.001 |
| Mean (SD) pre-BD $FEV_1$ % | 114 | 69.66% (23.05) | 79.93% (22.04) | <.001 | 95 | 70.67% (21.25) | 81.30% (21.15) | <.001 |
| Mean (SD) pre-BD $FEV_1$ z-score | 117 | -2.11 (1.56) | -1.61 (1.49) | <.001 | 94 | -2.04 (1.42) | -1.54 (1.39) | <.001 |

Abbreviations: ACT, Asthma Control Test; BD, bronchodilator; $FEV_1$, forced expiratory volume in the first second; NP, nasal polyposis.
[a]*P*<.05 for intergroup difference at baseline.
[b]*P*<.05 for intergroup difference at 12 months.
[c]*P*<.05 for intergroup difference of change.

polyps) and lower airway disease [9]. CRSwNP usually has greater impact on asthma burden than other comorbidities in terms of longer duration of nasal symptoms, poorer health-related quality of life, and greater exposure to systemic corticosteroids [3,10].

Eosinophils and overexpression of IL-5 play a critical role in the pathogenesis of severe asthma and CSRwNP, stimulating, on the one hand, the cysteinyl leukotriene pathway, which is associated with nasal congestion, rhinorrhea, and loss of smell, and contributing, on the other hand, to prostaglandin D2 signaling, which is responsible for smooth muscle contraction and bronchoconstriction [11]. Eosinophils and overexpression of IL-5 are involved in tissue remodeling, airway hyperresponsiveness, epithelial integrity, and mucus viscosity [12,13]. Therefore, inhibiting the IL-5 pathway may reduce the overlapping symptoms for both diseases, leading to better overall control. Mepolizumab is the only anti–IL-5 agent approved by the United States Food and Drug Administration and European Medicines Agency for severe eosinophilic asthma, CRSwNP, and the systemic eosinophilic diseases eosinophilic granulomatosis with polyangiitis and hypereosinophilic syndrome. Treatment with mepolizumab could therefore provide a concomitant benefit in the upper and lower respiratory tract in patients with severe asthma and comorbid NP, as described in recent literature examples [4,14]. Expectations for biologic therapy in severe asthma are high, since they are administered to improve not only symptoms, but also comorbid conditions, especially concomitant nasal polyps [15,16]. A multidisciplinary approach involving respiratory physicians, allergists, and ENT specialists is essential for adequate diagnosis and treatment.

The main limitation of our work is that it was a post hoc analysis of a retrospective real-world study, and, as such, we were unable to incorporate data that were not previously collected in the REDES study (eg, nasal outcomes). In addition, our results may be affected by potential bias due to missing data, although they are from one of the largest cohorts to assess the effectiveness and safety of mepolizumab and are consistent with those from previous clinical trials and real-world studies, suggesting that patients with severe asthma and comorbid nasal polyps constitute a phenotype that appears to respond particularly well to mepolizumab in real life.

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*Conflicts of Interest*

- EA reports the following: honoraria from lectures, presentations, speakers bureaus, manuscript writing, and educational events from GSK, AstraZeneca, Chiesi, GebroPharma, Sanofi, and Merck; support for attending meetings from GSK, AstraZeneca, Chiesi, and Sanofi; and receipt of equipment, materials, drugs, medical writing, gifts, and other services from GSK, Chiesi, and Merck.
- CC reports the following: grants or contracts from AstraZeneca, Chiesi, GSK, Novartis, and Sanofi; consulting fees from AstraZeneca, GSK, Novartis, and Sanofi; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, and educational events from AstraZeneca, Chiesi, GSK, Mundipharma, Novartis, Pfizer, and Sanofi; payment for expert testimony from AstraZeneca, Chiesi, GSK, Novartis, and Sanofi; support for attending meetings and/or travel from Chiesi, GebroPharma, Mundipharma, Pfizer, and Sanofi; participation on Data Safety Monitoring Boards or Advisory Boards from AstraZeneca, GSK, Novartis, and Sanofi; and receipt of equipment, materials, drugs, medical writing, gifts, and other services from GSK and Sanofi.
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- MGSH was an employee of GSK when this manuscript was written and holds shares in GSK.
- DBC and ALM are employees of GSK and hold stocks/shares in GSK.

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