Mepolizumab for Treatment of Severe Eosinophilic Asthma: A 5-Year Real-World Experience

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Mepolizumab is a humanized monoclonal antibody (mAb) that binds to and neutralizes interleukin (IL) 5, which is the main cytokine involved in the proliferation, maturation, activation, recruitment, and survival of eosinophils [1]. It is indicated for the treatment of patients with severe eosinophilic asthma (SEA), as its efficacy has been confirmed in clinical trials, which demonstrated a significant reduction in exacerbation rates and need for oral corticosteroids (OCS) and an improvement in both asthma control and quality of life [1-4].

The primary objective of our study was to evaluate the effectiveness of mepolizumab in daily clinical practice, 5 years after its authorization in Spain in 2017.

We performed a single-center, retrospective review of the medical records of patients with SEA who initiated mepolizumab at the Severe Asthma Unit of Hospital Clinic, Barcelona, Spain between March 2017 and April 2022. All patients met the criteria for severe uncontrolled asthma despite receiving step 5 treatment according to the Spanish Asthma Management Guidelines (GEMA 5.2) [5]. We included patients who had received at least 6 doses of mepolizumab. Data were collected at baseline and every 6-12 months after initiation of treatment. The database was last updated in January 2023.

We included 44 patients with SEA (70.5% women; median [range] age at initiation of treatment, 57 years [18-81 years]). The most frequently associated comorbidities were anxiety and/or depression in 50% of patients, chronic rhinosinusitis with nasal polyps (CRSwNP) in 45.5%, and allergic rhinitis in 31.8%. Concerning treatment duration, 18.2% of patients received mepolizumab for more than 60 months (5 years), 47.7% for 37 to 60 months, 27.3% for 13 to 36 months, and 4.5% for 6 to 12 months. One patient was treated for only 5 months. The baseline clinical characteristics of asthma patients are summarized in Supplementary Table 1. We observed a significant improvement in asthma outcomes after treatment with mepolizumab. Mepolizumab decreased asthma exacerbations in the last 12 months by 70.2% compared to the previous year, while asthma exacerbations requiring hospitalization decreased by 71.9%. Regarding lung function, the median forced expiratory volume in 1 second (FEV_1, L) increased by 0.29 L (range, –0.79 to 1.21 L); 2 patients experienced an improvement of >1 L, in FEV_1 (+9%) and in their forced expiratory flow at 25%-75% (FEF_{25-75}) (+11%). The median (IQR) annual cumulative dose of oral corticosteroids (OCS) decreased from 900 mg (555-2565 mg) in the previous year to 0 mg (0.0-1364 mg). Almost all the asthma patients (42 [95.5%]) required at least 1 dose of OCS during the previous year of treatment, although this number fell to 21 (47.7%) during treatment with mepolizumab. Finally, the Asthma Control Test (ACT) scores increased from 13.9 to 20.1 points (+44.6%). We also observed a reduction in the mean blood eosinophil count from 657/µL to 111/µL (–83.1%), while total IgE decreased from 229 to 145 kU/L (–36.7%). These results are summarized in Supplementary Table 2.

The criteria proposed by the 2020 Consensus Document of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) [6] were used to evaluate the response to mepolizumab. This consensus classifies the response to asthma treatment as no response, partial response, control, and complete response based on exacerbations, ACT score, FEV_1, and the use of OCS (Supplementary Table 3). We observed a good response in 63.6% of patients (complete response in 38.6% [n=17] and control in 25% [n=11] patients), a partial response in 25% (n=11), and no response in 11.4% (n=5). The initial response to mAbs was assessed after a median of 4 months (3-5 months), with a median increase in the ACT score from 14 (11-17.5) to 22 (19-24). Out of those who experienced no response (n=5), 60% (n=3) initially experienced a clinical improvement, although control was lost

after a mean of 17 months. In 2 cases, a search for antidrug antibodies yielded negative results. Mepolizumab was discontinued in 6 cases (13.6%) owing to a lack of efficacy and switch to a different mAb (3 cases), adverse events (intense arthralgia and myalgia, 2 cases), and remission of asthma symptoms after 8 months of treatment (1 case). We also assessed the the FEV_1, Exacerbations, Oral corticosteroids, and Symptoms (FEOS) score [7] to quantify the response to mAbs (median score, 70 [51.75-76]) (Supplementary Tables 2 and 4). In patients with CRSwNP, we also observed an improvement in the nasal polyps score and use of OCS (Supplementary Table 5).

Our results support those of the DREAM [2], MENSA [3], and MUSCA [4] clinical trials in terms of reduction in annual exacerbations, improvement in lung function, and increased asthma control. In addition, these findings are concordant with those of other real-world studies reported by Harrison et al [8] in the REALITI-A study and Domingo Ribas et al [9] in the REDES study. REALITI-A [8] is a multicenter observational study (7 countries), in which 368 patients with SEA were treated with mepolizumab. The patients' clinical condition improved significantly in terms of the annual exacerbation rate (decreased by 69% from 4.63 to 1.43 per person-year). Exacerbations requiring hospitalization decreased by 71.6% (from 0.60 to 0.17 per person-year), and the daily OCS maintenance dose decreased from 10.0 (5.0-15.0) mg/d to 5.0 (0.0-7.5) mg/d. The REDES study [9] is a Spanish multicenter study including 318 patients with SEA treated with mepolizumab, as in our series. The authors reported a decrease in exacerbation rates (from 4.48 to 1.0 per person-year [77.5%]), in exacerbations requiring hospitalization (from 0.33 to 0.07 per person-year [78.8%]), and in the daily OCS maintenance dose (12.1 mg/d to 4.9 mg/d [59.9%]). After 12 months of treatment with mepolizumab, an improvement was observed in FEV_1 (1.88 to 2.08 L [10.4%]) and the ACT score (from 14.1 to 20.8 points). A comparison with the results of our study is shown in Supplementary Table 6.

In conclusion, compared with the pivotal studies, we found that treatment with mepolizumab in a real-world setting seemed to sustain long-term effectiveness, with increased asthma control, reduction in the exacerbation rate, and improvement in lung function in most cases. The overall failure rate was only 11.4%. Further studies will help to corroborate the real-world efficacy of this treatment.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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