# Mepolizumab treatment for severe eosinophilic asthma: a 5-years real-life experience

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

The main of our study was to evaluate the effectiveness of mepolizumab in real life, 5 years after its commercialization in Spain in 2017.

We performed a single-centre retrospective review of medical records of patients suffering from severe eosinophilic asthma, that initiated mepolizumab at the Severe Asthma Unit of the Hospital Clinic of Barcelona, since March 2017 to 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 in the study the patients who have received at least 6 doses of mepolizumab, and the data has been collected at baseline and every 6-12 months after treatment onset. Last update of the database: January 2023.



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We included 44 patients with SEA, 70.5% of them female, with a median age of 57 years (range: 18-81 years) at the beginning of treatment. The most frequently associated comorbidities were anxiety and / or depression in 50% of the patients, chronic rhinosinusitis with nasal polyps (CRwNP) in 45.5% and allergic rhinitis in 31.8% patients. Concerning treatment duration, 18.2% patients received mepolizumab during more than 60 months (5 years), 47.7% during 37 to 60 months, 27.3% during 13 to 36 months, 4.5% during 6 to 12 months, while one patient was treated during only 5 months. Clinical baseline characteristics of asthma patients are summarized in Supplementary Table 1. Overall, we observed a significant improvement in asthma outcomes after mepolizumab treatment. Mepolizumab decreased asthma exacerbations in the last 12 months by 70.2% compared to the previous year, while asthma exacerbations requiring hospitalization were reduced by 71.9%. Regarding lung function, the median forced expiratory volume in 1 s ($FEV_1$, L) increased +0.29L, with a range from –0.79L to 1.21L (two patients showing an improvement of >1L), $FEV_1$ (%) improving +9% and the forced expiratory flow at 25-75% ($FEF_{25-75}$) +11%. The median annual cumulative dose of oral corticosteroids (OCS, in milligrams) decreased from 900mg (Q1-Q3: 555-2565mg) in the previous year, to 0 mg (Q1-Q3: 0.0-1,364mg). About 95.5% (n=42) of asthma patients required at least one dose of OCS during the previous year of treatment, this being reduced to 47.7% (n=21) during mepolizumab treatment. Finally, the Asthma Control Test (ACT) scores increased from 13.9 to 20.1 points (+44.6%). In addition, we observed a reduction of the mean blood eosinophil count from 657 to 111 cells/µL (-83.1%) while total IgE was decreased from 229 to 145 kU/L (-36.7%). These results are summarized in Supplementary Table 2.





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The criteria proposed by the 2020 Consensus of Spanish Society of Pneumology and Thoracic Surgery (SEPAR) [6], was used to evaluating 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, $FEV_1$ and the use of OCS (Supplementary Table 3). We observed that a good response was achieved in 63.6% of our patients (complete response in 38.6% (n=17) and control in 25% (n=11) patients); partial response in 25% (n=11) patients; and no response in 11.4% (n=5) patients. The initial response to mAbs was assessed in a median of 4 months (Q1-Q3: 3-5 months) with a median increase of ACT Score from 14 (11 – 17.5) to 22 (19 - 24). Out of those with no response (n=5), 60% (n=3) initially presented a clinical improvement but lost control after a mean of 17 months. In 2 of them we searched for anti-drug antibodies with negative results. Mepolizumab was discontinued in 7 cases (15.9%), 3 patients due to lack of efficacy and switched to a different mAb, 2 patients due to adverse events (intense arthralgias and myalgias) while one patient discontinued treatment with mepolizumab after 8 months due to the remission of asthma symptoms. We also assessed the The FEV1, Exacerbations, Oral corticosteroids, and Symptoms (FEOS) Score [7] to quantify the response of mAbs, with a median score of 70 (Q1-Q3: 51.75 - 76) (Supplementary Table 2 and 4). In patients with CRwNP we also observed an improvement in nasal polyps scores and use of OCS (Supplementary Table 5).

Our results support those from DREAM [2], MENSA [3] and MUSCA [4] clinical trials, in terms of reduction of annual exacerbations, improvement of lung function, and asthma control achievement. In addition, these findings are concordant with other real-world studies reported by Harrison et al. in the REALITI-A study [8] and Domingo Ribas et al. in the REDES study [8]. The REALITI-A [7] is a multicentric (7 countries) observational study in which 368 patients with SEA were treated with mepolizumab. They showed a significant clinical improvement in the rates of annual exacerbations (reduced by 69% from 4.63 to 1.43 per person





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and year). Exacerbations requiring hospitalization were reduced by 71.6% (from 0.60 to 0.17 per person and year), 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 [8] is a multicentric study including 318 patients with SEA treated with mepolizumab in Spain, as our series. It reported a decrease in the exacerbation rates by 77.5% (from 4.48 to 1.0 per person and year), in the exacerbations requiring hospitalization (by 78.8% from 0.33 to 0.07 per person and year), in the daily OCS maintenance dose (by 59.9%, from 12.1 mg/d to 4.9mg/d), while showing an overall improvement in the $FEV_1$ (by 10.4%, from 1.88 to 2.08L) and in the ACT score (from 14.1 to 20.8 score points) after 12 months of mepolizumab treatment. A comparison with the results of our study is shown in Supplementary Table 6.

In conclusion, in our series, treatment with mepolizumab in a real-world setting seemed to demonstrate a sustained long-term effectiveness, obtaining an increased asthma control, reduction of exacerbations and improvement of lung function in most of our patients when compared to the pivotal studies, with an overall failure rate of only 11.4%. Further studies will help to corroborate the real-life efficacy of this treatment.





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**Consent to publication**

Patients gave consent for publication of their cases.

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