Tezepelumab in Patients With Severe Asthma: Response at 3 Months

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Severe asthma is a complex disease that is difficult to manage [1]. Tezepelumab is a human monoclonal immunoglobulin G2λ antibody targeting the cytokine thymic stromal lymphopoietin (TSLP). It prevents TSLP from binding to its receptor and reduces the stimuli that TSLP can induce in different endotypes of asthma. Tezepelumab reduces downstream biomarkers of inflammation, such as blood and airway eosinophils, fractional exhaled nitric oxide (FeNO), IgE, IL-5, and IL-13 [2].

In clinical trials, tezepelumab has been shown to reduce the annualized asthma exacerbation rate in patients with high and low levels of T2 inflammation biomarkers (although the effect was greater among those with high levels), to improve asthma control, quality of life, and lung function, and to reduce airway hyperresponsiveness [3-6].

Data on tezepelumab in daily clinical practice are scarce. Our study provides one of the few real-life evaluations of tezepelumab, in contrast with other biologics for treatment of severe asthma, such as anti–IL-5 agents [7,8] and dupilumab [9], which have been widely assessed in real-world studies.

We report the results of an observational, prospective, and multicenter study performed by the Registry of Severe Asthma of the Region of Murcia under routine clinical practice conditions in 8 centers in Murcia, Spain. The study was approved by a local ethics committee (Comité Ético de Investigación Clínica del Hospital Universitario Santa María del Rosell, Cartagena, Spain).

We present a series of 32 patients receiving tezepelumab for severe, uncontrolled asthma confirmed by experienced pulmonologists and allergologists from one of the participating asthma units.

Our aim was to assess early response to tezepelumab, measuring changes in lung function (prebronchodilator FEV_1 and FVC), asthma control (Asthma Control Test [ACT]), and quality of life (Mini Asthma Quality of Life Questionnaire [AQLQ]). In addition, blood eosinophils and FeNO were analyzed. The methods are described in Supplementary Appendix 2.

We performed a descriptive analysis. The quantitative variables are expressed as means and standard deviations and the qualitative variables as absolute frequencies and percentages. The normality of the variables was studied for the comparative analysis. The *t* test was used for paired samples in the case of a normal distribution; the Wilcoxon test was used in the case of a nonnormal distribution. Significance was set at α=0.05. Stata V14.0 (StataCorp LLC) was used for the analysis.

The mean age was 53.1 years, and 23 participants were women (72%). The average body mass index was 29.5. Ten patients (31.2%) were current or former smokers, and 19 (59.4%) were atopic. Twenty-eight patients were T2-high (sensitization to a perennial allergen that triggers symptoms and/or peripheral blood eosinophils >150/μL and/or FeNO >25 ppb), and 4 patients were T2-low (no sensitization to a perennial allergen that triggers symptoms, peripheral blood eosinophils <150/μL, and FeNO <25 ppb) [1].

Onset of disease was after 18 years of age for most patients (28 [75%]). Only 6 patients (18.7%) had rhinosinusitis, and 3 (9.4%) were corticosteroid-dependent. Mean baseline blood eosinophils were 387/μL, total IgE 244 IU/mL, and FeNO 30.6 ppb.

The baseline mean number of exacerbations was 2.8. A total of 21 patients (65.6%) had made at least 1 visit to the emergency department, and 6 (18.7%) had to be admitted to hospital. The mean values recorded were as follows: ACT, 11.4; AQLQ, 3.1; FEV_1, 2031 mL (71.4%); and FVC, 2752 mL (77.2%).

Table. Results After 3 Months' Treatment With Tezepelumab.[a]

N=32	Baseline	3 mo	Mean difference	*P* Value
ACT	11.4 (3.7)	16.4 (5.7)	5 (5)	<.00001
AQLQ	3.1 (1)	4.1 (1.5)	1.1 (1.4)	.0007
FVC, %	77.2 (17.9)	82 (15.8)	4.85 (9.57)	.0123
FVC, mL	2752 (870)	2929 (880)	176 (328)	.0085
FVC Z-score	−1.68 (1.22)	−1.30 (1.03)	0.38 (0.69)	.0098
FEV_1, %	71.4 (18.2)	77.2 (18)	5.79 (10.62)	.0076
FEV_1, mL	2031 (130)	2196 (700)	163 (52)	.0039
FEV_1 Z-score	−1.98 (0.94)	−1.58 (1.03)	0.40 (0.69)	.0084
Eosinophils	387 (592)	149 (128)	238 (576)	.050
FeNO	30.6 (21.9)	18.3 (12.6)	12.33 (15.5)	.0003

Abbreviations: ACT, Asthma Control Test; AQLQ, Mini Asthma Quality of Life Questionnaire; FeNO, fractional exhaled nitric oxide.
[a]Data are presented as mean (SD).

The demographic and clinical characteristics are detailed in Supplementary Table 1.

Remarkably, biologics had failed in 17 patients (9 omalizumab, 9 mepolizumab, 4 benralizumab, 3 dupilumab) (Supplementary Material).

No cases of nasal polyposis were recorded, probably because patients with this condition had been treated with other indicated biologics.

The Table summarizes the results after 3 months of treatment with tezepelumab.

Asthma control improved with a mean difference of 5 points (*P*<.00001), above the clinically minimal important difference of 3 points and higher than the increase found by Biener et al [10] of 2 points after 15 weeks of treatment with tezepelumab in a retrospective real-life study of 129 patients. An improvement in the ACT score was also reported with tezepelumab by Jiménez-Gómez et al [11] in 5 of 9 patients who did not respond to other biological treatments. Only 1 patient in our series had a baseline ACT score ≥20, while 7 patients had an ACT score ≥20 after tezepelumab.

Patients' quality of life improved with an increase of 1.1 points (*P*=.0007) in the mini AQLQ score, clearly above the clinically minimally important difference of 0.5 points.

We found an improvement in lung function: mean difference in FEV_1, 163 mL (*P*=.0039), 5.79% (*P*=.0076), and Z-score 0.40 (0.0084); and mean difference in FVC, 176 mL (*P*=.0085), 4.85% (*P*=.0123), and Z-score 0.38 (0.0098). This improvement in FEV_1 is higher than that reported in another real-life study with tezepelumab [9]. FEV_1 was ≥80% in 9 patients at baseline and in 13 patients after 3 months of tezepelumab.

Eosinophil values decreased by a mean of 238/µL (*P*=.050) and FeNO by a mean of 12.33 ppb (*P*=.0003).

We compared variables between patients who had previously used another biologic and biologic-naïve patients and found no significant differences in lung function or ACT score. We did find differences in quality of life, with a higher increase in AQLQ in naïve patients (1.72 vs 0.54, *P*=.0348), showing that treatment had a greater impact on quality of life in biologic-naïve patients.

Before starting treatment, 3 patients were taking daily doses of oral corticosteroids (1 patient 40 mg and 2 patients 15 mg). After 3 months of tezepelumab, only 1 patient was taking 10 mg/d.

The mean number of exacerbations in the previous year was 2.8, with 21 patients having to visit the emergency department and 6 patients requiring admission to hospital (Supplementary Table 1). After starting tezepelumab, 1 patient reported 1 exacerbation, 2 patients 2 exacerbations, and 1 patient 3 exacerbations. Two patients had to visit the emergency department, and no hospital admissions were reported.

No severe adverse effects were reported by the 32 patients included. One patient was excluded because he had to withdraw tezepelumab owing to general malaise and intense and severe eye itching.

Our study is subject to limitations. The limited cohort size and brief evaluation time restricted our ability to evaluate the impact on exacerbations and corticosteroid intake. Moreover, ours is a real-life study and not a controlled study. Nevertheless, we recorded an improvement in asthma control, quality of life, and lung function. Notably, other biologic drugs had failed in more than half of the patients.

In conclusion, our 3-month real-life study showed that tezepelumab improved asthma control, quality of life, lung function, and type 2 biomarker levels.

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Conflicts of Interest

Juan Carlos Miralles López has received consultancy fees from AstraZeneca and speaker's fees from Novartis, GSK, AstraZeneca, Sanofi, Chiesi, and Gebro. Rubén Espinosa Andújar has received speaker's fees from GSK, AstraZeneca, Sanofi, FAES, and Chiesi. Francisco Javier Bravo Gutiérrez has received speaker's fees from Novartis, Ferrer, GSK, AstraZeneca, Sanofi, and Chiesi. José Valverde Molina has received consultancy fees from AstraZeneca and speaker's fees from Novartis, GSK, Astra Zeneca, Sanofi, and GEBRO. Sheila Cabrejos has received speaker's fees from GSK, Novartis, Sanofi, Stallergenes, ASAC Pharma, Inmunotek, Chiesi, and Allergy Therapeutics. The remaining authors declare that they have no conflicts of interest.

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