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SHORT COMMUNICATION

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Real-life effectiveness of tezepelumab in severe asthma

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effectiveness;
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Abstract
Background: Tezepelumab is a human monoclonal antibody which inhibits the cytokine thymic stromal lymphopoietin and is effective in different asthma endotypes.
Methods: This is a prospective, multicenter study of the Register of Severe Asthma of the Region of Murcia (RE-ASGRAMUR) Group performed under routine clinical practice conditions.
Results: We present a series of 57 patients who completed at least 6 months of treatment with tezepelumab. The exacerbations decreased from a baseline mean of 2.63 in the previous year to a *mean annualized rate of* 0.38 after 6 months of tezepelumab (85.6% decrease). The Asthma Control Test score increased by 5.3 points, and the Mini Asthma Quality of Life Questionnaire score increased by 0.94 points. Regarding lung function, we obtained a significant increase

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of 188 mL in forced expiratory volume in 1 s and 166 mL in forced vital capacity. Finally, type-2 (T2) biomarkers, such as eosinophils and nitric oxide, showed a significant decrease. We compared the results in patients with or without previous biological treatment as well as in patients with or without allergy sensitization, and we did not obtain significant differences in any variable.

Conclusions: Tezepelumab is an effective treatment for severe asthma, lessening exacerbations, controlling the disease, and improving quality of life and lung function in patients with and without high T2 biomarkers, regardless of previous biological treatment.

Introduction

Severe asthma (SA) is a complex disease, which is difficult to manage, and in spite of the current available treatments, a proportion of patients are not able to achieve complete control of asthma.[1]

Tezepelumab is a human monoclonal immunoglobulin G2λ antibody targeting the cytokine thymic stromal lymphopoietin (TSLP). It inhibits TSLP from binding to its receptor, thereby reducing the stimuli that TSLP induces in different asthma endotypes. It lowers inflammation-related biomarkers, including blood and airway eosinophils, fractional exhaled nitric oxide (FeNO), immunoglobulin E (IgE), interleukin (IL)-5, and IL-13.[2]

In clinical trials, tezepelumab is shown to reduce the annualized asthma exacerbation rate in patients with high and low levels of type-2 (T2) inflammation biomarkers to improve asthma control, quality of life, and lung function, and to reduce airway hyperresponsiveness.[3-5] Unlike other biological treatments, tezepelumab has shown effectiveness across various severe asthma phenotypes, with better results in eosinophilic severe asthma and allergic severe asthma than in type-2 low asthma.[6]

Data on treatment with tezepelumab in daily clinical practice are scarce.[7] Hence, we have recently published data of severe asthma patients after having 3 months of tezepelumab treatment.[8]

Our study aimed to check the response to 6-month tezepelumab treatment, under routine clinical practice, regarding exacerbations, asthma control, quality of life, and lung function in a series of severe asthma patients.

Methods

This was a prospective, multicenter study of the Register of Severe Asthma of the Region of Murcia Group (RE-ASGRAMUR) performed at nine hospitals of the Region of Murcia (Spain) under conditions of routine clinical practice. The study was conducted ethically according to the World Medical Association Declaration of Helsinki. The patients gave their written informed consent, and the Research Ethics Committee approved the study (approval No. E.O. 2021-77).

We included patients diagnosed with severe asthma (according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria), having completed at least 6 months of tezepelumab treatment. Patients treated with tezepelumab for <6 months, having other severe respiratory illnesses, and not accepting participation in the study were excluded from this work.

We analyzed clinical characteristics, drug tolerance, and effectiveness: exacerbations, Asthma Control Test (ACT), Mini Asthma Quality of Life Questionnaire (mini-AQLQ), and lung function (FEV1 – forced expiratory volume in 1 s).

A descriptive analysis of the study variables was performed. Absolute frequencies and percentage values were used for qualitative variables, and mean, standard deviation, median, interquartile range, and maximum and minimum were used for quantitative variables. The normality of quantitative variables was studied with the Kolmogorov–Smirnov test, and the Student's T-test for paired samples was used to compare baseline data and data at 6 months.

Results

We presented a series of 64 patients diagnosed with severe asthma and treated with tezepelumab. Seven patients stopped the treatment, three because of loss of follow-up, two because of treatment failure, and two because of adverse effects: one presented nausea, internal burning, and severe oculonasal itching, and another had subconjunctival effusion, general malaise with nausea and dizziness, numb hands, and hip pain. In all, 57 patients completed at least 6 months of treatment with tezepelumab.

The baseline patient characteristics are shown in Table 1. The mean age was 54.8 years; 65% of the patients were women, and most of the patients (76%) had the disease after 18 years of age.

A total of 35 patients (61.4%) were allergic, 17 patients were nonallergic with ≥150 blood eosinophils/μL and/or ≥25 parts per billion (ppb) FeNO, and 5 patients had T2 low biomarkers (eosinophils < 150 cells/μL and FeNO < 25 ppb).

We want to highlight that 29 patients were previously treated with a biological drug, and 11 of them with more than one biological drug. 19 were treated with omalizumab, 12 with mepolizumab, 7 with benralizumab, 7 with dupilumab, and 2 with reslizumab.

Table 2 shows the results with tezepelumab treatment.

Table 1 Baseline patient characteristics.

Parameter	N = 57
Women n (%)	37 (65)
Age (mean ± SD)	54.8 ± 13.5
BMI (mean ± SD)	31.1 ± 7.2
Smoking	
Never smoker, n (%)	37 (64.9)
Ex-smoker, n (%)	20 (35.1)
Age onset of symptoms	
0–18 years, n (%)	10 (24)
>18 years, n (%)	31 (76)
Allergy sensitization, n (%)	35 (61.4)
Rhinosinusitis, n (%)	13 (23)
Polyposis, n (%)	5 (8.8)
Corticosteroid-dependent, n (%)	5 (8.8)
Eosinophils (mean ± SD)	392 ± 530
IgE (mean ± SD)	218 ± 350
FeNO (mean ± SD)	30.1 ± 31.8
ACT (mean ± SD)	11.6 ± 3.8
AQLQ (mean ± SD)	3.2 ± 1.1
Exacerbations (mean ± SD)	2.63 ± 2.81
≥1 ED visit, n (%)	27 (47.4)
≥1 Hospital admission, n (%)	9 (15,8)
FVC, mL (mean ± SD)	2606 ± 974
FVC, % (mean ± SD)	74.9 ± 17.4
FEV1, mL (mean ± SD)	1883 ± 747
FEV1, % (mean ± SD)	67.9 ± 17.6
Prior treatment with a biological agent	29 (50.9)
Omalizumab, n (%)	19 (33.3)
Mepolizumab, n (%)	12 (21)
Benralizumab, n (%)	7 (12.3)
Dupilumab, n (%)	7 (12.3)
Reslizumab, n (%)	2 (3.5)

ACT: asthma control test; AQLQ: Asthma Quality of Life Questionnaire; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; FeNO: nitric oxide; ED: emergency department; IgE: immunoglobulin E; BMI: body mass index.

In all, 27 patients (47.4%) attended emergency department (ED), and 9 were hospitalized prior to the treatment. Only one patient attended ED and no hospitalization was recorded after tezepelumab treatment.

Five patients took oral corticosteroids daily (3 patients, 20 mg/d; 1 patient, 15 mg/d; and 1 patient, 5 mg/d) prior to treatment. After tezepelumab treatment, one patient took 10 mg/d and another 5 mg/d of oral corticosteroids.

Discussion

The exacerbations decreased from a baseline mean of 2.63 in the previous year to a *mean annualised rate* of 0.38 after 6 months of tezepelumab therapy (85.6% decrease; P < 0.00001). A significant decrease in the annualized exacerbation rate was also reported by Biener et al. in a patient series in Germany.[7]

The ACT score increased by 5.3 points, above the minimally important difference (3 points) and similar to the improvement we observed after 3 months of tezepelumab treatment,[8] and higher than the score reported by Biener et al.[7] The mini-AQLQ score raised by 0.94 points, also above the minimally important difference of 0.5 points.

Regarding lung function, we obtained a significant increase of 188 mL in FEV1 and 166 mL in forced vital capacity (FVC). Finally, T2 biomarkers, such as eosinophils and FeNO, showed a significant decrease.

In all, 13 patients (22.8%) had no exacerbations, no intake of oral corticosteroid, an ACT score ≥ 20, and a FEV1 ≥ 80% after 6 months of tezepelumab treatment, fulfilling the criteria of complete response.[9]

We compared exacerbations like ACT, AQLQ, FVC, FEV1, eosinophils, and FeNO—in patients with or without previous biological treatment and patients with or without allergy manifestations, and we obtained no significant difference in any variable.

We also checked differences between patients with allergic sensitization and patients without allergic sensitization with high T2 biomarkers (eosinophils ≥ 150 cells/μL

Table 2 Results after six months of tezepelumab treatment.

N = 57	Baseline	6 Months	Mean difference	P
Exacerbations	2.63 ± 2.81	0.38 ± 0.15	2.25 ± 2.74	0.001
ACT	11.6 ± 3.8	17 ± 5	5.3 ± 5.8	0.001
AQLQ	3.25 ± 1.1	4.2 ± 1.4	0.94 ± 1.4	0.001
FVC, %	74.9 ± 17.4	78.2 ± 18.2	3.3 ± 9.8	0.02
FVC, mL	2606 ± 974	2772 ± 946	166 ± 513	0.02
FEV1, %	67.9 ± 17,6	73.2 ± 19.1	5.3 ± 11.7	0.002
FEV1, mL	1883 ± 747	2071 ± 762	188 ± 439	0.003
Eosinophils	393 ± 530	150 ± 153	241 ± 516	0.002
FeNO	30.1 ± 31.8	23.2 ± 25.2	6.9 ± 23.1	0.04

ACT: asthma control test; AQLQ: Asthma Quality of Life Questionnaire; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; FeNO: nitric oxide; Data are presented as mean ± SD.

and/or FeNO ≥ 25 ppb) and T2 low biomarkers; however, no significant differences were observed.

In summary, we observed a significant lessening of exacerbations (85% decrease), and improved asthma control, quality of life, and lung function after 6 months of tezepelumab therapy. We had a good response with tezepelumab therapy in patients with failure to other biological drugs. In our series, tezepelumab was effective in patients with or without allergy as well as with or without high T2 biomarkers.

Authors Contributions

Juan Carlos Miralles-López and José Valverde-Molina designed the study and wrote the manuscript. Virginia Pérez-Fernández performed the informational analysis. All the authors contributed to data collection, and all read and approved the final manuscript.

Conflict of Interest

Juan Carlos Miralles-López received consultancy fees from AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, Chiesi, and Gebro. Francisco-José Bravo-Gutierrez received speaker fees from Novartis, Ferrer, GSK, AstraZeneca, Sanofi, and Chiesi. Rubén Andújar-Espinosa received speaker fees from GSK, AstraZeneca, Sanofi, FAES, and Chiesi. Manuel Castilla-Martínez received consultancy fees from GSK and AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and Chiesi. Sheila Cabrejos-Perotti received speaker fees from Sanofi. Maria Jesús Avilés-Inglés received speaker fees from Chiesi. Inmaculada Ibarra-Calabuig received speaker fees from Roxall, Hall Allergy, Asacpharma, Inmunotek, Diater, Sanofi, and Allergy Therapeutics. Miguel Henrique Reyes-Cotes received speaker fees from GSK and AstraZeneca. Manuel José Pajarón-Fernández received speaker fees from GSK. María Loreto Alemany-Francés received speaker fees from Novartis, GSK, AstraZeneca, and Chiesi. José Valverde-Molina received consultancy fees from AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and GEBRO. The remaining authors declared that they had no conflict of interest.

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Appendix

Members of the Register of Severe Asthma of the Region of Murcia Group

REgistro de Asma GRAve de la Región de MURcia (RE-ASGRAMUR) Steering Group
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