LETTER TO EDITOR

Real-life efficacy of Tezepelumab in patients with failure to other biologic drugs

Juan Carlos Miralles-López[1], Juan José Cortés Collado[2], Yulia Petryk Petryk[3], Francisco-Javier Bravo-Gutierrez[4,], Rubén Andújar-Espinosa[5], Mercedes Ramírez Hernández[6], Manuel Castilla-Martínez[7], Cayetano Díaz-Chantar[8], Inmaculada Ibarra-Calabuig[3], José Valverde-Molina[9,10], Virginia Pérez-Fernández[11], RE-ASGRAMUR GROUP*

[1]Department of Allergy, University General Hospital Reina Sofía, Murcia, Spain

[2]Department of Allergy, Hospital Virgen del Castillo, Yecla, Murcia, Spain

[3]Department of Allergy, University General Hospital Rafael Mendez, Lorca, Murcia, Spain

[4]Department of Pulmonology, University General Hospital Santa Lucia, Cartagena, Murcia, Spain

[5]Department of Pulmonology, University Clinic Hospital Virgen de la Arrixaca, Murcia, Spain

[6]Department of Allergy, University General Hospital Santa Lucia, Cartagena, Murcia, Spain

[7]Department of Pulmonology, University General Hospital Los Arcos, San Javier, Murcia, Spain

[8]Department of Pulmonology, Hospital de la Vega Lorenzo Guirao, Cieza, Murcia, Spain

[9]Department of Paediatrics, University General Hospital Santa Lucia, Cartagena, Murcia, Spain

[10]IMIB Biomedical Research Institute, Murcia, Spain

[11]Department of Public Health Sciences, University of Murcia School of Medicine, Murcia, Spain.

[*]Members of the RE-ASGRAMUR (Register of Severe Asthma of the Region of Murcia) Group are listed in Appendix 1.

Key words

Tezepelumab; severe asthma; real-life efficacy; failure previous drugs.

To the Editor,

Tezepelumab is a human monoclonal IgG2λ antibody that targets the cytokine thymic stromal lymphopoietin (TSLP). By blocking TSLP from binding to its receptor, Tezepelumab helps inhibit the immune responses TSLP initiates across various asthma endotypes. This results in a reduction of key inflammatory biomarkers, such as blood and airway eosinophils, fractional exhaled nitric oxide (FeNO), immunoglobulin E (IgE), interleukin-5 (IL-5), and interleukin-13 (IL-13) [1].

Tezepelumab has been shown to reduce asthma exacerbations and to improve asthma control, quality of life, and lung function in clinical trials [2,3].

Real-world data on tezepelumab have been reported [4,5], and our group has published 3-month and 6-month results of tezepelumab treatment in real-life settings [6,7]. Our objective has been to study the effectiveness of tezepelumab in patients with severe asthma who had previously experienced failure with another biologic drug.

We report the results of an observational, prospective, and multicenter study performed by the Registry of Severe Asthma of the Region of Murcia (RE-ASGRAMUR) under

routine clinical practice conditions in 9 centers in Murcia, Spain. The study was conducted ethically in accordance with 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) who had completed at least 6 months of tezepelumab treatment. We analyzed exacerbations, changes in lung function (pre-bronchodilator FEV1), asthma control (ACT), and quality of life (mini AQLQ). Additionally, T2 biomarkers, including blood eosinophils and exhaled nitric oxide (FeNO), were also analyzed.

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 assessed using the Kolmogorov–Smirnov test, and the Student's t-test for paired samples was employed to compare baseline data and data at 6 months.

We present a series of 35 patients diagnosed with severe asthma treated with tezepelumab who had previously experienced failure with another biologic drug. The reason for switching biological drugs was loss of efficacy. Six patients stopped the treatment, two 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.

Twenty-nine patients completed at least 6 months of treatment with tezepelumab. Table I shows the baseline characteristics of our patients.

The mean age was 51.9 years, with the majority of patients (67%) being women. The mean age of symptom onset was 28 years. Eighteen patients (62.1%) were atopic, 9 (31%) had rhinitis, and 3 (10.3%) had nasal polyps.

The mean of exacerbations in the previous year was 2.9; fifteen patients (51.7%) had to visit the ED, and six (20.7%) needed hospital admission.

Overall, patients were not well controlled, with a mean ACT score of 10.65, and experienced impaired quality of life, as indicated by a mean miniAQLQ score of 3.19.

The whole group of 29 patients had a previous failure with another biological drug: 19 (33.3%) with omalizumab, 12 (21%) with mepolizumab, 7 (12.3%) with benralizumab and dupilumab, and 2 (3.5%) with reslizumab. Eleven patients had been previously treated with more than one biological drug.

The results after tezepelumab treatment are shown in Table II. The mean exacerbation rate decreased from 2.9 to 0.62 (annualized), with a mean difference of 2.28, and the mean ED visits fell from 1.48 to 0.03.

The mean ACT score rose from 10.65 to 16.52, and the AQLQ score from 3.19 to 4.01. The mean FEV1 increased by 260 mL (7.04%). Eosinophils showed a significant mean reduction of 351. Finally, mean FeNO had a nonsignificant decrease of 5.6 ppb.

The mean rate of exacerbation decreased by 78.8%, a finding consistent with that reported in other real-life studies involving tezepelumab. [4,5,8]. On the other hand, the rate of ED visits dropped a 98%. We consider these figures highly significant because all patients had previously failed at least one biological drug, and 11 of them had failed more than one. Furthermore, all patients had severe T2-high asthma, previously treated with biological drugs targeting the T2 pathway. Patients with T2-high asthma treated with mepolizumab had increased sputum proteins, including TSLP [9], and this feature may explain the favorable response to tezepelumab in patients with poor response to anti-IL5 drugs.

Besides exacerbations, tezepelumab also improved asthma control, with an increase in ACT score of 5.86 points, exceeding the minimal important difference (MID) of 3 points, and quality of life, as evidenced by the rise in miniAQLQ score of 0.82 points.

Regarding T2 biomarkers, we found a significant reduction in blood eosinophils and a non-significant reduction in FeNO.

By blocking the action of TSLP early in the inflammatory cascade, tezepelumab inhibits several downstream inflammatory pathways, which may explain its success compared to other biologics that target single inflammatory pathways.

Tezepelumab reduces blood eosinophil counts, as well as levels of fractional exhaled nitric oxide (FeNO) and IgE, by decreasing the levels of IL-5, IL-13, and IL-4.

Furthermore, tezepelumab may directly affect mast cell function, which plays a central role in the allergic response[10]. These actions could explain the success of Tezepelumab in severe allergic asthma. The majority of our patients were atopic, and tezepelumab has demonstrated broad efficacy in patients with severe allergic asthma, representing a valuable therapeutic option for these patients.

In summary, Tezepelumab is an effective treatment for patients with T2-high severe asthma who have failed another biological drug, improving exacerbations, asthma control, quality of life, and lung function.

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Author 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 has received consultancy fees from AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, Chiesi, and Gebro. Juan José Cortés Collado has received speaker fees from AstraZeneca, Sanofi, and GSK. Yulia Petryk Petryk has received speaker fees from AstraZeneca, Sanofi, and Chiesi. Francisco Javier Bravo Gutiérrez has received speaker fees from Novartis, Ferrer, GSK, AstraZeneca, Sanofi, and Chiesi. Rubén Espinosa Andújar has received speaker fees from GSK, AstraZeneca, Sanofi, FAES, and Chiesi. Manuel Castilla-Martínez has received consultancy fees from GSK and AstraZeneca and speaker fees from Novartis, GSK, AstraZeneca, Sanofi, and Chiesi. Inmaculada Ibarra Calabuig has received speaker fees of Roxall, Hall allergy, Asacpharma, Inmunotek, Diater, Sanofi, and Allergy Therapeutics. José Valverde Molina has received consultancy fees from AstraZeneca and speaker fees from Novartis, GSK, Astra Zeneca, Sanofi, and GEBRO. The remaining authors declare that they have no conflicts of interest.

The authors declare that none of the conflicts of interest described are related to the article.

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Table I. Baseline patient characteristics

Parameter	**N=29**
Women n (%)	20 (67)
Age (mean ± SD)	51.9 ± 11.9
BMI (mean ± SD)	30 ± 7
Age onset symptoms (mean ± SD)	28 ± 16
Atopic, n (%)	18 (62.1)
Rhinitis, n (%)	9 (31)
Polyposis, n (%)	3 (10.3)
Eosinophils (mean ± SD)	482 ± 691
IgE (mean ± SD)	297.6 ± 463.8
FeNO (mean ± SD)	26.3 ± 21
ACT (mean ± SD)	10.65 ± 4.05
AQLQ (mean ± SD)	3.19 ± 1.23
Exacerbations (mean ± SD)	2.9 ± 3.17
≥ 1 ED visit n (%) ≥ 1 Hospital admission n (%)	15 (51.7) 6 (20.7)
FEV1 ml (mean ± SD)	1864 ± 773
FEV1 % (mean ± SD)	67.78 ± 15.73
Prior treatment with a biological agent Omalizumab, n (%) Mepolizumab, n (%) Benralizumab, n (%) Dupilumab, n (%) Reslizumab, n (%)	29 (100) 19 (33.3) 12 (21) 7 (12.3) 7 (12.3) 2 (3.5)

Table II. Results in patients with previous treatment with another biological drug

N=29	Previous	6 months	Mean difference	P
Exacerbations	2.9 ± 3.17	0.62 ± 1.5	2.28 ± 3.03	0.0004
ED visits	1.48 ± 1.94	0.03 ± 0.19	1.45 ± 1.92	0.0004
ACT	10.65 ± 4.05	16.52 ± 5.06	5.86 ± 5.86	0.00001
AQLQ	3.19 ± 1.23	4.01 ± 1.27	0.82 ± 1,32	0.0085
FEV1, %	67.78 ± 15.73	74.82 ± 15.46	7.04 ± 11.77	0.0046
FEV1, ml	1864 ± 773	2133 ± 653	268 ± 508	0.0094
Eosinophils	482 ± 691	130 ± 115	351 ± 681	0.0163
FENO	26.3 ± 21	20.7 ± 18	5.6 ± 16	NS

Appendix 1

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

Manuel Castilla Martínez (Hospital Universitario Los Arcos del Mar Menor, San Javier, Spain), Juan Carlos Miralles López (Hospital Universitario Reina Sofía, Murcia, Spain), José Valverde Molina (Hospital General Universitario Santa Lucía, Cartagena, Spain)

Investigators (alphabetical order of centers)

Manuel Castilla Martínez, Lelia Gacías-Pedrós, José Valverde Molina, Andres Barrios Recio (Hospital Universitario Los Arcos del Mar Menor, San Javier, Spain), Loreto Alemany Francés, Roberto Bernabeu Mora, Ana Mora González (Hospital General Universitario Morales Meseguer, Murcia, Spain), Miguel Henrique Reyes Cotes, Isabel M. Flores Martín (Hospital Comarcal del Noroeste, Caravaca, Spain), El Molaka Zouhair, Inmaculada Ibarra Calabuig, Yulia Petryk-Petryk (Hospital General Universitario Rafael Méndez, Lorca, Spain), Juan Carlos Miralles López, María Jesús Avilés Inglés, Consuelo Alcalde Rumayor, Cristina Navarro Garrido (Hospital General Universitario Reina Sofía, Murcia, Spain), Javier Bravo Gutiérrez, Rocío Ibáñez Meléndez, Sheila Cabrejos-Perotti, Mercedes-Ramírez Hernández, Carolina Díaz García, Francisco Javier Rodriguez-Dominguez (Hospital General Universitario Santa Lucía, Cartagena, Spain), Manuel José Pajarón Fernández, Cayetano Díaz Chantar, Carmen Alvarez Santacruz (Hospital Comarca La Vega, Cieza, Spain), Rubén Andújar Espinosa, José Meseguer Arce, Mariola Navarro Guerrero (Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain), Antonio Carbonell Martínez (Centro Médico la Fama, Murcia, Spain).