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RESEARCH LETTER

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Real-life experience after 3 months with tezepelumab before marketing approval

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ABSTRACT

Background: Tezepelumab is a monoclonal antibody targeting thymic stromal lymphopoietin (TSLP), implicated in asthma pathogenesis, and that has been approved for patients with severe uncontrolled asthma in Spain in October 2023. This study evaluates our experience with Tezepelumab for those patients who received the indicated drug off-label prior to its commercialization.

Methods: We conducted a real-life observational study on three patients from the Severe Asthma Unit of the Hospital Universitario de Fuenlabrada, Spain, who received Tezepelumab off-label before its official approval. We analyzed symptoms control based on ACT, exacerbations, reductions in the doses of oral corticosteroid, lung function, blood changes and safety at 3 months of treatment.

Results: Tezepelumab demonstrated efficacy in improving asthma control and a notable reduction in emergency department visits. OCS use decreased, with one patient halving their prednisone dose. Lung function, particularly FEV1 and FEV1/FVC parameters, improved, but no significant changes were observed in FeNO levels, blood eosinophil counts and total IgE. The treatment exhibited a favorable safety profile with no reported adverse effects during the study period.

Conclusions: In this preliminary real-world experience prior to the official approval of tezepelumab in Spain, this monoclonal antibody showed promising results and suggests its potential as a valuable alternative for the treatment of severe asthma.

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Tezepelumab is a human monoclonal antibody that blocks activity of the thymic stromal lymphopoietin (TSLP), an epithelial cell-derived cytokine implicated in asthma pathogenesis. TSLP is released by the airway epithelial cells in response to allergens and other environmental triggers and drives airway inflammation by initiating both T2 and non-T2 processes through its downstream inflammatory effects, involving a wide range of cells, such as hematopoietic progenitor cells, eosinophils, basophils, mast cells, airway smooth muscle cells (ASMCs), group 2 innate lymphoid cells (ILC2s), lymphocytes, dendritic cells, and monocytes/macrophages.¹

In a recent published *post hoc* analysis from the two clinical trials PATHWAY and NAVIGATOR, it was demonstrated that tezepelumab showed clinically meaningful reductions in exacerbations and improvement in different outcomes across patient subgroups defined by various inflammatory biomarker levels, such as reduction in eosinophil counts, fractional exhaled nitric oxide (FeNO), and total immunoglobulin E (IgE) levels from baseline, and clinical characteristics, such as subgroups with evidence of both T2 or non-T2 inflammation.^{2,5}

However, because of a very recent marketing approval (October 1, 2023) of tezepelumab in Spain, few real-life data are available to date, except for the patients who received tezepelumab off-label.

The aim of this contribution was to report our experience with three patients who were administered tezepelumab at the Severe Asthma Unit of the Hospital Universitario de Fuenlabrada between April and July 2023 prior to its marketing approval.

We analyzed symptoms control based on asthma control test (ACT), exacerbations, reduction in the doses of oral corticosteroids (OCS), lung function, blood changes, and safety at 3 months of treatment. Written informed consent was obtained from the participants before administration of tezepelumab. Table 1 describes the clinical profile of each patient and summarizes clinical, functional, and laboratory data at both baseline and 3-month follow-up.

The first patient was a 42-year-old male, an ex-smoker. He was diagnosed with uncontrolled severe T2-phenotype asthma, allergic rhinitis, aspirin-exacerbated respiratory disease (AERD), and alpha-1 antitrypsin deficiency (AATD) low-risk phenotype. He was refractory to previous treatment with omalizumab (February 2019-June 2022) and benralizumab (June 2022-March 2023); hence in April 2023, it was decided to switch him to tezepelumab.

The second patient was a 46-year-old female, also diagnosed with uncontrolled severe T2-phenotype asthma, with no comorbidities other than allergic rhinitis, refractory to previous treatment with benralizumab for 1 year (May 2022-June 2023). In July 2023, she was started treatment with tezepelumab.

The third patient was a 77-year-old female with severe non-T2 phenotype asthma, having a daily treatment with 10-mg prednisone, and diagnosed with gastroesophageal reflux. She started her first biologic treatment with tezepelumab in July 2023.

As illustrated in Table 1, patients showed improved asthma control based on the ACT scores at 3 months of treatment, compared with baseline (7 ± 15 vs. 16 ± 19). This improvement in the perception of asthma control was objectively accompanied by reduction in the number of emergency department visits at 3 months, compared with baseline (1 ± 4 visits annually vs. 0 visits at 3 months). Regarding OCS use, the number of prednisone cycles because of the exacerbations at 3 months of tezepelumab treatment, compared to baseline, decreased in both first and second patient (1 ± 4 cycles per year vs. 0 cycles at 3 months). In the third patient, the daily dose of prednisone decreased by 50% (from 10 mg to 5 mg), with no increase in prednisone dose because of exacerbations in these months.

Although a larger sample size is needed to draw conclusions, lung function, measured as both volume in milliliter and percentage, improved in our patients, especially for both forced expiratory volume in the 1st second (FEV1) and

Table 1. The clinical profile of each patient and summarizes clinical, functional, and laboratory data.

Patient	Basal pre-Tezepelumab			3m with Tezepelumab		
	1	2	3	1	2	3
Total IgE (UI/ml)	256	169	48.7	33.5	344.3	64.7
Peripheral blood eosinophils (cels/mcL)	0 Eo (previous Benralizumab)	10 Eo (previous Benralizumab)	30 Eo (no previous biologic treatment)	100 Eo	10 Eo	20 Eo
FeNO (ppb)	< 5	25	8	<5	14	4
FVC	4.66L (86.3%)	3.40L (104.6%)	2.07L (98.2%)	4.79L (88.8%)	3.89L (106%)	2.02L (95.8%)
FEV1	3.01L (68.8%)	2.47L (88.4%)	1.20L (70%)	3.18L (72.6%)	3.17L (107%)	1.31L (76.6%)
FEV1/FVC	64.64%	72.82%	58.03%	66.25%	81.32%	65.08%
Asthma control Test (ACT)	7	10	15	18	16	19
Exacerbations/year	4	1	1	0	0	0
Oral corticosteroid cycles	4	1	1*	0	0	0**

* Patient with basal 10mg/24h of Prednisone

** Patient with reduced basal 5mg/24h of Prednisone

FEV1/forced vital capacity (FVC) parameters at 3 months, compared with baseline. However, no major changes were observed when analyzing FeNO levels, blood eosinophil counts, and total IgE. In terms of safety, no adverse effects were reported during the course of treatment.

Conclusion

Our first real-life results prior to the marketing approval of tezepelumab in Spain confirmed that in a real-life setting, a 3-month tezepelumab treatment improved lung function and specially asthma control. It also decreased emergency department visits and reduced the use of OCS; this all was in line with pivotal studies.

It is likely that the failure to demonstrate a decrease in FeNO levels, eosinophilia, and total IgE was due to the short period of time over which the patients were followed.

Authors contributions

Victoria Villalobos Violán and Mar Gandolfo-Cano made substantial contributions to the acquisition, analysis, and interpretation of data, drafted and revised it critically, and provided their approval to the final version. Beatriz González Cano, Miguel Ángel Racionero Casero, Eloína González-Mancebo, Ester Mohedano Vicente, and Maria Jesus Trujillo Trujillo made substantial contributions to the acquisition of data, drafted and revised it critically, and provided their approval to the final version.

Conflict of interest

Victoria Villalobos Violán, Eloína González-Mancebo, Ester Mohedano Vicente, MJ Trujillo Trujillo, and Mar Gandolfo-Cano received honoraria as speakers from Astra-Zeneca. Miguel Ángel Racionero had received honoraria as a speaker and for participation in a clinical study from Astra-Zeneca. Beatriz González Cano declared no conflict of interest.

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