

Successful Desensitization to Tezepelumab in a Polysorbate-Allergic Patient

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Hypersensitivity reactions (HSRs) are defined as noxious and unintended responses to a drug that occur at doses normally used in humans for the prophylaxis, diagnosis, or treatment of disease or for modification of physiological function [1]. The mechanisms responsible for HSRs are not fully understood and may vary between IgE-mediated, non-IgE-mediated, and unclear pathogenic events [2]. Typically, medications are avoided after HSRs unless there is a pressing medical need and no alternative. Desensitization to drugs that cause allergy is not risk-free, although it is a useful procedure and has been applied for

drug HSRs involving mast cell degranulation and IgE- and non-IgE-mediated mechanisms.

Tezepelumab, a human monoclonal antibody (immunoglobulin G2λ), binds specifically to thymic stromal lymphopoietin (TSLP). By blocking TSLP, tezepelumab has demonstrated efficacy across known asthma phenotypes and acts upstream of all biomarkers used in daily clinical practice [3]. According to the summary of product characteristics, the frequency of allergic reactions to tezepelumab cannot be estimated from currently available data [4]. The excipients of tezepelumab include polysorbate 80, a widely used additive in many liquid and solid formulations of medications, including most biological agents currently used for the treatment of severe asthma [5].

We present the case of a polysorbate-allergic patient with severe asthma who was successfully desensitized to tezepelumab.

A 47-year-old man was diagnosed with asthma in 2018 and with severe asthma in 2020, when he started treatment with omalizumab, which was interrupted owing to lack of efficacy. Dupilumab was initiated in 2021, although it proved to be inefficient and was switched to benralizumab.

Less than an hour after the first dose of benralizumab, the patient developed scalp pruritus that later became generalized, palpebral angioedema, facial erythema, and throat tightness with no visible pharyngeal angioedema. These symptoms resolved in less than 2 hours with corticosteroid and antihistamine treatment.

Since benralizumab contains polysorbate 20, skin tests were performed with the polysorbate available in our pharmacy, which was polysorbate 80. Prick tests and intradermal skin tests with polysorbate 80 performed at 0.0004 mg/mL and 0.004 mg/mL [6] yielded a positive result (7-mm wheal with surrounding erythema after 15 minutes) at 0.004 mg/mL in the intradermal skin test.

Table. Tezepelumab Desensitization Protocol

Step	Dose administered, mg	Tezepelumab concentration	Volume, mL	Time, min
1	2.12	0.1 cc solution B + 0.9 cc SS ^a	1	30
2	4.25	0.2 cc solution B + 0.8 cc SS	1	30
3	8.51	0.4 cc solution B + 0.6 cc SS	1	30
4	17.02	0.8 cc solution B + 0.2 cc SS	1	30
5	34.04	1.6 cc solution B + 0.4 cc SS	2	30
6	65.96	0.6 cc solution A + 0.4 cc SS ^b	1	30
7	76.96	0.7 cc solution A + 0.3 cc SS	1	30
Total	208.86			210 min (3h 30)

Abbreviation: SS, saline solution.

^aSolution B – 21.27 mg/mL (0.6 mL of solution A + 2.5 mL of saline solution, giving a total of 65.96 mg/3.1 mL).

^bSolution A – 210 mg/1.91 mL (undiluted tezepelumab).

As a result, benralizumab was discontinued and reslizumab (which does not contain polysorbate or polyethylene glycol) was started and well tolerated, although it was subsequently discontinued owing to lack of effectiveness.

At this point, given the ineffectiveness of the previous treatments, we offered the patient desensitization to tezepelumab, which he accepted. The patient gave his written informed consent for desensitization and for the publication of results.

We developed a protocol for desensitization to tezepelumab (Tezspire) similar to other desensitization protocols for subcutaneous biological treatments [7].

We used 2 solutions: solution A, at 210 mg/1.91 mL (undiluted tezepelumab); and solution B, at 21.27 mg/mL (created with 0.6 mL of solution A, plus 2.5 mL of saline solution, giving a total of 65.96 mg/3.1 mL).

The patient was admitted to the intensive care unit, where he was monitored. We decided not to start specific pretreatment, because he was already taking montelukast 10 mg, cetirizine 10 mg, and prednisone 15 mg daily and had been diagnosed with hypersensitivity to nonsteroidal anti-inflammatory drugs.

Before starting desensitization, skin testing was performed using tezepelumab at a 1/100 dilution (1.01 mg/mL), yielding a negative result in the prick test and a positive result in the intradermal skin test (even though the patient was taking cetirizine daily). The same concentration revealed a negative result in 2 healthy controls.

The desensitization protocol was administered subcutaneously following the steps shown in the Table. Twenty minutes after step 4, the patient developed pharyngeal and genital pruritus, wheezing, and pruritic erythema, with a few hives on his upper abdomen. However, there were no changes in saturation, blood pressure, or other vital signs. He was treated immediately with methylprednisolone, dexchlorpheniramine, and salbutamol, with complete resolution of symptoms in 20 minutes. We decided to resume desensitization by repeating the same dose as in step 4 (17.02 mg). In order to reduce costs, we agreed not to use a new vial: therefore, we decided to divide step 5 into 2 doses. As the full dose in step 5 was 34.04 mg/2 mL, we administered 1 mL of step 5 (17.02 mg) and, after 30 minutes, the remaining 1 mL of step 5. The doses were well tolerated. The rest of the procedure was uneventful, and the patient was discharged.

One month later, the second desensitization procedure was performed following the original protocol (Table). No changes were necessary, the doses were well tolerated, and no reactions were observed.

Our protocol was safe in the patient treated, who was able to tolerate what we believe is the best therapeutic option for him at this time.

The disadvantages of the procedure are the need for in-hospital administration, the human and material resources required, and the time involved. Administration times could be shortened in the future if tolerance continues to be adequate, as shown in other series [8]. However, the clinical benefit of being able to select optimal treatment safely in a patient with severe disease outweighs the disadvantages. Considering

the biologics used for severe asthma, published data for desensitization procedures is limited to omalizumab and dupilumab [7,8]. The largest cohort on record that underwent desensitization to omalizumab includes only 12 patients [7]. Data on desensitization to other biologics for severe asthma are lacking, although current guidelines recommend protocols used successfully for monoclonal antibodies such as rituximab or infliximab, which are used to treat diseases other than severe asthma [9]. We report our experience in the desensitization of a patient with a proven allergy to tezepelumab due to polysorbate, an excipient that is currently included in all subcutaneous monoclonal antibodies for severe asthma. Further studies will be needed to test the safety of this protocol in a larger cohort of patients.

To our knowledge, we present the first desensitization protocol for tezepelumab (Tezspire) in a polysorbate-allergic patient.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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