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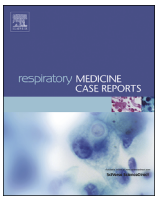

Case Report

Tezepelumab improved chronic rhinosinusitis with nasal polyps in a Patient with aspirin exacerbated respiratory disease

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ABSTRACT

Introduction: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) and aspirin-exacerbated respiratory disease (AERD) have more severe sinus disease than those without AERD. CRSwNP associated with type 2 inflammation and AERD can be difficult to control with standard medical therapy and sinus surgery.

Case study: 74-year-old Japanese woman with chronic sinusitis since age 50 and asthma since age 60. At age 64, she began to experience asthma exacerbations and was started on short-term corticosteroid therapy with prednisolone. At age 70, she experienced urticaria, nasal congestion, and wheezing after taking an NSAID; based on an NSAID provocation test, we diagnosed the patient with AERD and CRSwNP. A diagnosis of severe eosinophilic chronic rhinosinusitis was also made based on the scoring system and algorithm used in the Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis.

Results: Treatment with benralizumab (30 mg), formoterol–fluticasone combination via pressurized metered inhaler (1000 μg), and leukotriene receptor antagonist improved the asthma symptoms and exacerbations so the short-term prednisolone was stopped; however, nasal congestion and olfactory dysfunction (hyposmia) persisted, and peripheral blood eosinophil count (peak, 1500 cells/μL) and fractional exhaled nitric oxide (peak, 42 ppb) became elevated. Swapping the benralizumab for monthly tezepelumab (210 mg) improved not only the asthma symptoms but also the nasal congestion, olfactory dysfunction, eosinophil count (< 300 cells/μL), and fractional exhaled nitric oxide level [8ppb].

Conclusion: Changing from benralizumab to tezepelumab improved asthma symptoms, nasal obstruction, and olfactory dysfunction in elderly, female, Japanese patient with AERD and CRSwNP.

1. Background

Aspirin-exacerbated respiratory disease (AERD) is characterized by moderate-to-severe asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and intolerance of Nonsteroidal anti-inflammatory drug (NSAIDs). The cause of the disease is overproduction of

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cysteinyl leukotrienes following dysregulation of arachidonic acid metabolism, resulting in an increase of type 2 eosinophilic inflammation. [1–3]. Compared with the general asthma population, the prevalence of severe asthma among patients with AERD (15 %) is approximately double, and most AERD patients report upper airway symptoms from as early as 5 years prior to receiving a diagnosis of asthma [4].

CRSwNP is an inflammatory condition of the nasal passages, is confirmed nasal polyps and paranasal sinuses that is diagnosed based on the presence of two or more symptoms, one of which should be either rhinorrhea or nasal congestion/obstruction, with or without facial pain or pressure or loss of sense of smell for at least 12 weeks. [5]. About 10 % of patients with difficult-to-treat CRSwNP have comorbid AERD. [6]. Patients with CRSwNP and N-ERD have more severe sinus disease and worse health-related quality of life than those without AERD. [1].

CRS (with or without NP) has three endotypes: T1 is characterized by the type 1 cytokines interferon gamma and transforming growth factor beta; T2 by the type 2 inflammatory proteins and cytokines immunoglobulin E, interleukin (IL)-4, IL-5, and IL-13; and T3 by the cytokine IL-17A produced by T helper 17 cells. [7]. In T2 CRSwNP, eosinophils make up the predominant inflammatory cells in the mucous lining of the sinuses, although type 2 innate lymphoid cells, B cells, macrophages, dendritic cells, mast cells, and basophils are also found. [8]. Patients with the T2 endotype may also present with increased fractional exhaled nitric oxide level and either normal or elevated serum total immunoglobulin E. [9].

Biologics are promising agents for the treatment of AERD, especially in difficult-to-treat asthmatics. Omalizumab use in AERD patients is associated with reduction in steroid use and decreased hospitalization, [10], and decreased nasal polyp score in two phase III trials. [11]. Mepolizumab was shown recently to be effective for the treatment of nasal polyposis in patients with co-morbid asthma in a trial in which AERD subjects were included. [12]. Benralizumab, when added to standard-of-care therapy, reduced nasal polyp score (NPS), decreased nasal blockage, and reduced difficulty with sense of smell compared with placebo in patients with CRSwNP. [13]. Benralizumab decrease asthma exacerbation in severe asthma patients with or without NPS. [14]. In patients with uncontrolled severe CRSwNP, dupilumab significantly improved objective measures and patient-reported symptoms to a greater extent in the presence of comorbid AERD than without, [15], with similar findings being reported from two randomized placebo-controlled phase III trials. [16].

Thymic stromal lymphopoietin (TSLP) is an epithelial cell–derived cytokine that has recently been identified as a key factor in type 2 inflammation. [17]. TSLP receptor expression is significantly higher in the inflammatory infiltrate and in the epithelial cells of both CRSwNP and chronic rhinosinusitis without nasal polyps (CRSsNP) patients compared to controls. [18]. TSLP activity is increased in the nasal polyps of patients with chronic rhinosinusitis. [19]. Tezepelumab is a human monoclonal antibody that blocks thymic stromal lymphopoietin from binding to its heterodimeric receptor. Tezepelumab reduced asthma exacerbations and type 2 inflammatory biomarkers in patients with and without nasal polyps; [20–22]; however, the efficacy of tezepelumab against nasal polyps is yet to be evaluated.

Here, we present a patient with AERD who did not respond to benralizumab for the treatment of sinusitis symptoms including nasal congestion and olfactory dysfunction and who was subsequently switched to tezepelumab. After switch in therapy, the asthma symptoms, nasal congestion, anosmia, and computed tomography (CT) imaging findings all showed improvements.

2. Case

The patient was a 74-year-old Japanese woman with allergic rhinoconjunctivitis since age 45, chronic sinusitis since age 50, and asthma since age 60. She was atopic, with positive immunoglobulin E radioallergosorbent test results for house-dust mite and cedar pollen and total serum IgE level was 2595 IU/mL (normal, ≤232 IU/mL) Since the initial diagnosis, her asthma had been kept in control by treatment with 800 μg inhaled fluticasone propionate plus salmeterol (50 μg) twice daily, leukotriene receptor antagonist, and 300 mg of sustained-release theophylline. However, at age 64 she began to experience asthma exacerbations more than three times a year, 18 level of asthma control test (ACT), so her polytherapy was expanded to include 1000 μg of formoterol–fluticasone via pressurized metered inhaler as needed plus short-term steroid therapy with 20 mg/day prednisolone for five to seven days during exacerbations.

At age 70, the patient began to experience urticaria, nasal congestion, and wheezing after taking NSAIDs, although she did not experience the onset of these symptoms after taking aspirin until she was 40 years old. We obtained written informed consent from the patient to perform an oral provocation test for aspirin, and the test was performed in accordance with the protocol of Stevenson et al. [23] She was admitted to NHO Yokohama Medical Center on October 4, 2022 for an aspirin challenge test. Three hours and 20 min after taking 60 mg of aspirin, the patient exhibited clinically observable nasal congestion, urticaria, dyspnea, and wheezing, and her forced expiratory volume (FEV) in 1 second had decreased from 1.57 to 1.33 L. Findings from a CT scan showed that her anosmia was complicated by sinusitis with mucosal hypertrophy in the bilateral ethmoid and maxillary sinuses and revealed white blood cells (8100/μL, of which 1782 cells were eosinophils) in peripheral blood. Based on these observations and findings, we gave a final diagnosis of AERD with CRSwNP. A further diagnosis of severe eosinophilic chronic rhinosinusitis was made based on the scoring system and algorithm used in the Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis. [24]. The total subjective nasal and Sino-Nasal Outcome Test (SNOT)-22 score was 51. [25].

Fig. 1 shows the clinical course of the patient. At age 70 and the onset of the NSAID-exacerbated symptoms, she did not receive short-term prednisolone after the start of treatment with 30 mg of benralizumab every two months. Then leukotriene receptor antagonist was continued and the dose of formoterol–fluticasone combination aerosol was reduced to 500 μg,

Asthma symptoms including dyspnea and cough improved, ACT increased from 18 to 22, %FEV_1 increased from 81.0 % to 104.8 % and the asthma exacerbations stopped.; however, nasal obstruction and olfactory disorder (hyposmia) persisted. SNOT-22

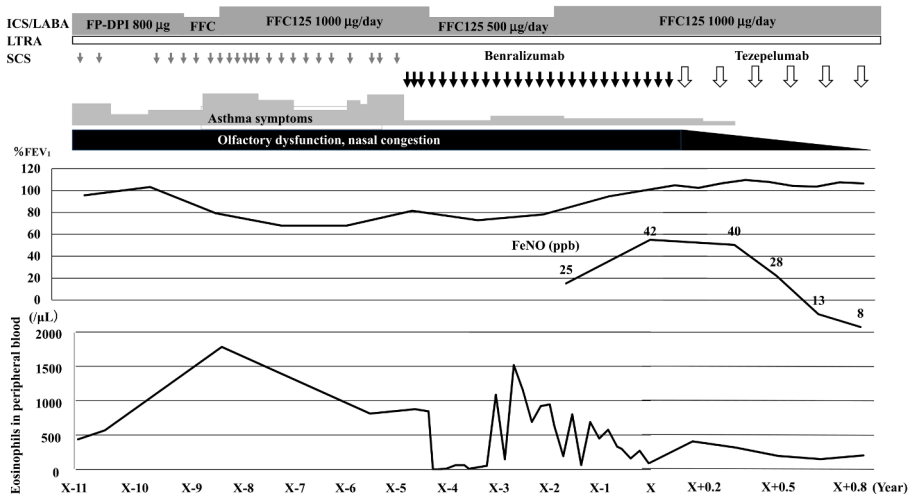

Fig. 1. Clinical course of our patient with non-steroidal anti-inflammatory aspirin exacerbated respiratory disease (AERD) complicated with chronic rhinosinusitis with nasal polyps.
In this patient with AERD, short-term systemic corticosteroid (SCS) therapy was stopped and treatment with benralizumab was started; however, olfactory dysfunction (hyposmia), asthma symptoms such as wheezing, coughing attacks, and shortness of breath, increased peripheral blood eosinophil count, and increased fractional exhaled nitric oxide (FeNO) level remained. After the switch from benralizumab to tezepelumab, olfactory dysfunction and nasal obstruction improved, and FeNO level and eosinophil count decreased. The middle X-axis shows percentage of predicted FEV_1 and the lower X-axis shows the peripheral blood eosinophil count. The degree of asthma symptoms shown in gray indicates the degree of wheezing, coughing attacks, and shortness of breath, and the relative strength of the symptoms is shown by the height of the gray color. Additionally, SCS indicates short-term steroid therapy (20 mg per day in PSL equivalent for 3–5 days) for asthma exacerbation.
AERD, aspirin exacerbated respiratory disease; FEV_1, forced expiratory volume in 1 second; FFC, formoterol–fluticasone combination aerosol; FP-DPI, fluticasone propionate dry power inhaler; ICS, inhaled corticosteroid; LABA, long-acting β2 agonist; LTRA, leukotriene receptor antagonist; SCS, systemic corticosteroid. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

score increased to 54. In addition, peripheral blood eosinophil count, which had initially decreased, increased again until it peaked at 1500 cells/mL before decreasing thereafter, and fractional exhaled nitric oxide level increased from 25 to 42 ppb before remaining at the high level even after administering 25 times of benralizumab over 4 years. At four years after the start of treatment with benralizumab, the patient still had sinusitis in the left dominant maxillary and ethmoid sinuses (Fig. 2b–f) compared with two months after the start of benralizumab (Fig. 2a–e). Therefore, the benralizumab was replaced with 210 mg of tezepelumab every month, which resulted in improvements not only in the asthma symptoms and dyspnea, ACT increased from 22 to 25, $\%FEV_1$ increased from 104.8 % to 109.0 %, FeNO decreased from 42 to 8 ppb but the nasal congestion and olfactory dysfunction also gradually improved, SNOT-22 score decreased to 14, the eosinophil count was reduced to less than 300 cells/μL, and the fractional exhaled nitric oxide level was de-

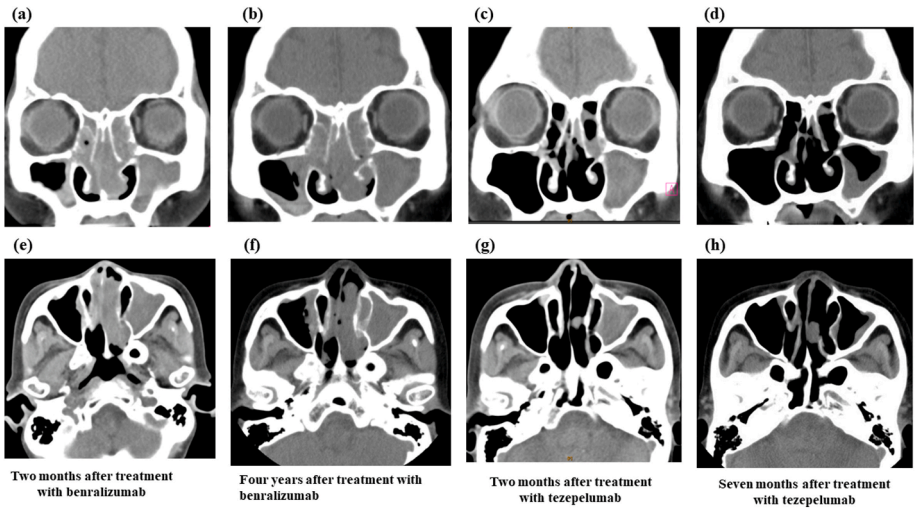

Fig. 2. Changes in sinusitis, as observed on computed tomography images.
Coronal (a–d) and transverse (e–h) sections of the sinuses at two months (a, e) and four years (b, f) after the start of treatment with benralizumab, and at two months (c, g) and seven months (d, h) after the start of treatment with tezepelumab. After treatment for four years with benralizumab, the patient still had sinusitis in the left dominant maxillary and ethmoid sinuses; however, after the switch to tezepelumab, the sinusitis in both the ethmoid and maxillary sinuses improved.

creased to normal. She did not need systemic corticosteroids. The sinusitis in both the ethmoid and maxillary sinuses had gradually improved at two months (Fig. 2c–g) and seven months (Fig. 2d–h) after switching to tezepelumab.

Written Informed Consent was obtained from the subject for the publication of the case report.

3. Discussion

AERD should be suspected if a patient reports respiratory symptoms occurring after ingestion of aspirin or other NSAIDs. Aspirin challenge remains the gold standard to diagnose AERD because reliable in vitro biomarkers are yet not to be identified. Therapeutic approaches for the treatment of AERD should be based on disease severity with avoidance of culprit agents and cross-reacting NSAIDs.[2] On chest CT scan, which is the gold standard imaging modality, AERD patients have a more severe sinus opacification and extension than do CRSwNP patients without AERD. [26].

Combination therapy with inhaled corticosteroid and a long-acting beta-2 adrenergic agonist provides sufficient asthma control in most AERD patients. [1]. However, some patients require more specific measures. Overexpression of 5-lipoxygenase pathway of arachidonic acid and overproduction of cysteinyl leukotrienes provides a rational for treating AERD patients with leukotriene-modifying drugs. [3]. Although CRSwNP associated with type 2 inflammation and AERD can be difficult to control with standard medical therapy and sinus surgery, biologics are promising treatment options for such patients, with phase III clinical trials for omalizumab, dupilumab, mepolizumab, and benralizumab in CRSwNP demonstrating favorable outcomes. [27]. Fifty-two of 98 patients (53.0 %) with AERD were treated with omalizumab, mepolizumab, reslizumab, benralizumab, and/or dupilumab and 84 patients (85.7 %) reported undergoing aspirin desensitization. Among these biologics, dupilumab had the highest patient-reported efficacy. [28]. In another study, 4 of 10 patients with severe asthma and CRSwNP reported improved olfaction after long-term treatment with omalizumab, mepolizumab, reslizumab, or benralizumab, with no significant differences for improved olfaction among the four biologics or between the AERD and non-AERD patients. [29]. However, in the present case, the patient had severe sinusitis in the bilateral maxillary and ethmoid sinuses that persisted at four years after the start of administration of benralizumab.

Mepolizumab and reslizumab act by blocking circulationg IL-5 would prevent its adhesion to IL-5R on mainly eosinophils. On the other hand, benralizumab interacts with the subunit of the IL-5R on the surface of eosinophils, basophils and ILC2 cells by acting antibody-dependent cell cytotoxicity. [30]. We considered the possibility that downregulation of IL-5R.

This is consistent with the finding that 50 % of patients with AERD treated with an *anti*-IL-5/IL-5 receptor alpha therapy, such as benralizumab, did not improve ACT score, sense of smell, or total SNOT-22 score. [15].

In the PATHWAY study, a phase IIb trial of tezepelumab versus placebo in adults with severe, uncontrolled asthma, tezepelumab significantly reduced annualized asthma exacerbation rate and improved lung function and symptom control. [20]. Nasal polyp tissue extracts significantly enhanced IL-1β–dependent IL-5 production in mast cells compared with uncinate tissue homogenates, and responses were significantly inhibited by *anti*-TSLP, suggesting that nasal polyps contain biologically relevant levels of TSLP activity. [19]. No significant difference was observed in the expression of TSLP receptor by immunohistochemistry of inflammatory infiltrate and epithelial cells in CRSwNP compared to CRSsNP. [18]. A sub-analysis of the phase 3 NAVIGATOR trial reported that asthma with NP decreased asthma exacerbation rate and lower SNOT-22 scores compared to asthma without NP [31]. There is a report that a reduction in NP was observed after administration of tezepelumab in a case of severe asthma with CRSsNP and eosinophilic otitis media [32].

Here, we report a patient with AERD who was unresponsive to benralizumab but who was successfully relieved not only her asthma symptoms but also her nasal congestion and olfactory dysfunction after switching to tezepelumab. To date, no randomized controlled trials of tezepelumab with AERD patients have been performed; [33], therefore, future trials are needed to verify the effects of tezepelumab on sinusitis.

4. Bullet points

1. CRSwNP associated with type 2 inflammation and AERD can be difficult to control with standard medical therapy and sinus surgery.
2. This is consistent with the finding that 50 % of patients with AERD treated with an *anti*-IL-5/IL-5 receptor alpha therapy, such as benralizumab, did not improve ACT score, sense of smell, or total SNOT-22 score.
3. Nasal polyps contain biologically relevant levels of TSLP activity.
4. Tezepelumab decreased asthma exacerbation rate of asthma with nasal polyps and lower SNOT-22 scores compared to asthma without nasal polyps.

CRediT authorship contribution statement

Yuga Yamashita: Writing – original draft, Data curation, Conceptualization. **Kosuke Terada:** Investigation, Data curation. **Yuka Kodama:** Investigation, Data curation. **Ryo Nakadegawa:** Investigation, Data curation. **Hinako Masumitsu:** Investigation, Data curation. **Yuto Motobayashi:** Investigation, Data curation. **Reeko Osada:** Investigation, Data curation. **Hirokazu Takayasu:** Investigation, Data curation. **Nami Masumoto:** Investigation, Data curation. **Takeshi Kaneko:** Supervision. **Naomi Tsurikisawa:** Writing – review & editing, Project administration, Investigation, Data curation, Conceptualization.

Declaration of competing interest

Have no conflicts of interest to disclose about this study.

References

[1] M.L. Kowalski, I. Agache, S. Bavbek, et al., B Diagnosis and management of NSAID-Exacerbated Respiratory Disease (N-ERD)-a EAACI position paper, Allergy 74 (2019) 28–39.
[2] S.D. Woo, Q.Q. Luu, H.S. Park, NSAID-exacerbated respiratory disease (NERD): from pathogenesis to improved care, Front. Pharmacol. 11 (2020) 1147.
[3] T.M. Laidlaw, J.A. Boyce, Updates on immune mechanisms in aspirin-exacerbated respiratory disease, J. Allergy Clin. Immunol. 151 (2023) 301–309.
[4] K. Mascia, T. Haselkorn, Y.M. Deniz, et al., Aspirin sensitivity and severity of asthma: evidence for irreversible airway obstruction in patients with severe or difficult-to-treat asthma, J. Allergy Clin. Immunol. 116 (2005) 970–975.
[5] W.J. Fokkens, V.J. Lund, C. Hopkins, et al., Epos 2020: European position paper on rhinosinusitis and nasal polyps 2020, Rhinology 58 (2020) 1–464.
[6] J.P. Rajan, N.E. Wineinger, D.D. Stevenson, et al., Prevalence of aspirin-exacerbated respiratory disease among asthmatic patients: a meta-analysis of the literature, J. Allergy Clin. Immunol. 135 (2015) 676–681.e671.
[7] I. Striz, K. Golebski, Z. Strizova, et al., New insights into the pathophysiology and therapeutic targets of asthma and comorbid chronic rhinosinusitis with or without nasal polyposis, Clin. Sci. 137 (2023) 727–753.
[8] W.W. Stevens, R.J. Lee, R.P. Schleimer, et al., Chronic rhinosinusitis pathogenesis, J. Allergy Clin. Immunol. 136 (2015) 1442–1453.
[9] T.F. Olonisakin, J.A. Moore, S. Barel, et al., Fractional exhaled nitric oxide as a marker of mucosal inflammation in chronic rhinosinusitis, Am. J. Rhinol. Allergy 19458924221080260 (2022).
[10] T. Jean, V. Eng, J. Sheikh, et al., Effect of omalizumab on outcomes in patients with aspirin-exacerbated respiratory disease, Allergy Asthma Proc. 40 (2019) 316–320.
[11] P. Gevaert, T.A. Omachi, J. Corren, et al., Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials, J. Allergy Clin. Immunol. 146 (2020) 595–605.
[12] P. Gevaert, N. Van Bruaene, T. Cattaert, et al., Mepolizumab, a humanized anti-IL-5 mAb, as a treatment option for severe nasal polyposis, J. Allergy Clin. Immunol. 128 (2011) 989–995.
[13] C. Bachert, J.K. Han, M.Y. Desrosiers, et al., Efficacy and safety of benralizumab in chronic rhinosinusitis with nasal polyps: a randomized, placebo-controlled trial, J. Allergy Clin. Immunol. 149 (2022) 1309–1317.e12.
[14] S. Nolasco, C. Crimi, C. Pelaia, A. Benfante, M. Caiaffa, C. Calabrese, et al., Benralizumab effectiveness in severe eosinophilic asthma with and without chronic rhinosinusitis with nasal polyps: a real-world multicenter study, J. Allergy Clin. Immunol. Pract. 9 (2021) 4371–4380.e4.
[15] H. Wangberg, S.R. Spierling Bagsic, et al., Appraisal of the real-world effectiveness of biologic therapies in aspirin-exacerbated respiratory disease, J. Allergy Clin. Immunol. Pract. 10 (2022) 478–484.e3.
[16] J. Mullol, T.M. Laidlaw, C. Bachert, et al., Efficacy and safety of dupilumab in patients with uncontrolled severe chronic rhinosinusitis with nasal polyps and a clinical diagnosis of NSAID-ERD: results from two randomized placebo-controlled phase 3 trials, Allergy 77 (2022) 1231–1244.
[17] L. Klimek, J. Hagemann, H.J. Welkoborsky, et al., Epithelial immune regulation of inflammatory airway diseases: chronic rhinosinusitis with nasal polyps (CRSwNP), Allergol Select 6 (2022) 148–166.
[18] M. Boita, M. Garzaro, L. Raimondo, et al., The expression of TSLP receptor in chronic rhinosinusitis with and without nasal polyps, Int. J. Immunopathol. Pharmacol. 24 (2011) 761–768.
[19] D.R. Nagarkar, J.A. Poposki, B.K. Tan, et al., Thymic stromal lymphopoietin activity is increased in nasal polyps of patients with chronic rhinosinusitis, J. Allergy Clin. Immunol. 132 (2013) 593–600.e12.
[20] C. Emson, J. Corren, K. Sałapa, et al., Efficacy of tezepelumab in patients with severe, uncontrolled asthma with and without nasal polyposis: a *post hoc* analysis of the phase 2b pathway study, J. Asthma Allergy 14 (2021) 91–99.
[21] S. Nolasco, C. Pelaia, G. Scioscia, R. Campisi, C. Crimi, Tezepelumab for asthma, Drugs Today 58 (2022) 591–603.
[22] C. Pelaia, G. Pelaia, C. Crimi, A. Maglio, L. Gallelli, R. Terracciano, et al., Tezepelumab: a potential new biological therapy for severe refractory asthma, Int. J. Mol. Sci. 22 (2021) 4369.
[23] D.D. Stevenson, R.A. Simon, D.A. Mathison, Aspirin-sensitive asthma: tolerance to aspirin after positive oral aspirin challenges, J. Allergy Clin. Immunol. 66 (1980) 82–88.
[24] T. Tokunaga, M. Sakashita, T. Haruna, et al., Novel scoring system and algorithm for classifying chronic rhinosinusitis: the JESREC Study, Allergy 70 (8) (2015) 995–1003.
[25] P. Schalek, L. Otruba, A. Hahn, Quality of life in patients with chronic rhinosinusitis: a validation of the Czech version of SNOT-22 questionnaire, Eur. Arch. Oto-Rhino-Laryngol. 267 (2010) 473–475.
[26] M.L. Kowalski, B. Bienkiewicz, R. Pawliczak, P. Kordek, Nasal polyposis in aspirin-hypersensitive patients with asthma (aspirin triad) and aspirin-tolerant patients, Allergy Clin Immunol Int - J World Allergy Org. 6 (2003) 246–250.
[27] X. Xu, S. Reitsma, Y. Wang, et al., Updates in biologic therapy for chronic rhinosinusitis with nasal polyps and NSAID-exacerbated respiratory disease, Allergy 77 (2022) 3593–3605.
[28] J. Mullur, C.M. Steger, D. Gakpo, et al., Aspirin desensitization and biologics in aspirin-exacerbated respiratory disease: efficacy, tolerability, and patient experience, Ann. Allergy Asthma Immunol. 128 (2022) 575–582.
[29] B. Barroso, M. Valverde-Monge, I. Alobid, et al., Improvement in olfaction in patients with CRSwNP and severe asthma taking anti-IgE and anti-IL-5 biologics: a real-life study, J Investig. Allergol. Clin. Immunol. 33 (2023) 37–44.
[30] A. Bakakos, N. Rovina, P. Bakakos, Treatment challenges in severe eosinophilic asthma: differential response to anti-IL-5 and anti-IL-5R therapy, Int. J. Mol. Sci. 22 (2021) 3969.
[31] T.M. Laidlaw, A. Menzies-Gow, S. Caveney, et al., Tezepelumab efficacy in patients with severe, uncontrolled asthma with comorbid nasal polyps in NAVIGATOR, J. Asthma Allergy 16 (2023) 915–932 PMID: 37692126.
[32] K. Kawashima, O. Matsuno, M. Okuno, et al., Successful treatment of eosinophilic chronic rhinosinusitis and secretory otitis media in refractory asthma with thymic stromal lymphopoietin (TSLP) receptor monoclonal antibody, Cureus 15 (2023), e47798 PMID: 38022039.
[33] R.J.L. van der Lans, W.J. Fokkens, S. Reitsma, Therapeutic options for chronic rhinosinusitis in N-ERD patients, Front Allergy 2 (2021) 734000.