Biological therapy in chronic rhinosinusitis with nasal polyposis: a retrospective study

Original Article

Authors

Beatriz de Sá Nicolau
Unidade Local de Saúde de São José, Lisboa

Cláudia Geraldes
Unidade Local de Saúde de São José, Lisboa

André Alves Pereira
Instituto Superior Técnico, Lisboa

Tiago Infante Velada
Unidade Local de Saúde de São José, Lisboa

Jorge Mexia
Unidade Local de Saúde de São José, Lisboa

Herédio de Sousa
Unidade Local de Saúde de São José, Lisboa

Correspondence:
Beatriz de Sá Nicolau
beanicolau98@gmail.com

Article received on May 8, 2025.
Accepted for publication on October 14, 2025.

Abstract

Objectives: To describe the case series of patients with CRSwNP under biological therapy in a tertiary hospital.
Study Design: Retrospective observational study.
Material and Methods: Patients with CRSwNP who started biological therapy between April 2023 and December 2024 were included. Patients were evaluated at weeks 0, 4 and 16. Therapeutic response was assessed according to the EPOS/EUFOREA 2023 criteria, using the NPS, NOSE, SNOT-22, VAS for smell and nasal obstruction, and the Sniffin' Sticks test. Statistical analysis was performed using Friedman and Wilcoxon tests ($p<0.05$).
Results: A total of 23 patients under treatment with Dupilumab or Mepolizumab were included. There was a significant reduction in NPS, SNOT-22, olfaction and nasal obstruction VAS ($p<0.0001$) and an increase in Sniffin' Sticks scores ($p<0.001$) between week 0 and week 16 of treatment.
Conclusions: Biological therapy showed symptomatic efficacy and improved quality of life in CRSwNP patients who do not respond to conventional therapy.

Keywords: Chronic rhinosinusitis; Monoclonal antibodies; Dupilumab; Mepolizumab; Sniffin' sticks

Introduction

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) affects approximately 1–2% of the European population and is frequently associated with a significant reduction in the patients' quality of life.[1]

CRSwNP is a multifactorial inflammatory disease of the nasal mucosa and paranasal sinuses, which is predominantly associated with a type 2 inflammatory response.[2–4] In this condition, pro-inflammatory cytokines, namely interleukin (IL)-4, IL-5, and IL-13, are responsible for inducing and maintaining type 2 inflammation. The inflammatory

response induced by these mediators involves the recruitment and activation of eosinophils, basophils, mast cells, goblet cells, M2 macrophages, and B lymphocytes.[3,4] The activation of these immune cells leads to the production of immunoglobulin (Ig) E, increased number of smooth muscle cells in the nasal mucosa, albeit with reduced functionality, enhanced fibrinogen, excessive mucus secretion, and local edema.[3,4] Furthermore, cytokine-induced structural changes lead to the formation of nasal polyps and remodeling of the nasal epithelium, perpetuating epithelial barrier dysfunction, another characteristic of this disease.[3,4] Given the underlying pathophysiology, patients with CRSwNP often present with comorbidities such as bronchial asthma, atopic dermatitis, or allergic rhinitis.[2] The classic symptoms of CRSwNP include nasal obstruction, rhinorrhea, facial pain, and olfactory disorders. Diagnosis is based on the presence of characteristic clinical features, supported by suggestive findings on nasal endoscopy or computed tomography of the paranasal sinuses.[5] Recently, alongside advances in understanding the disease's pathophysiology, criteria have been established for the use of biologic therapy in CRSwNP that is refractory to conventional treatment, with improvement demonstrated in both the symptoms and quality of life.[2] therapy) and in patients who have previously undergone endoscopic sinus surgery (ESS), provided they meet at least three of the five criteria listed in Table 1.[2,5]

According to the EPOS/EUFOREA 2023 criteria, response to biologic therapy is defined by a reduction in the size of the nasal polyps, as measured by the Nasal Polyp Score (NPS); reduction in the need for systemic corticosteroids for symptom control; improvement in the quality of life; improvement in olfactory function; and reduced impact of comorbidities.[2]

Thus, the objective of this study was to describe the characteristics of patients with CRSwNP who underwent biologic therapy at a tertiary hospital.

Materials and methods

This retrospective observational study analyzed the clinical records of patients with CRSwNP who began biologic therapy with mepolizumab or dupilumab between April 2023 and December 2024 at the Local Health Unit of São José. Patients were evaluated at 0, 4, and 16 weeks of treatment. Demographic (age and sex) and clinical data were collected, including the number of criteria fulfilled for initiation of biologic therapy, peripheral eosinophilia, and serum IgE levels measured before treatment initiation and at week 16 of treatment. Therapeutic success was evaluated according to the EUFOREA/EPOS 2023 criteria, which include serial assessments using the NPS, Nasal Obstruction and Septoplasty

Table 1
Indications for biologic Therapy in CRSwNP, EUFOREA/EPOS 2023

Bilateral nasal polyps in patients undergoing ESS	
↓ Three criteria required	
Criteria	**Cut-off**
Evidence of type 2 inflammation	Tissue eosinophils ≥ 10/HPF OR eosinophilia ≥ 150 × 106/L or total IgE ≥ 100 kIU/L)
Need for systemic corticosteroid therapy or contraindication	≥ 2 cycles per year OR long-term low-dose corticosteroid therapy (> 3 months)
Reduced quality of life	SNOT-22 ≥ 40
Significant olfactory disfunction	Anosmia confirmed by olfactory testing
Diagnosis of asthma	Regular use of inhaled corticosteroids

ESS, Endoscopic Sinus Surgery; HPF, High Power Field; SNOT-22, Sinonasal Outcome Test

Effectiveness Scale (NOSE), Sinonasal Outcome Test (SNOT-22), olfactory and nasal obstruction Visual Analog Scale (VAS), and psychophysical olfactory assessment using the Sniffin' Sticks test (Burghart Sniffin' Sticks, Burghart Messtechnik GmbH, Wedel, Germany). Adverse effects of biologic therapy were also recorded, as well as the number of cases in which treatment discontinuation was required and the reasons for suspension. All collected data were anonymized to ensure patient confidentiality.

Statistical analysis

The Friedman test was used for comparison of multiple non-categorical variables, while the Wilcoxon signed-rank test was used for paired non-categorical variables. A p-value < 0.05 was considered statistically significant.

Descriptive data analysis was conducted using Microsoft Excel®, and statistical analysis was performed using Python® version 3.12.4 (Python Software Foundation, Wilmington, DE, USA).

Results

A total of 23 patients with CRSwNP were included in the study, comprising 13 men (M) and 10 women (W) (M:W = 1.3). All of them received subcutaneous biologic therapy with dupilumab (70%, n = 16) or mepolizumab (30%, n = 7). The mean age of the participants was 54.2 ± 13.9 years (28–78 years). Among them, 78% (n = 18) had asthma; 78% (n = 18) presented with anosmia and 17% (n = 4) with hyposmia, confirmed with the Sniffin' Sticks test; and 48% (n = 11) required at least two courses of systemic corticosteroids in the year preceding the commencement of biologic therapy. Regarding the eligibility criteria for biologic treatment initiation, 17% (n = 4) patients met three criteria, 65% (n = 15) met four criteria, and 17% (n = 4) met all five criteria. Baseline demographic characteristics of the participants are presented in Table 2.

Before therapy initiation, the mean scores were: NPS (0–8), 5.6 ± 1.6; SNOT-22 (0–110), 72.0 ± 16.0; NOSE (0–20), 16.7 ± 3.3; olfactory VAS (0–10), 9.7 ± 0.6; nasal obstruction VAS, 8.9 ± 1.0; and total Sniffin' Sticks TDI, 13.4 ± 6.9.

A statistically significant reduction in the NPS was observed between weeks 0 and 4 ($p < 0.001$) and between weeks 0 and 16 ($p < 0.05$).

A decrease in total IgE was also observed between weeks 0 and 16 ($p < 0.001$). However, peripheral eosinophilia did not differ significantly between weeks 0 and 16 ($p = 0.4$).

In the psychophysical olfactory assessment, Sniffin' Sticks testing demonstrated improvement in TDI scores across weeks 0, 4, and 16 ($p < 0.001$).

Significant improvements were also observed in the Sniffin' Sticks discrimination ($p < 0.05$) and identification ($p < 0.05$) subtests, although the threshold test showed no statistically significant variation over the weeks ($p = 0.65$).

Regarding patient-reported outcome measures (PROMs), significant reductions were observed in SNOT-22 ($p < 0.001$), NOSE ($p < 0.001$), nasal obstruction VAS ($p < 0.001$), and olfactory VAS ($p < 0.001$) between weeks 0 and 16 of treatment. Of the 23 participants, seven (30%) completed 52 weeks of biologic therapy. At week 52, the mean scores were: NPS, 1.5 ± 2.1; SNOT-22, 18.0 ± 14.7; NOSE, 3.1 ± 3.3; olfactory VAS, 3.3 ± 3.8; nasal obstruction VAS, 2.7 ± 2.8; and total Sniffin' Sticks TDI, 24.4 ± 8.1.

In this subgroup, statistically significant improvements were observed in the NPS ($p < 0.05$), SNOT-22 ($p < 0.05$), NOSE ($p < 0.05$), olfactory VAS ($p < 0.05$), and nasal obstruction VAS ($p < 0.05$) from baseline to week 52. For the Sniffin' Sticks test, a statistically significant improvement was observed only in the identification subtest ($p < 0.05$). No significant differences were found in the threshold ($p = 0.63$), discrimination ($p = 0.30$), or total TDI ($p = 0.06$) scores, possibly due to the small sample size of this subgroup.

Regarding the adverse effects, 26% (n = 6) of the participants reported some form of medication-related reaction, as shown in Table 2. In one case, biologic therapy was discontinued due to the development of pancreatitis without any other identifiable cause.

Table 2
Demographic characteristics of the participants

Demographic characteristics	n total = 23
Age, mean ± SD (minimum–maximum)	54.2 ± 13.9 (28-75) anos
Sex	
Female, n (%)	10 (43%)
Male, n (%)	13 (57%)
Biologic therapy	
Dupilumab, n (%)	16 (70%)
Mepolizumab, n (%)	7 (30%)
Peripheral eosinophilia, mean ± SD	505.6x106 ± 307.2x106/L
Total serum IgE, mean ± SD	364.8 ± 489.1 kUI/L
NPS, mean ± SD	5.6 ± 1.6
SNOT-22, mean ± SD	72.0 ± 15.9
NOSE, mean ± SD	16.7 ± 3.3
Olfactory VAS, mean ± SD	9.7 ± 0.6
Nasal obstruction VAS, mean ± SD	8.9 ± 1.0
Criteria for initiating biologic therapy	
Asthma, n (%)	18 (78%)
Peripheral eosinophilia ≥ 150× 106/L or total serum IgE ≥ 100 kIU/L, n (%)	22 (96%)
Need for systemic corticosteroid therapy (≥ 2 cycles per year or low-dose corticosteroid therapy for > 3 months), n (%)	11 (48%)
Significant impact of symptoms on the quality of life (SNOT-22 ≥ 40), n (%)	23 (100%)
Significant olfactory dysfunction*, n (%)	18 (78%)
Number of criteria fulfilled to initiate biologic therapy	
3 criteria, n (%)	4 (17%)
4 criteria, n (%)	15 (65%)
5 criteria, n (%)	4 (17%)

SD, Standard Deviation; NPS, Nasal Polyp Score; SNOT-22, Sinonasal Outcome Test; NOSE, Nasal Obstruction and Septoplasty Effectiveness Scale; VAS, Visual Analog Scale.
*Total Threshold, Discrimination, Identification (TDI) score with Sniffin' Sticks test ≤ 30.5

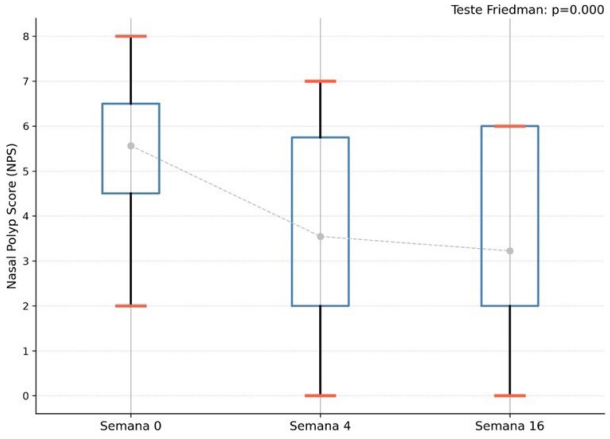
Discussion

The results of this study support the efficacy of biologic therapy in CRSwNP that is unresponsive to conventional medical and surgical treatment. The findings are consistent with previously published data and highlight the positive impact of biologic therapy on clinical, laboratory, and quality-of-life outcomes in affected patients.

Demographic and clinical characteristics

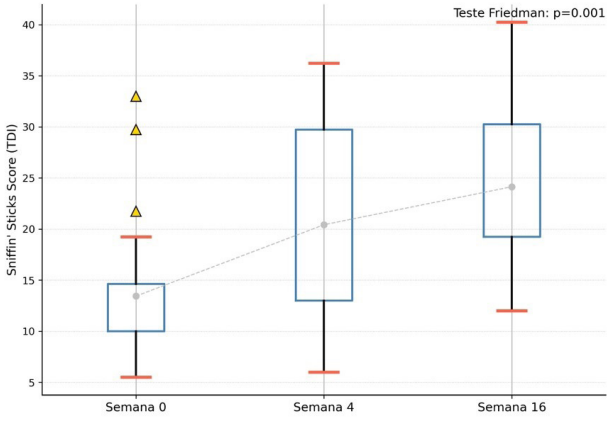
As previously described, CRSwNP is a disease associated with the type 2 inflammatory response, which explains its frequent association with other allergic diseases such as bronchial asthma. The high prevalence of asthma in this study sample (78%) reflects this well-established association. Silver et al. reported that among 5,997 patients with CRSwNP, 89.1% of those requiring biologic therapy had comorbid asthma.[11]

Figure 1
NPS scores at 0, 4, and 16 weeks of biologic therapy



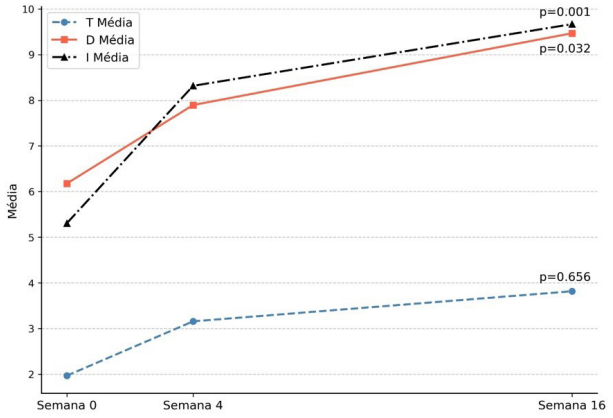
NPS, Nasal Polyp Score
NPS, Nasal Polyp Score
Boxplots illustrate the NPS distribution and boxes represent the interquartile ranges (IQRs).
The gray circles represent the mean NPS values at 0, 4, and 16 weeks. Statistical analysis was conducted using the Friedman test ($p < 0.001$).

Figure 2
Total TDI scores with Sniffin' Sticks test at 0, 4, and 16 weeks of biologic therapy



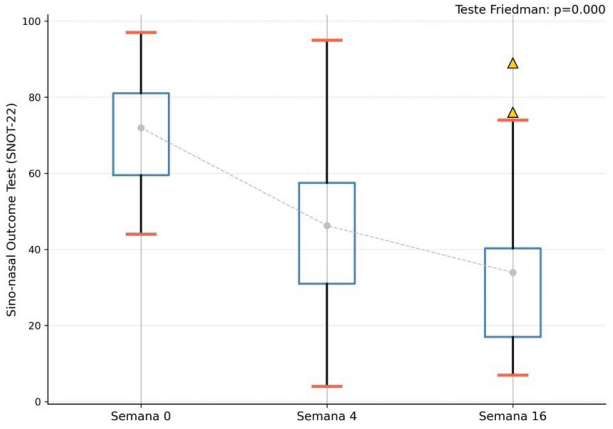
TDI, Threshold, Discrimination, and Identification Score
Boxplots illustrate the distribution of TDI scores and boxes represent the interquartile ranges (IQRs).
The gray circles represent the mean TDI values at 0, 4, and 16 weeks.
Yellow triangles depict outliers.
Statistical analysis was conducted using the Friedman test ($p = 0.001$).

Figure 3
Threshold, discrimination, and identification scores of the Sniffin' Sticks test at 0, 4, and 16 weeks of biologic therapy



T, Threshold; D, Discrimination; I, Identification
Statistical analysis was conducted using the Friedman test.

Figure 4
SNOT-22 scores at 0, 4, and 16 weeks of biologic therapy

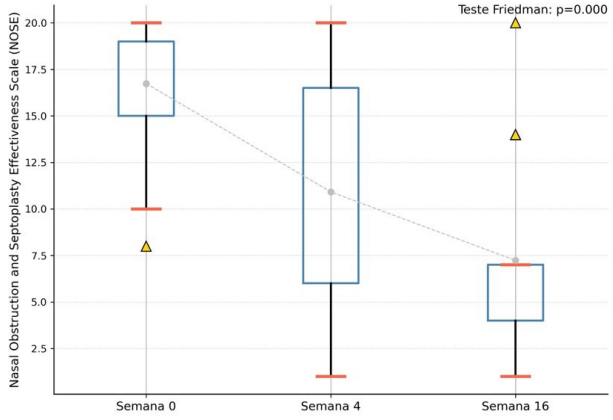


SNOT-22, Sinonasal Outcome Test
Boxplots illustrate the distribution of SNOT-22 scores and boxes represent the interquartile ranges (IQRs).
Gray circles represent the mean SNOT-22 scores at weeks 0, 4, and 16.
Yellow triangles depict outliers.
Statistical analysis was conducted using the Friedman test ($p < 0.001$).

Furthermore, according to the EUFOREA/EPOS 2023 criteria, the presence of asthma is one of the parameters to consider when initiating biologic therapy in patients with CRSwNP.[2]

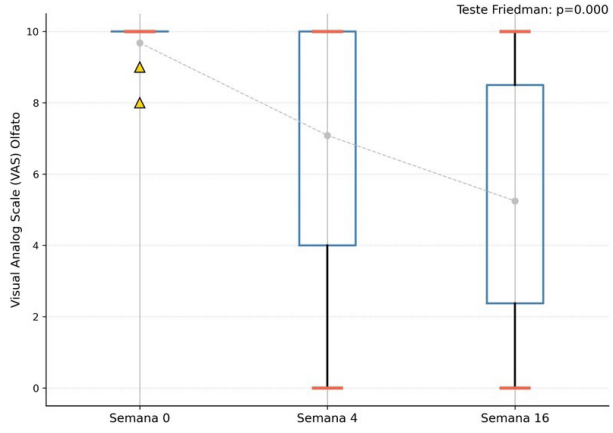
Anosmia was confirmed in 78% of the participants through psychophysical olfactory assessment (Sniffin' Sticks), corresponding to a TDI score ≤ 16.5 points before biologic treatment initiation. Hyposmia was observed in 17% of the participants (TDI > 16.5 and ≤ 30.5). These findings align with those of previous studies that identified olfactory dysfunction as a key marker of disease severity. In a study of 724 patients with CRSwNP, Soler et al. reported that the prevalence of anosmia was

Figure 5
NOSE scores at 0, 4, and 16 weeks of biologic therapy



NOSE, Nasal Obstruction and Septoplasty Effectiveness Scale
Boxplots illustrate the distribution of the NOSE scores and boxes represent the interquartile ranges (IQRs).
The gray circles represent the mean NOSE scores at 0, 4, and 16 weeks.
Yellow triangles represent outliers.
Statistical analysis was conducted using the Friedman test ($p < 0.001$).

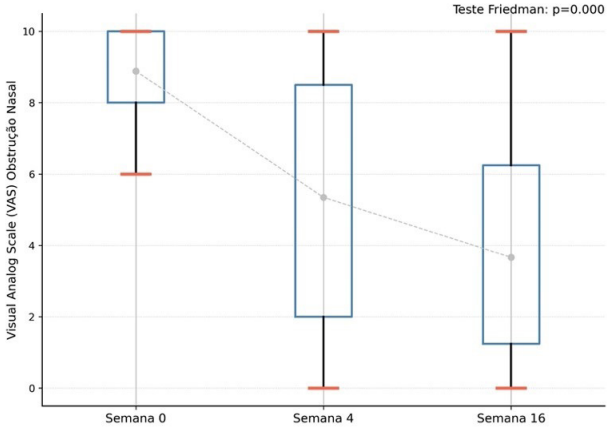
Figure 6
Olfactory VAS scores at 0, 4, and 16 weeks of biologic therapy



VAS, Visual Analog Scale
Boxplots illustrate the distribution of olfactory VAS scores and boxes represent the interquartile ranges (IQRs).
Gray circles represent the mean olfactory VAS scores at 0, 4, and 16 weeks.
Yellow triangles represent outliers.
Statistical analysis was conducted using the Friedman test ($p < 0.001$).

83%.[12] Similar to asthma, significant olfactory loss is one of the criteria for initiating biologic therapy, which helps to explain the high prevalence of this symptom in patients with CRSwNP.

Figure 7
Nasal obstruction VAS scores at 0, 4, and 16 weeks of biologic therapy



VAS, Visual Analog Scale
Boxplots illustrate the distribution of nasal obstruction VAS score, and boxes represent the interquartile ranges (IQRs).
Gray circles represent the mean nasal obstruction VAS scores at 0, 4, and 16 weeks.
Yellow triangles represent outliers.
Statistical analysis was conducted using the Friedman test ($p < 0.001$).

Table 3
Reações adversas associadas a terapêutica biológica

Adverse effects	Number of patients (n total = 23)
Pruritus, n (%)	1 (4%)
Gastrointestinal symptoms, n (%)	2 (9%)
Headache, n (%)	1 (4%)
Arthralgia, n (%)	1 (4%)
Pancreatitis*, n (%)	1 (4%)

* Biologic therapy discontinuation due to adverse event with no other apparent cause

Impact of biologic therapy – Physician-reported outcomes

The mean NPS significantly decreased between weeks 0 and 4 ($p < 0.001$), and between weeks 0 and 16 ($p < 0.05$) in the subgroup that completed 52 weeks of biologic therapy ($p < 0.05$). Comparable findings were reported in the SINUS-24/-52 and SYNAPSE trials, which demonstrated a significant improvement in the NPS in patients treated with dupilumab or mepolizumab compared with placebo.[7,8,10]

Additionally, the observed reduction in the total serum IgE levels ($p < 0.001$) is consistent with the mechanism of action of biologic agents, specifically modulation of the type 2 immune response.

Psychophysical olfactory assessment using the Sniffin' Sticks test demonstrated a significant improvement in the total TDI score ($p < 0.001$), as well as the discrimination and identification subtests ($p < 0.05$). Galleti et al. also reported sustained improvement in olfactory function measured by the Sniffin' Sticks identification test after 6 and 12 months of biologic therapy with dupilumab.[13] This effect can be attributed to reduced inflammation in the upper airways because of inhibition of pro-inflammatory cytokines by biologic agents. The present study used the extended version of the Sniffin' Sticks test, incorporating the threshold, discrimination, and identification components. This is the first study to document a statistically significant improvement in olfactory discrimination in patients with CRSwNP undergoing biologic therapy.

Impact of biologic therapy – Patient-reported outcomes

Most PROMs showed a statistically significant improvement throughout the treatment period. In CRSwNP refractory to conventional treatment, the effect of biologic therapy in improving the SNOT-22 scores has been well established in the literature.[14] Similar improvements were observed in the NOSE ($p < 0.001$) and olfactory and nasal obstruction VAS scores (both $p < 0.001$), confirming clinically significant benefits as perceived by patients. These results were maintained in the subgroup that completed 52 weeks of treatment, demonstrating a sustained favorable therapeutic response over time.

This study has some limitations, such as its retrospective design and small sample size, which may affect the generalizability of the findings. Nevertheless, the results align with those reported in the literature. Additionally, this study did not explore specific differences between outcomes obtained with dupilumab versus mepolizumab in specific subgroups. Such analyses could prove valuable in developing patient-specific treatment allocation criteria. Future prospective studies with larger cohorts are necessary to enable direct comparisons among different biologic agents and to better elucidate their relative outcomes.

Conclusion

In this study, biologic therapy with dupilumab or mepolizumab proved effective in reducing the symptoms and improving the quality of life of patients with CRSwNP unresponsive to conventional medical and surgical treatment. Thus, biologic therapy represents a viable and effective option for patients with CRSwNP who fail to respond to conventional treatment, providing an important alternative for the management of this disease.

Conflict of Interests

The authors declare that they have no conflict of interest regarding this article.

Data Confidentiality

The authors declare that they followed the protocols of their work in publishing patient data.

Human and animal protection

The authors declare that the procedures followed are in accordance with the regulations established by the directors of the Commission for Clinical Research and Ethics and in accordance with the Declaration of Helsinki of the World Medical Association.

Privacy policy, informed consent and Ethics committee authorization

The authors declare that they have obtained signed consent from the participants and that they have local ethical approval to carry out this work.

Financial support

This work did not receive any grant contribution, funding or scholarship.

Scientific data availability

There are no publicly available datasets related to this work.

References

1. Fokkens W, Van Der Lans R, Reitsma S. Dupilumab for the treatment of chronic rhinosinusitis with nasal polyposis. Expert Opin Biol Ther. 2021 May;21(5):575-585. doi: 10.1080/14712598.2021.1901881.
2. Fokkens WJ, Viskens AS, Backer V, Conti D, De Corso E, Gevaert P. et al. EPOS/EUFOREA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. Rhinology. 2023 Jun 1;61(3):194-202. doi: 10.4193/Rhin22.489.
3. Bachert C, Marple B, Schlosser RJ, Hopkins C, Schleimer RP, Lambrecht BN. et al. Adult chronic rhinosinusitis. Nat Rev Dis Primers. 2020 Oct 29;6(1):86. doi: 10.1038/s41572-020-00218-1.
4. Bachert C, Hicks A, Gane S, Peters AT, Gevaert P, Nash S. et al. The interleukin-4/interleukin-13 pathway in type 2 inflammation in chronic rhinosinusitis with nasal polyps. Front Immunol. 2024 Apr 16:15:1356298. doi: 10.3389/fimmu.2024.1356298.
5. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S. et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020 Feb 20;58(Suppl S29):1-464. doi: 10.4193/Rhin20.600.
6. Infarmed. Autoridade Nacional do Medicamento e Produtos de Saúde I.P. Autorização de introdução no mercado [Internet]. Lisboa: Infarmed; [cited 2025 Apr 15]. Available from: https://www.infarmed.pt/web/infarmed/entidades/medicamentos-uso-humano/autorizacao-de-introducao-no-mercado
7. Sanofi. A randomized, 24-week treatment, double-blind, placebo-controlled efficacy and safety study of dupilumab 300 mg every other week, in patients with bilateral nasal polyposis on a background therapy with intranasal corticosteroids [Internet]. clinicaltrials.gov; 2019 Jul. Report No.: NCT02912468. [cited 2025 Apr 15]. Available from: https://fdaaa.trialstracker.net/trial/NCT02912468/
8. Sanofi. A randomized, double-blind, 52-week, placebo controlled efficacy and safety study of dupilumab, in patients with bilateral nasal polyposis on a background therapy with intranasal corticosteroids [Internet]. clinicaltrials.gov; 2019 Oct. Report No.: NCT02898454. [cited 2025 Apr 15]. Available from: https://fdaaa.trialstracker.net/trial/NCT02898454/
9. Hoffmann-La Roche. A phase III, randomized, multicenter, double-blind, placebo-controlled clinical trial of omalizumab in patients with chronic rhinosinusitis with nasal polyps [Internet]. clinicaltrials.gov; 2020 Mar. Report No.: NCT03280537. [cited 2025 Apr 15]. Available from: https://fdaaa.trialstracker.net/trial/NCT03280537/
10. Han JK, Bachert C, Fokkens W, Desrosiers M, Wagenmann M, Lee SE. et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2021 Oct;9(10):1141-1153. doi: 10.1016/S2213-2600(21)00097-7.
11. Silver J, Packnett E, Park J, Deb A. Biologic use and treatment patterns in patients with chronic rhinosinusitis with nasal polyps: a US real-world study. Allergy Asthma Clin Immunol. 2023 Dec 8;19(1):104. doi: 10.1186/s13223-023-00855-7.
12. Soler ZM, Patel ZM, Mullol J, Mattos J, Nash S, Xia C. et al. Association between smell loss, disease burden, and dupilumab efficacy in chronic rhinosinusitis with nasal polyps. Am J Rhinol Allergy. 2025 Jan;39(1):6-12. doi: 10.1177/19458924241274501.
13. Galletti C, Ragusa M, Sireci F, Ciodaro F, Barbieri MA, Giunta G. et al. Dupilumab in chronic rhinosinusitis with nasal polyps: Real life data in a multicentric Sicilian experience. Am J Otolaryngol. 2024 Jan-Feb;45(1):104106. doi: 10.1016/j.amjoto.2023.104106.
14. Book R, Eligal S, Tal Y, Eliashar R. Biological treatment for uncontrolled chronic rhinosinusitis with nasal polyps: preliminary real-world results from a Tertiary Medical Center. J Clin Med. 2023 May 25;12(11):3671. doi: 10.3390/jcm12113671.