


Biologic Therapies in Chronic Rhinosinusitis with Nasal Polyposis: Current Evidence and Future Perspectives

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ABSTRACT

Chronic rhinosinusitis with nasal polyposis (CRSwNP) is a common type 2 inflammatory disease affecting approximately 1–4% of the population. It is characterized by persistent nasal obstruction, olfactory dysfunction, facial pain, and substantial impairment of quality of life. Although standard therapies, such as intranasal corticosteroids and endoscopic sinus surgery, remain the mainstay of treatment, a significant proportion of patients experience recurrent or inadequately controlled disease. Improved understanding of the immunopathogenesis of CRSwNP has highlighted the central role of type 2 inflammation driven by cytokines including interleukin-4, interleukin-5, interleukin-13, and immunoglobulin E, thereby enabling the development of targeted biological therapies. Biologic agents such as dupilumab, mepolizumab, benralizumab, and omalizumab have demonstrated consistent efficacy in phase III randomized controlled trials and real-world studies, leading to significant reductions in nasal polyp burden, improvements in Sino-Nasal Outcome Test (SNOT-22) scores, restoration of olfactory function, and decreased need for systemic corticosteroids and revision surgeries. Patient selection is increasingly guided by clinical phenotypes and biomarkers, including blood eosinophil counts, total serum IgE levels, and the presence of comorbid asthma or aspirin-exacerbated respiratory disease. Emerging evidence supports the integration of biological therapy with surgical management in refractory cases, while ongoing trials targeting upstream mediators, such as interleukin-33 and thymic stromal lymphopoietin, may further expand therapeutic options. Overall, biologic therapies represent a paradigm shift in the management of severe CRSwNP, paving the way for precision-based, individualized treatment strategies.

Biologics, Chronic Rhinosinusitis, Nasal Polyposis, Dupilumab, Precision Medicine

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INTRODUCTION

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a persistent inflammatory disorder involving the nasal passages and paranasal sinuses, affecting an estimated 1.1% of the adult population in the United States [1,2]. This condition significantly impairs patients' health-related quality of life, manifesting through prominent symptoms, including nasal congestion or blockage, reduced or absent sense of smell (hyposmia/anosmia), facial pain or pressure, and associated issues such as disrupted sleep, heightened anxiety, and depressive symptoms [3,4]. Worldwide, both the incidence and prevalence of chronic rhinosinusitis appear to be increasing, highlighting its importance as a public health concern. Although the precise mechanisms underlying CRSwNP pathogenesis are not yet fully elucidated, the disease is predominantly linked to type 2 inflammatory processes, featuring prominent tissue eosinophilia and upregulation of key cytokines, including interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13). Nevertheless, alternative inflammatory profiles, such as type 1 and type 3 endotypes, have been documented, particularly among individuals in non-Western regions and among non-White ethnic groups. Moreover, overlapping or mixed inflammatory

pathways can frequently occur within the same patient, complicating accurate endotype classification and influencing variability in therapeutic responses [5-7].

Standard treatment approaches for chronic rhinosinusitis with nasal polyps (CRSwNP) typically involve intranasal corticosteroids (INCS), regular nasal saline irrigation, and short courses of oral corticosteroids. Endoscopic sinus surgery (ESS) is generally considered for patients who do not respond adequately to conservative measures. Nevertheless, a considerable proportion of individuals continue to experience persistent or uncontrolled symptoms despite optimal medical therapy. The introduction of biologic agents targeting type 2 inflammatory pathways has significantly broadened the available treatment options for this condition. As of the latest approvals by the US Food and Drug Administration (FDA), three monoclonal antibodies have been authorized specifically for CRSwNP: dupilumab (2019), omalizumab (2020), and mepolizumab (2021). This narrative review consolidates existing clinical evidence and explores promising future developments in the application of biologic therapies for managing CRSwNP [8-10].

Current FDA-Approved Biologics for Chronic Rhinosinusitis with Nasal Polyps

As of 2025, three biologic agents have received approval from the United States Food and Drug Administration (FDA) for the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP): dupilumab, omalizumab, and mepolizumab [11]. These monoclonal antibodies selectively target key components of the type 2 inflammatory pathway, which underlies most CRSwNP cases. Evidence from pivotal randomized controlled trials and accumulating real-world studies consistently demonstrates that these therapies effectively reduce nasal polyp burden, improve sinonasal symptoms, including nasal obstruction, facial pressure, and olfactory dysfunction, and enhance overall disease control in patients with refractory or inadequately controlled disease [12,13].

Table 1. Pivotal Phase 3 Randomized Controlled Trials of FDA-Approved Biologics for Chronic Rhinosinusitis with Nasal Polyps

Biologic	Key Phase 3 Trials	Primary Endpoints	Selected Secondary Endpoints	Key Clinical Outcomes
Dupilumab	LIBERTY NP SINUS-24 LIBERTY NP SINUS-52	Endoscopic nasal polyp score (NPS) Daily nasal congestion score	Lund–Mackay CT score SNOT-22 total score UPSIT olfactory test Need for systemic corticosteroids or surgery	Significant and sustained reductions in NPS and nasal congestion at 24 and 52 weeks; marked improvement in olfaction and health-related quality of life; reduced need for rescue corticosteroids and revision surgery
Omalizumab	POLYP 1 POLYP 2	Endoscopic nasal polyp score (NPS) Daily nasal congestion score	SNOT-22 total score UPSIT olfactory test	Clinically meaningful reductions in NPS and congestion at 24 weeks; consistent improvement in sinonasal symptoms and quality-of-life indices
Mepolizumab	SYNAPSE	Endoscopic nasal polyp score (NPS) Nasal congestion VAS score	Lund–Mackay CT score SNOT-22 total score Need for systemic corticosteroids or surgery	Significant reductions in polyp burden and nasal obstruction at 52 weeks; prolonged time to surgery; greatest benefit observed in patients with elevated baseline eosinophil counts

Dupilumab is a fully human monoclonal antibody that inhibits signaling through the interleukin-4 receptor alpha (IL-4Rα) subunit, thereby blocking the biological effects of IL-4 and IL-13 [14]. Initially approved in 2017 for moderate-to-severe atopic dermatitis, dupilumab became the first biologic agent approved for CRSwNP in 2019, following robust results from the phase III LIBERTY NP SINUS-24 and SINUS-52 trials [15,16].

Table 2. FDA-Approved Indications and Safety Profiles of Biologic Therapies Used in CRSwNP

Biologic	Relevant FDA-Approved Indications	Common Adverse Events	Serious or Notable Adverse Events
Dupilumab	Atopic dermatitis; asthma; CRSwNP; eosinophilic esophagitis; chronic spontaneous urticaria; COPD	Injection-site reactions; conjunctivitis; transient eosinophilia	Hypersensitivity reactions; rare cases of clinically significant eosinophilia
Mepolizumab	Severe eosinophilic asthma; CRSwNP; eosinophilic granulomatosis with polyangiitis; hypereosinophilic syndrome	Injection-site reactions; headache; fatigue	Herpes zoster reactivation; hypersensitivity reactions
Omalizumab	Moderate-to-severe persistent asthma; CRSwNP; chronic spontaneous urticaria; IgE-mediated food allergy	Injection-site reactions; headache; upper respiratory symptoms	Anaphylaxis (boxed warning); serum sickness-like reactions

These studies demonstrated statistically significant and clinically meaningful reductions in endoscopic nasal polyp score (NPS), improvements in nasal congestion severity, and substantial gains in sinonasal-related quality of life compared with placebo, alongside a reduced need for systemic corticosteroids and revision sinus surgery [15–17]. Omalizumab, an anti-IgE monoclonal antibody that binds to circulating free IgE and prevents its interaction with the high-affinity FcεRI receptor on mast cells and basophils, was originally approved in 2003 for moderate-to-severe persistent allergic asthma [18]. In 2020, omalizumab received FDA approval for CRSwNP based on favorable outcomes from the phase III POLYP 1 and POLYP 2 trials [19,20]. In these studies, omalizumab significantly reduced nasal polyp size and nasal congestion scores while producing clinically meaningful improvements in patient-reported symptom burden and quality of life when added to standard intranasal corticosteroid therapy [19–21].

Mepolizumab, a humanized monoclonal antibody targeting interleukin-5 (IL-5), is the most recent FDA-approved biologic for CRSwNP, having gained approval in 2021 [22]. Data from the phase III SYNAPSE trial demonstrated that mepolizumab significantly reduced nasal polyp burden, alleviated nasal obstruction, and prolonged the time to revision sinus surgery [23]. The therapeutic benefit was particularly pronounced in patients with elevated baseline eosinophil counts, underscoring the relevance of eosinophilic inflammation as a driver of disease severity and treatment response [23,24].

Type 2 Inflammatory Cascade in CRSwNP

Damage to the sinonasal epithelial barrier initiates the release of epithelial-derived alarmins, including thymic stromal lymphopoietin (TSLP),

Table 3. Selected Completed and Ongoing Clinical Trials Targeting Upstream Inflammatory Pathways in CRSwNP

Target Pathway	Representative Biologic	Trial Phase	Study Population	Primary Endpoint
IL-4 receptor α	TQH2722	Phase II	CRSwNP ± CRSsNP	Change in NPS and/or Lund–Mackay score
TSLP	Tezepelumab	Phase III (Completed)	CRSwNP	Change in NPS and nasal congestion at 52 weeks
TSLP receptor	Verekitug	Phase II	CRSwNP	Change in NPS at 24 weeks
TSLP	CM-326	Phase Ib/IIa	CRSwNP	Safety and change in NPS
TSLP	SHR-1905	Phase II	CRSwNP	Change in NPS at 24 weeks
TSLP	TQC2731 (with INCS)	Phase II	CRSwNP	Change in NPS at 24 weeks

interleukin-25 (IL-25), and interleukin-33 (IL-33) [25]. These upstream cytokines activate group 2 innate lymphoid cells (ILC2s) and T helper 2 (Th2) lymphocytes, leading to the secretion of canonical type 2 cytokines IL-4, IL-5, and IL-13 [26]. Collectively, these mediators drive B-cell class switching with subsequent IgE production, recruitment and activation of eosinophils, goblet cell hyperplasia, and excessive

mucus secretion [27]. Sustained activation of these pathways promotes tissue remodeling, extracellular matrix deposition, and ultimately the formation and persistence of nasal polyps, particularly in patients with concomitant allergic sensitization (Figure 1) [28].

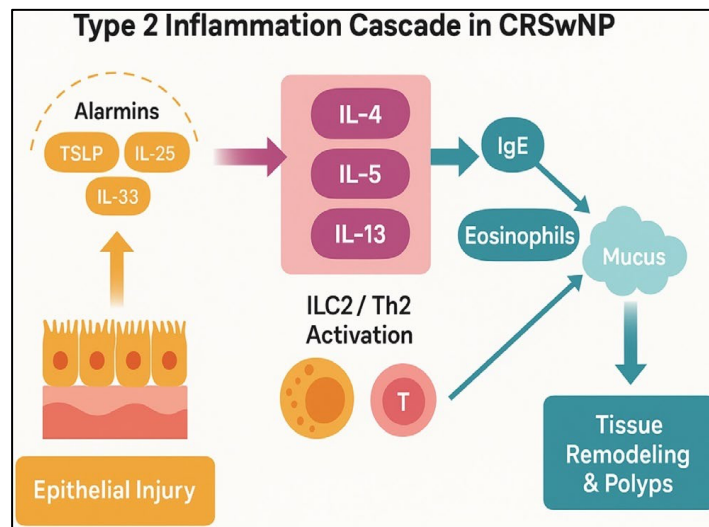


Figure 1. Type 2 Inflammation Cascade in CRSwNP

Candidates for Biologic Therapy

Current clinical guidelines, including the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) and subsequent international expert consensus statements, recommend the consideration of biologic therapy for patients with CRSwNP who exhibit objective evidence of type 2 inflammation and remain symptomatic despite optimized conventional medical therapy and, when appropriate, prior endoscopic sinus surgery [29,30].

Eligible patients typically present with refractory disease characterized by persistent nasal obstruction, substantial polyp burden, impaired olfaction, or recurrent polyp regrowth following surgery, supported by biomarkers of type 2 inflammation such as elevated blood or tissue eosinophils, increased total serum IgE, or dominant type 2 cytokine signatures [30,31]. A comprehensive evaluation by an otolaryngologist is essential prior to biologic initiation to confirm the endoscopic presence and severity of nasal polyps and to exclude alternative pathologies that may mimic polyposis, including benign or malignant sinonasal tumors or inverted papilloma [32]. Reports of misdiagnosis in the absence of specialist assessment further highlight the importance of expert confirmation to ensure appropriate patient selection [33].

Comparative Outcomes of Biologic Therapy and Endoscopic Sinus Surgery

Endoscopic sinus surgery (ESS) has long been the cornerstone treatment for patients with CRSwNP who fail maximal medical therapy. [34]. Comparative studies evaluating ESS versus biologic therapy suggest that surgery produces more rapid and pronounced early reductions in the nasal polyp burden. Dharmarajan et al. reported greater early improvements in polyp size following ESS than those following biologics [35], while a multicenter cohort study by Miglani et al. demonstrated that ESS yielded SNOT-22 improvements comparable to dupilumab and superior to omalizumab at 24 and 52 weeks, alongside significantly greater reductions in endoscopic polyp scores [36].

Systematic reviews and meta-analyses indicate that although ESS provides superior short-term polyp reduction, longer-term outcomes may differ. At one year, dupilumab was associated with comparable polyp control and superior improvement in olfactory function compared with surgery [37]. Health economic analyses further suggest that both approaches yield meaningful gains in quality-adjusted life years (QALYs), with mixed findings regarding the relative cost-effectiveness across healthcare systems [38,39].

Combination and Sequential Strategies

Growing evidence suggests that biologic therapy and ESS should not be viewed as mutually exclusive but rather as complementary modalities [40]. Perioperative or postoperative biological administration has been associated with reduced polyp recurrence, enhanced olfactory recovery, and more durable symptom control than surgery alone [41,42]. Early observational studies have indicated potential synergistic effects when biologics are used as adjuvant therapy, although the optimal timing, duration, and patient selection criteria remain to be clearly defined [43]. Large prospective randomized trials are needed to establish evidence-based recommendations for integrated treatment strategies.

Emerging Therapies and Future Directions

Despite substantial progress, important unmet needs persist in the management of CRSwNP. Head-to-head randomized trials directly comparing currently approved biologics remain limited, and predictive biomarkers capable of guiding individualized biologic selection have not been sufficiently validated for routine clinical use [44]. Emerging agents targeting upstream mediators, including TSLP and IL-33, and long-acting IL-5 inhibitors, such as depemokimab, represent promising therapeutic avenues [45–47]. In parallel, expanding research on non-type 2 inflammatory endotypes is essential, as these patients remain poorly responsive to existing biologic options [48].

CONCLUSION

Biologic therapies have fundamentally reshaped the therapeutic landscape for chronic rhinosinusitis with nasal polyps (CRSwNP), providing highly effective treatment alternatives for individuals with refractory disease who fail to achieve satisfactory symptom control despite optimized medical management and/or endoscopic sinus surgery. The approval and integration of dupilumab, omalizumab, and mepolizumab mark significant milestones in type 2 inflammation-targeted therapy. Emerging long-acting and upstream-acting agents, including depemokimab and tezepelumab, are advancing toward potential FDA approval and are poised to expand therapeutic options. Moving forward, priority research areas should include head-to-head comparative effectiveness studies, rigorous cost-effectiveness evaluations, development of evidence-based algorithms for initiating, tapering, and discontinuing biologic therapy, optimal integration of biologics with endoscopic sinus surgery, and advancement of biomarker-driven precision medicine approaches to enhance patient selection and long-term outcomes.

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The author has made substantial contributions to this narrative review. GWS conceptualized the study, conducted the literature search and data synthesis, and drafted the initial manuscript. The author critically revised the manuscript and approved the final version for publication and is accountable for all aspects of the work, ensuring its accuracy and integrity.

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REFERENCE

1. Laidlaw TM, Mullol J, Woessner KM, Amin N, Mannent LP. Chronic rhinosinusitis with nasal polyps and asthma. *J Allergy Clin Immunol Pract.* 2021;9(3):1133–1141.
2. Mullol J, Alobid I, Marino-Sanchez F, et al. Furthering the understanding of loss of smell in chronic rhinosinusitis. *J Allergy Clin Immunol.* 2020;145(3):773–776.
3. Min JY, Metson R, Misono S, et al. Epidemiology and burden of chronic rhinosinusitis. *JAMA Otolaryngol Head Neck Surg.* 2022;148(7):649–658.
4. Wu D, Bleier BS, Wei Y, et al. Regional and racial variations in chronic rhinosinusitis endotypes. *Allergy.* 2021;76(4):1076–1086.
5. Hao M, Jiang Y, Li W, et al. Coexistence of multiple endotypes in chronic rhinosinusitis with nasal polyps: implications for personalized treatment. *Clin Exp Allergy.* 2022;52(6):776–786.
6. Bachert C, Zhang N, Hellings PW, Bousquet J. Biologics in type 2 inflammatory diseases: targets and clues for diseases. *Int Forum Allergy Rhinol.* 2018;8(8):793–806.
7. Bachert C, Han JK, Desrosiers M, et al. Dupilumab for nasal polyposis in chronic rhinosinusitis. *N Engl J Med.* 2019;381(1):55–69.
8. Gevaert P, Omachi TA, Corren J, et al. Efficacy and safety of omalizumab in nasal polyposis: two randomized phase 3 trials. *J Allergy Clin Immunol.* 2020;146(3):595–605.
9. Han JK, Bachert C, Fokkens WJ, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps: results from the randomized, double-blind, placebo-controlled phase 3 SYNAPSE study. *J Allergy Clin Immunol.* 2021;147(6):1899–1909.
10. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology.* 2020;58(S29):1–464.
11. Laidlaw TM, Mullol J, Woessner KM, Amin N, Mannent LP. Chronic rhinosinusitis with nasal polyps and asthma. *J Allergy Clin Immunol Pract.* 2021;9(3):1133–1141.
12. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, et al. Dupilumab for nasal polyposis in chronic rhinosinusitis. *N Engl J Med.* 2019;381(1):55–69.
13. Gevaert P, Omachi TA, Corren J, Mullol J, Han JK, et al. Efficacy and safety of omalizumab in nasal polyposis: two randomized phase 3 trials. *J Allergy Clin Immunol.* 2020;146(3):595–605.
14. Bachert C, Zhang N, Hellings PW, Bousquet J. Biologics in type 2 inflammatory diseases: targets and disease mechanisms. *Int Forum Allergy Rhinol.* 2018;8(8):793–806.
15. Han JK, Bachert C, Desrosiers M, Gevaert P, Fokkens WJ, et al. Efficacy of dupilumab in chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol.* 2021;147(6):1899–1909.
16. Holgate ST, Chuchalin AG, Hebert J, Lötvall J, Persson GB, et al. Efficacy and safety of omalizumab in allergic asthma. *N Engl J Med.* 2004;351(4):268–279.
17. Hao M, Jiang Y, Li W, Zhang Y, Li H, et al. Coexistence of multiple endotypes in chronic rhinosinusitis with nasal polyps. *Clin Exp Allergy.* 2022;52(6):776–786.
18. Wu D, Bleier BS, Wei Y, Zhou B, Wang Y, et al. Regional and racial variations in chronic rhinosinusitis endotypes. *Allergy.* 2021;76(4):1076–1086.
19. Xu X, Reitsma S, Wang DY, Fokkens WJ. Updates in biologic therapy for chronic rhinosinusitis with nasal polyps and NSAID-exacerbated respiratory disease. *Allergy.* 2022;77(11):3593–3605.
20. Licona-Limon P, Kim LK, Palm NW, Flavell RA. TH2, allergy and group 2 innate lymphoid cells. *Nat Immunol.* 2013;14(6):536–542.
21. Akdis CA, Arkwright PD, Brüggen MC, Busse W, Gadina M, et al. Type 2 immunity in allergic disease. *Nat Rev Immunol.* 2020;20(9):475–490.
22. Van Bruaene N, Pérez-Novo CA, Basinski TM, Van Zele T, Holtappels G, et al. T-cell regulation in nasal polyposis. *J Allergy Clin Immunol.* 2008;121(6):1439–1446.

23. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020;58(29):1–464.
24. Han JK, Bachert C, Desrosiers M, Hellings PW, Amin N, et al. EUFOREA consensus on biologics for chronic rhinosinusitis with nasal polyps. *Allergy*. 2021;76(10):2946–2967.
25. Yan CH, Hwang PH, Woodworth BA. The role of biomarkers in chronic rhinosinusitis with nasal polyps. *Laryngoscope Invest Otolaryngol*. 2022;7(2):390–397.
26. Monk AS, Thorp BD, Ebert CS Jr, Senior BA. Ensuring appropriate use of biologics in chronic rhinosinusitis with nasal polyps. *Int Forum Allergy Rhinol*. 2021;11(6):1053–1055.
27. Smith TL, Litvack JR, Hwang PH, Loehrl TA, Mace JC, et al. Outcomes of endoscopic sinus surgery for chronic rhinosinusitis. *Otolaryngol Head Neck Surg*. 2010;142(1):55–63.
28. Dharmarajan H, Falade O, Lee SE, Wang EW. Dupilumab versus endoscopic sinus surgery outcomes in CRSwNP. *Int Forum Allergy Rhinol*. 2022;12(9):986–995.
29. Miglani A, Soler ZM, Smith TL, Mace JC, Schlosser RJ. Endoscopic sinus surgery versus biologics for CRSwNP. *Int Forum Allergy Rhinol*. 2023;13(1):116–128.
30. Kim J, Kim DH, Hwang SH. Dupilumab treatment for chronic rhinosinusitis with nasal polyposis: a systematic review and meta-analysis. *J Rhinol*. 2023;30(2):62–68.
31. Parasher AK, Gliksman M, Segarra D, Rudmik L, Quast T, et al. Economic evaluation of dupilumab versus endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2022;12(6):813–820.
32. Scangas GA, Wu AW, Ting JY, Metson R, Holbrook EH, et al. Cost-utility analysis of dupilumab versus endoscopic sinus surgery. *Laryngoscope*. 2021;131(1):26–33.
33. Pelletier A, Mfuna Endam L, Gonzalez E, Jannat S, Irani T, et al. Perioperative adjuvant dupilumab with endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2025;15(3):227–238.
34. Liu CN, Nguyen TD, Tang DH, Pham TT, Tran TQ, et al. Dupilumab as adjuvant therapy after endoscopic sinus surgery in type 2 CRSwNP. *Eur Arch Otorhinolaryngol*. 2025;282(6):3319–3328.
35. Garvey WJ, Damask CC, Meleca RJ, Patadia MO. Outcomes of biologic therapy with and without endoscopic sinus surgery. *Am J Rhinol Allergy*. 2022;36(5):677–683.
36. Oykhman P, Nair P, Wurman C, Smith SG, Sehmi R, et al. Comparative efficacy of biologics in CRSwNP: a network meta-analysis. *J Allergy Clin Immunol Pract*. 2023;11(1):232–241.
37. Cai Y, Chen H, Xie S, Zhang Y, Liu J, et al. Comparative efficacy of biologics for chronic rhinosinusitis with nasal polyps. *Allergy*. 2023;78(4):1026–1037.
38. Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, et al. Tezepelumab in severe, uncontrolled asthma. *N Engl J Med*. 2021;384(19):1800–1809.
39. Wechsler ME, Colice G, Griffiths JM, Almqvist G, Skärby T, et al. Depemokimab in eosinophilic disease. *Lancet Respir Med*. 2022;10(11):1141–1152.
40. Tomassen P, Vandeplass G, Van Zele T, Cardell LO, Arebro J, et al. Inflammatory endotypes of chronic rhinosinusitis. *J Allergy Clin Immunol*. 2016;137(5):1449–1456.
41. Rudmik L, Soler ZM. Medical therapies for adult chronic sinusitis: a systematic review. *JAMA*. 2015;314(9):926–939.
42. Hopkins C, Browne JP, Slack R, Lund VJ, Brown P. The Lund–Mackay staging system for chronic rhinosinusitis: how is it used and what does it predict? *Otolaryngol Head Neck Surg*. 2007;137(4):555–561.
43. DeConde AS, Smith TL. Outcomes after sinus surgery: chronic rhinosinusitis with nasal polyps. *Otolaryngol Clin North Am*. 2016;49(1):101–113.
44. Oykhman P, Nair P. Biologic therapies for chronic rhinosinusitis with nasal polyps. *J Allergy Clin Immunol Pract*. 2021;9(9):3347–3356.
45. Bachert C, Sousa AR, Lund VJ, et al. Reduced need for surgery in severe nasal polyposis with mepolizumab. *J Allergy Clin Immunol*. 2017;140(4):1024–1031.
46. Menzies-Gow A, Corren J, Bourdin A, et al. Tezepelumab in adults and adolescents with severe, uncontrolled asthma. *N Engl J Med*. 2021;384(19):1800–1809.

47. Wechsler ME, Colice G, Griffiths JM, et al. Long-acting anti-IL-5 therapy with depemokimab in eosinophilic disease. *Lancet Respir Med.* 2022;10(11):1141–1152.
48. Van Zele T, Claeys S, Gevaert P, et al. Differentiation of chronic sinus diseases by measuring inflammatory mediators. *J Allergy Clin Immunol.* 2006;118(6):1289–1296.