

Review

Biologics: Its Role in Treating Chronic Rhinosinusitis and Nasal Polyps

Leyla Çevirme*  and Susamber Dik Kahramanoğulları 

Division of Immunology and Allergy, Adana City Training and Research Hospital, Adana 01250, Türkiye

* Correspondence: laylacevirme@gmail.com**Received:** 7 April 2026; **Revised:** 27 April 2026; **Accepted:** 29 May 2026; **Published:** 5 June 2026

Abstract: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a clinically heterogeneous inflammatory disorder characterized by persistent sinonasal inflammation and a notable tendency for recurrence, even in patients receiving appropriate medical and surgical treatment. This heterogeneity largely reflects differences in underlying inflammatory endotypes, which in turn influence clinical presentation, risk of postoperative relapse, and response to therapy. In the majority of patients, type 2 (T2) inflammation represents the dominant immunologic profile, driven by cytokines such as interleukin (IL)-4, IL-5, IL-13, and thymic stromal lymphopoietin (TSLP). Targeting these pathways has become a central focus in recent therapeutic strategies. In this context, the introduction of biologic agents has substantially altered the management of patients with severe and difficult-to-control disease. Data from phase 3 randomized trials have consistently shown meaningful reductions in polyp burden and symptom severity, along with decreased reliance on systemic corticosteroids and a lower need for revision surgery. These findings are supported by real-world studies, which suggest that the benefits of biologic therapies extend to more heterogeneous patient populations, including those with comorbid asthma or aspirin-exacerbated respiratory disease. Despite these advances, several important questions remain unresolved. In particular, there is a need for more precise patient selection based on reliable biomarkers, as well as clearer guidance on long-term treatment strategies. Issues related to cost-effectiveness and the optimal timing of treatment discontinuation or switching also continue to represent areas of ongoing debate in clinical practice.

Keywords: Biologics; IL-5; IL-13/4; IgE; Mepolizumab; Omalizumab; Dupilumab; Tezepelumab

1. Introduction

Chronic rhinosinusitis (CRS) is a prevalent inflammatory disease affecting nearly 12% of the general population and showing considerable clinical heterogeneity [1]. Chronic rhinosinusitis with nasal polyps (CRSwNP) is a well-defined subtype marked by bilateral nasal polyp development and chronic inflammation of the sinonasal mucosa, with a global prevalence reported between 0.5% and 4.3% [2]. CRSwNP significantly affects quality of life and is often associated with anxiety, depression, sleep disturbances, asthma, AERD, and allergic rhinitis. In addition, patients exhibit considerable heterogeneity in inflammatory endotypes, histopathology, disease severity, and recurrence risk. This variability complicates treatment selection and represents a challenge when attempting to compare outcomes across trials of targeted biologic therapies. Although CRSwNP demonstrates substantial inflammatory heterogeneity, type 2 (T2) inflammation remains the dominant endotype in most patients and is commonly characterized by eosinophilia and increased IL-5 and IL-13 expression. This inflammatory pattern has been reported in nearly 70–90% of Western patients. Nevertheless, a substantial proportion of patients display mixed in-

flammatory patterns, reflecting the coexistence of type 1 (T1), type 2 (T2), and type 3 (T3) immune responses [3,4]. The relationship between inflammatory endotypes and clinical expression is evident in both CRSwNP and Chronic rhinosinusitis without nasal polyps (CRSsNP). T2-dominant disease is frequently associated with anosmia, concomitant asthma, allergic manifestations, and mucus hypersecretion, whereas T1 inflammation tends to be more common in female patients and is characterized by facial pain and pressure. Meanwhile, purulent nasal discharge has been reported to correlate significantly with T3 endotype activity [5].

Inflammatory pathways are generally categorized into three major patterns. T1 inflammation is mainly involved in immune defense against viral, bacterial, and fungal pathogens and is mediated by Th1 cells, Th17 cells, and type 1 innate lymphoid cells, with IFN- γ and TNF- α serving as key cytokines. In contrast, type 2 (T2) inflammation is associated with allergic responses and host defense against parasites and involves Th2 cells, type 2 innate lymphoid cells, eosinophils, mast cells, basophils, and IgE-producing B lymphocytes. The principal cytokines driving T2 inflammation are IL-4, IL-5, and IL-13 [6]. Produced predominantly by Th2 lymphocytes and type 2 innate lymphoid cells (ILC2s), IL-4 and IL-13 play a pivotal role in enhancing T2 inflammation, particularly by stimulating IgE-producing plasma cell differentiation from B cells [7]. The interaction of IgE with receptors on mast cells, together with IL-4/IL-13-driven upregulation of IL-5 and eotaxin, facilitates eosinophil development and their migration into inflamed tissues [8]. Furthermore, IL-13 contributes to goblet cell hyperplasia, excessive mucus production, and structural remodeling of the airway mucosa. In CRSwNP, this inflammatory milieu remains dysregulated, with persistently elevated levels of IL-4, IL-5, and IL-13 observed in both eosinophilic and non-eosinophilic polyp tissues [8,9]. In CRSwNP, epithelial-derived cytokines, including IL-25, IL-33, and thymic stromal lymphopoietin (TSLP), act as upstream drivers of type 2 (T2) inflammation. Disruption of the epithelial barrier by environmental stimuli such as pathogens, proteases, or irritants triggers the release of these alarmins, particularly TSLP [10]. These cytokines activate type 2 innate lymphoid cells (ILC2s), leading to the production of downstream T2 cytokines, including IL-4, IL-5, and IL-13, which orchestrate the characteristic inflammatory response [6]. T3 inflammation contributes primarily to immune defense against extracellular bacteria and fungi and is driven by Th17 cells and type 3 innate lymphoid cells. IL-17 and IL-22 are the principal cytokines involved in this inflammatory pathway [6]. Collectively, these inflammatory cells, receptors, and cytokines have become important therapeutic targets in CRSwNP.

Biologics targeting IgE, IL-5, IL-5R α , IL-4R α , and TSLP have been approved for severe asthma by the U.S. Food and Drug Administration and the European Medicines Agency. Some of these agents, including omalizumab, mepolizumab, dupilumab, and tezepelumab, are also approved for CRSwNP, whereas depemokimab has recently demonstrated encouraging results in both asthma and CRSwNP [11].

2. Indications for Biologic Treatment in CRSwNP

Criteria for identifying patients with CRSwNP who may benefit from biologic therapy, along with the appropriate timing for treatment initiation, have been outlined in several expert consensus statements [12]. Assessment of treatment response, and decisions regarding discontinuation or switching of biologic agents, are also discussed within these consensus frameworks. The 2023 EPOS/ EUFOREA update recommends biologic treatment for patients with bilateral nasal polyps and previous sinus surgery who meet at least three of five defined criteria. Biologic therapy is generally considered in patients who remain uncontrolled despite prior sinus surgery and appropriate medical treatment. The main selection criteria recommended by EPOS/ EUFOREA are presented in **Table 1**.

Table 1. Indication for biological treatment in CRSwNP.

Clinical Criterion	Suggested Threshold
Evidence of T2 inflammation	Tissue eosinophils ≥ 10 /hpf, blood eosinophils ≥ 150 cells/ μ L, or total IgE ≥ 100 IU/mL
Systemic corticosteroid requirement	≥ 2 systemic steroid courses/year or long-term low-dose steroid use (>3 months)
Impaired quality of life	SNOT-22 score ≥ 40
Olfactory dysfunction	Anosmia or marked smell impairment on validated testing
Comorbid asthma	Regular inhaled corticosteroid requirement

Note: hpf: high power field, SNOT: Sinonasal Outcome Test.

According to the EPOS recommendations, prior surgical status should be considered when selecting candidates for biologic therapy in CRSwNP. In clinical practice, many rhinologists recommend endoscopic sinus surgery before

initiating biologic treatment, particularly in patients with severe obstructive disease. Complete ethmoidectomy may facilitate postoperative topical corticosteroid delivery and reduce inflammatory burden, thereby potentially optimizing subsequent medical and biologic treatment responses in patients with symptomatic recurrence [12,13]. Therefore, biologics are generally considered in patients with persistent or recurrent disease despite appropriate surgical and medical management.

3. Current Biologic Agents (Part I)

3.1. Omalizumab

Omalizumab is a recombinant humanized monoclonal antibody that targets free circulating IgE by binding to its Cε3 region, thereby inhibiting interaction with FcεRI receptors on mast cells and basophils [14]. By neutralizing free IgE, omalizumab disrupts a critical step in the IgE-driven inflammatory cascade underlying CRSwNP, which is characterized by enhanced systemic and local IgE production within polyp tissue [15]. Treatment with omalizumab has been shown to reduce levels of circulating IgE, as well as eosinophils, basophils, mast cells, and B lymphocytes, leading to decreased release of inflammatory mediators such as prostaglandins and leukotrienes [16]. In patients with CRSwNP, increased IgE levels within nasal tissue are often independent of systemic allergic sensitization and may originate from multiple distinct B-cell clones. In this context, *Staphylococcus aureus* enterotoxins are thought to function as superantigens, promoting polyclonal IgE production through activation of both B and T lymphocytes [17].

The phase 3 POLYP 1 and POLYP 2 trials demonstrated the efficacy of omalizumab in severe CRSwNP patients with inadequate response to intranasal corticosteroids, with baseline SNOT-22 scores indicating markedly impaired quality of life [18,19]. Participants were randomized to receive either omalizumab or placebo in addition to intranasal mometasone furoate for a treatment duration of 24 weeks. Compared with baseline, omalizumab produced significant improvements in the co-primary endpoints—nasal polyp score (NPS) and nasal congestion score (NCS)—at week 24. These findings were supported by secondary outcomes, including clinically meaningful reductions in SNOT-22 scores [18,19]. Olfactory performance, evaluated using the University of Pennsylvania Smell Identification Test (UPSIT), also improved significantly, along with other nasal symptoms such as postnasal drip and rhinorrhea [19]. In the open-label extension phase, continuation of omalizumab therapy for up to 52 weeks resulted in sustained efficacy and further improvements in NPS, NCS, and SNOT-22 scores [18]. Importantly, treatment with omalizumab was associated with a reduction in surgical interventions by approximately 25% and a 62.5% decrease in the need for rescue systemic corticosteroids compared with placebo [18,20]. Subgroup analyses demonstrated that the efficacy of omalizumab was maintained across various patient populations, including those with elevated eosinophil levels, prior sinus surgery, comorbid asthma, and AERD [21]. Notably, the therapeutic effect of omalizumab was observed irrespective of allergic status, suggesting that local IgE production within nasal polyp tissue, rather than systemic atopy, may represent a more relevant therapeutic target [15,22]. Omalizumab may be utilized as a targeted treatment in patients with severe CRSwNP refractory to intranasal corticosteroids, irrespective of underlying allergic sensitization [15,19,22]. The POLYP studies included patients with severe disease characterized by high nasal polyp scores and substantial impairment in quality of life [18,19]. Overall, subgroup analyses indicate that omalizumab provides a broad spectrum of efficacy in patients with CRSwNP, including those with elevated eosinophil levels, prior surgery, comorbid asthma, and AERD [21,22].

Patients included in the POLYP trials had severe CRSwNP and demonstrated an inadequate response to intranasal corticosteroid therapy throughout the 24-week treatment duration [18,19]. These studies demonstrated efficacy across a broad patient population, including those with or without prior surgery, with or without comorbid asthma, and irrespective of atopic status [21,22]. Overall, these data support the use of omalizumab as a suitable treatment strategy for a wide range of patients with severe CRSwNP who exhibit persistent symptoms despite intranasal corticosteroid use [18,19]. Anti-IgE therapy (omalizumab) is an effective treatment option in IgE-mediated/atopic diseases and, in appropriate candidates, improves nasal obstruction and related symptoms, with significant effects on nasopharyngeal symptoms [23].

Regarding adverse drug reactions, in addition to reactions commonly observed with other biologic agents—primarily affecting the respiratory and dermatologic systems, such as asthma exacerbation, dyspnea, cough, and fatigue—urticaria and lack of drug efficacy were reported at higher rates particularly with omalizumab [24].

3.2. Dupilumab

Dupilumab is a fully human monoclonal antibody targeting the IL-4 receptor alpha (IL-4R α) subunit, thereby inhibiting IL-4 and IL-13 signaling pathways that play central roles in type 2 inflammation [25,26]. Local *Staphylococcus aureus* colonization and enterotoxin release enhance immune activation and promote T2-skewed inflammation, supporting its pathogenic role in CRSwNP progression [14]. In CRSwNP, type 2 (T2) inflammation is characterized by eosinophilic infiltration, increased IgE production, and excessive mucus secretion, and represents a shared inflammatory pathway with comorbid diseases such as asthma, NERD, atopic dermatitis, and allergic rhinitis. Asthma is reported in up to 65% of CRSwNP patients, whereas NERD and atopic dermatitis are observed in approximately 26% and 9% of cases, respectively [3,27]. T2-driven inflammation also contributes to olfactory dysfunction through structural and functional impairment of the olfactory epithelium [6]. Experimental data indicate that IL-4 and IL-13 may directly disrupt olfactory neuron integrity, promoting neuronal loss and mucus overproduction [28,29]. These pathophysiological insights have supported the development of targeted biologic therapies, with dual IL-4/IL-13 blockade (dupilumab) emerging as an effective and approved treatment strategy in CRSwNP [30].

The phase 3 LIBERTY NP SINUS-24 and SINUS-52 studies evaluated dupilumab as add-on therapy in adults with severe CRSwNP. These multinational, randomized, placebo-controlled trials included patients with bilateral nasal polyps who remained symptomatic despite intranasal corticosteroid treatment. Eligible patients had a history of prior systemic corticosteroid use or sinus surgery within the previous two years and demonstrated severe bilateral disease with high nasal polyp scores accompanied by persistent symptoms such as nasal obstruction, loss of smell, or nasal discharge. In SINUS-24, 276 patients from 67 centers across 13 countries were randomized to receive either dupilumab 300 mg every two weeks or placebo for 24 weeks [25].

The SINUS-52 trial enrolled 448 patients across 117 centers in 14 countries and evaluated different dupilumab dosing regimens over 52 weeks. Patients, regardless of concomitant asthma status, were randomized to receive dupilumab every two weeks, dupilumab every two weeks followed by every four weeks, or placebo. The primary endpoints included changes in nasal polyp score, nasal congestion severity, and Lund–Mackay CT score. Safety analyses pooled data from the dupilumab and placebo arms of both SINUS-24 and SINUS-52. Overall, dupilumab significantly improved all major efficacy endpoints. Temporary elevations in peripheral eosinophil counts were observed and were considered to reflect reduced eosinophil migration into tissues rather than increased production. Common adverse events included nasopharyngitis, headache, epistaxis, asthma worsening, and injection-site reactions, most of which occurred more frequently in placebo-treated patients. During the 52-week follow-up of SINUS-52, cough, bronchitis, arthralgia, and injection-site reactions were reported slightly more often with dupilumab [25,27].

Across these studies, dupilumab therapy reduced multiple T2 inflammatory biomarkers, including IgE, thymus and activation-regulated chemokine (TARC), eotaxin-3, periostin, and eosinophil cationic protein (ECP). Temporary peripheral eosinophilia was also reported and is believed to reflect impaired eosinophil trafficking to tissues after IL-4/IL-13 inhibition [25].

Current standard treatment options for CRSwNP have important limitations. Intranasal corticosteroids, considered first-line therapy, provide modest effects on polyp size and symptom control. Systemic corticosteroids may offer short-term improvement but are limited by significant adverse effects with long-term use [31]. Endoscopic sinus surgery can be effective in refractory cases; however, recurrence is common if the underlying inflammatory process is not adequately controlled. Consequently, many patients undergo repeated courses of systemic corticosteroids and multiple surgical interventions. Therefore, the use of an agent targeting T2 inflammation and treating concomitant diseases such as asthma may provide clinical benefit [32]. Dupilumab has been approved by the U.S. Food and Drug Administration as add-on therapy for adults with inadequately controlled CRSwNP. It is also licensed in both the United States and Europe for moderate-to-severe atopic dermatitis in patients aged 12 years and older who do not achieve adequate control with topical treatment [33–35].

Real-world evidence supports the clinical benefits of dupilumab across different populations. In a Brazilian cohort, treatment was associated with significant improvements in olfactory function, quality of life, and both the size and extent of nasal polyps [36]. Consistent with these findings, the European CHRINOSOR study demonstrated sustained improvements across all assessed outcomes over 24 to 52 weeks compared with baseline [37]. Similarly, data from a Hungarian real-world cohort indicated that dupilumab was more effective than conventional treatment approaches and showed a favorable safety profile when used in accordance with recommended treatment proto-

cols [38]. Dupilumab currently appears to provide the most consistent clinical benefit among approved biologics for CRSwNP. However, caution may be warranted in patients with marked peripheral blood eosinophilia, as transient eosinophil elevation and, rarely, eosinophilic complications have been reported during treatment [39,40].

3.3. Stapokibart

Stapokibart is an IL-4R α -targeting biologic that blocks IL-4 and IL-13 signaling pathways and has been approved in China, although it has not yet received approval from the U.S. Food and Drug Administration [41]. This agent represents the first IL-4R α -targeting biologic to receive approval for seasonal allergic rhinitis. Phase 3 data suggest that stapokibart may improve nasal polyp size and symptom severity in severe CRSwNP patients receiving intranasal corticosteroids. However, long-term follow-up data remain limited, and the inclusion of only Chinese patients may restrict the generalizability of the findings [42].

3.4. Mepolizumab

Mepolizumab is a humanized monoclonal antibody directed against IL-5, a central cytokine in type 2 inflammation that plays a critical role in eosinophil maturation and survival [43,44]. By inhibiting the interaction between IL-5 and its receptor, mepolizumab reduces eosinophil maturation, survival, and tissue migration, thereby attenuating eosinophil-driven inflammation, a central feature of CRSwNP pathophysiology [43–45]. IL-5-mediated eosinophilic inflammation contributes to tissue damage and remodeling through the release of cytotoxic mediators, including major basic protein, eosinophil cationic protein, and eosinophil peroxidase [45]. Elevated IL-5 levels in nasal polyp tissue have been associated with increased eosinophil infiltration and disease severity, supporting the biological rationale for IL-5-targeted therapies, particularly in eosinophil-predominant CRSwNP [20,43–45].

The SYNAPSE trial was a phase 3, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of subcutaneous mepolizumab at a dose of 100 mg administered every four weeks over 52 weeks in patients with severe CRSwNP [46,47]. The trial included 407 adults with severe CRSwNP and prior sinus surgery who remained candidates for additional intervention. Mepolizumab significantly reduced nasal polyp burden and nasal obstruction compared with placebo [46–48]. A higher proportion of patients in the mepolizumab group achieved a ≥ 1 -point improvement in nasal polyp score and a reduction of more than 3 points in nasal obstruction VAS score [46]. Additionally, clinically meaningful improvements were observed in SNOT-22 scores, along with significant gains in olfactory function [48,49]. Subgroup analyses indicated that the therapeutic benefits of mepolizumab were evident regardless of the presence of comorbid asthma or aspirin-exacerbated respiratory disease (AERD). However, treatment effects were more pronounced in patients with baseline blood eosinophil counts of ≥ 150 and ≥ 300 cells/ μL [46].

Because disease characteristics may vary between Asian and European populations, the phase 3 MERIT trial evaluated mepolizumab in patients with CRSwNP/ECRS from China, Japan, and Russia. Add-on treatment with subcutaneous mepolizumab 100 mg significantly reduced nasal obstruction and polyp burden compared with placebo. The findings were consistent with those of the SYNAPSE trial and further supported the efficacy and safety of mepolizumab in CRSwNP [50]. Real-world studies have supported these findings by showing significant improvements in quality of life at both 6 and 12 months after mepolizumab treatment, as assessed using SNOT-22 and Rhinosinusitis Outcome Measure-31 (RSOM-31) scores [51]. In a cohort of patients with severe CRSwNP, partial recovery of olfactory function was observed in 22% of cases, while complete restoration was achieved in 14% [52].

In patients with type 2 CRSwNP, mepolizumab has been associated with reductions in eosinophilia, polyp size, nasal obstruction, and surgical or corticosteroid requirements [47]. Therefore, mepolizumab may be preferred in patients with marked eosinophilia, particularly those with elevated peripheral blood eosinophil levels, severe disease resistant to surgery, and recurrent postoperative disease [23,46]. Follow-up data from the SYNAPSE study after treatment discontinuation indicate that although there is partial loss of efficacy following cessation of mepolizumab, the chronic nature of CRSwNP suggests that most patients require continued biologic therapy to maintain disease control [53]. Mepolizumab was generally well tolerated in the SYNAPSE study, with no new safety concerns observed during 52 weeks of treatment. Additionally, by reducing the need for systemic corticosteroids, it demonstrated the potential to decrease the cumulative adverse effect burden associated with corticosteroid use [47,54].

Injection-site reactions, headache, and back pain were the most frequently observed adverse events with mepolizumab [48]. Serious adverse events are rare, and data from various indications indicate a reassuring long-

term safety profile [48]. However, pharmacovigilance reports have shown relatively higher rates of systemic symptoms such as fatigue and fever, issues related to missed doses (potentially associated with challenges in subcutaneous administration), and respiratory complications such as asthma and dyspnea compared with other biologic agents [24].

4. Current Biologic Agents (Part II)

4.1. Benralizumab

Benralizumab is an afucosylated IgG1 monoclonal antibody directed against IL-5R α that differs from IL-5-blocking agents by inducing profound eosinophil depletion. After binding to IL-5R α on the eosinophil surface, it enhances apoptosis of eosinophils via Fc γ R11a-mediated antibody-dependent cellular cytotoxicity (ADCC), primarily through natural killer (NK) cells, resulting in a rapid and profound reduction in circulating eosinophil levels [55,56]. Pharmacodynamic analyses from the Phase 3 OSTRO trial confirmed that this effect is also observed in patients with CRSwNP. Eosinophil counts in nasal polyp tissue were significantly reduced at week 56 in treated patients. Moreover, benralizumab therapy was associated with significant decreases in eosinophil-derived neurotoxin levels in nasal lining fluid, indicating marked suppression of local eosinophilic inflammation [57].

Current evidence for benralizumab in CRSwNP mainly comes from the phase 3 OSTRO trial, a randomized placebo-controlled study involving 413 adults with severe disease despite intranasal corticosteroid therapy. Patients received subcutaneous benralizumab 30 mg or placebo every 4 weeks for the first three doses and then every 8 weeks thereafter [58].

The coprimary outcomes were changes in endoscopic nasal polyp score and nasal blockage severity at week 40. Compared with placebo, benralizumab achieved significant improvement in both endpoints [58]. However, results for secondary endpoints were more limited. Improvement in SNOT-22 scores did not reach statistical significance, and although nominal improvement in sense of smell was reported, this was not adjusted for multiplicity [58,59]. Benralizumab did not significantly reduce the need for surgery or systemic corticosteroid use compared with placebo [58].

In addition to the OSTRO trial, the effects of benralizumab on sinonasal outcomes have been investigated through phase 2 studies, meta-analyses, and real-world evidence. A published systematic review and meta-analysis that combined data from three randomized controlled trials demonstrated statistically significant improvements in bilateral endoscopic nasal polyp score (NPS) and SNOT-22 outcomes in patients treated with benralizumab [60]. In a smaller phase 2 randomized trial, benralizumab achieved significant reductions in nasal polyp size compared with baseline, with a substantial proportion of patients demonstrating concurrent improvements in NPS, CT scores, SNOT-22, and smell tests [61]. Real-world data with follow-up up to 24 months have also shown sustained reductions in NPS and SNOT-22 scores and improvements in olfactory performance [62]. Subgroup analyses from OSTRO and post-hoc evaluations from asthma trials indicate that patients with comorbid asthma may experience greater sinonasal improvement with benralizumab [63]. Baseline peripheral blood eosinophil levels have been proposed as potential predictors of response, although no validated threshold has been established specifically for CRSwNP [58]. The ratio of blood eosinophil count to allergen skin test positivity has been reported to correlate with polyp reduction [61]. Pharmacodynamic data further support that clinical efficacy is closely linked to depletion of both circulating and tissue eosinophils [57].

Evidence from phase 2 and phase 3 trials, as well as real-world studies, indicates that benralizumab has a safety profile in CRSwNP that is comparable to that observed in patients with severe asthma [57,58]. Overall, the treatment is well tolerated, with commonly reported adverse events including injection-site reactions, headache, nasopharyngitis, arthralgia, and dizziness [63]. Importantly, no novel or unexpected safety concerns have been identified in the CRSwNP population. In addition, pharmacokinetic data suggest that drug exposure in patients with CRSwNP is similar to that reported in severe asthma [57].

Although benralizumab offers a biologically plausible strategy for targeting eosinophil-driven inflammation in CRSwNP, the available clinical evidence remains relatively limited and somewhat inconsistent. While the phase 3 OSTRO trial reported significant improvements in the co-primary endpoints, these benefits were not uniformly reflected across several secondary outcomes or in surgical endpoints. Moreover, the subsequent ORCHID trial did not meet its primary endpoint and was terminated early, ultimately resulting in the discontinuation of the CRSwNP

development program [64]. As a result, benralizumab has not been granted regulatory approval for the treatment of CRSwNP. Based on the currently available evidence, its role in this setting remains unclear, and there is still a lack of long-term controlled studies as well as direct comparative trials with other biologic agents.

4.2. Reslizumab

Reslizumab is a humanized IgG4 monoclonal antibody that targets interleukin-5 (IL-5), a key regulator of eosinophil function. By blocking the interaction between IL-5 and its receptor (IL-5R α), it inhibits IL-5-mediated signaling, thereby reducing eosinophil maturation and survival [65].

In a phase 1 study involving patients with bilateral grade 3–4 CRSwNP and recurrent nasal polyps after surgery, a single intravenous dose of reslizumab (3 mg/kg) was found to be safe and well tolerated. Treatment led to substantial reductions in eosinophil counts and eosinophil cationic protein levels in both serum and nasal secretions, along with improvements in nasal polyp scores in a subset of patients. Baseline nasal IL-5 levels above 40 pg/mL were suggested as a potential predictor of response to anti-IL-5 therapy [66]. Post hoc analyses of the phase 3 BREATH 1 and 2 asthma trials showed that intravenous reslizumab reduced asthma exacerbations by 83% in patients with eosinophilic asthma and coexisting CRSwNP. Significant improvements in lung function and asthma-related quality of life were also reported [67,68]. Moreover, reslizumab exhibited comparable efficacy in patients with eosinophilic CRSwNP regardless of the presence of aspirin sensitivity, suggesting that anti-IL-5 therapy may be beneficial across these subgroups [68]. Treatment was also associated with a lower incidence of upper respiratory tract infections compared with placebo. Although the underlying mechanism remains uncertain, this effect may be related to attenuation of eosinophilic inflammation in the upper airway, contributing to reduced polyp burden and improved sinus drainage [68]. Although intravenous reslizumab is an effective add-on therapy for severe eosinophilic asthma, it has not yet been approved for the treatment of CRSwNP [69].

4.3. Tezepelumab

Tezepelumab is a fully IgG2 lambda monoclonal antibody that targets thymic stromal lymphopoietin, a key epithelial alarmin implicated in the initiation and amplification of type 2 inflammation [70]. Disruption of the epithelial barrier is a key feature in the pathogenesis of CRSwNP and contributes to interactions with environmental triggers and pro-inflammatory signals. Structural and functional abnormalities within the sinonasal epithelium include defects in tight junction integrity, basal cell dysplasia, loss of ciliated cells, impaired function of secretory cells, subepithelial extracellular matrix accumulation, and the development of epithelial-mesenchymal transition (EMT) [10]. Released in response to epithelial injury triggered by external stimuli, TSLP functions as an upstream alarmin involved in both type 2 and non-type 2 inflammatory pathways associated with airway remodeling and bronchial hyperresponsiveness [71]. TSLP expression is not limited to nasal epithelial cells and basal stem cells; it has also been demonstrated in subepithelial fibroblasts and infiltrating inflammatory cells [5]. The NAVIGATOR trial evaluating tezepelumab included endpoints related to both asthma and CRSwNP and was designed as a multicenter, randomized, double-blind, placebo-controlled phase 3 trial [71]. In this trial, tezepelumab significantly decreased the rate of asthma exacerbations in adolescents and adults with severe, uncontrolled disease compared with placebo. Notably, this reduction was consistent across different seasons and was independent of sensitization to either perennial or seasonal aeroallergens. Among patients with coexisting CRSwNP, treatment with tezepelumab was also associated with improvements in olfactory function, nasal congestion, and SNOT-22 scores.

Increased TSLP mRNA expression has been observed in CRSwNP compared with CRSsNP and healthy controls, with expression predominantly localized to nasal polyp tissue [5]. Based on these findings and the concept of united airway pathophysiology, tezepelumab has begun to be investigated in patients with CRSwNP. The therapeutic effects of corticosteroids in CRSwNP are mediated through suppression of inflammatory pathways and eosinophilic inflammation driven by TSLP signaling [72]. In recent years, the development of biologic therapies targeting T2 inflammation-related factors has increased the number of targeted treatment options for patients with CRSwNP [12].

The phase 3 WAYPOINT trial investigated the efficacy and safety of tezepelumab, an anti-thymic stromal lymphopoietin monoclonal antibody, in patients with severe CRSwNP regardless of concomitant asthma status [73]. 203 patients received tezepelumab and 205 received placebo. After 52 weeks, tezepelumab significantly improved nasal polyp score and nasal congestion compared with placebo, along with additional benefits in olfactory function,

SNOT-22, Lund–Mackay CT, and overall symptom scores. In addition, treatment with tezepelumab substantially reduced the need for surgical intervention and significantly decreased systemic glucocorticoid requirements compared with placebo.

Tezepelumab represents a promising therapeutic option because it targets thymic stromal lymphopoietin (TSLP), an upstream regulator of type 2 inflammation. Because TSLP acts upstream in the inflammatory cascade, tezepelumab may offer broader modulation of airway inflammation compared with biologics targeting downstream cytokines. Nevertheless, additional real-world studies and long-term clinical data are still needed to better define its efficacy, safety profile, and positioning in CRSwNP management algorithms.

4.4. Depemokimab

Depemokimab is a novel affinity-matured humanized IgG1 monoclonal antibody targeting interleukin-5, a central cytokine involved in eosinophil differentiation, persistence, and tissue recruitment. Its mechanism of action is comparable to that of mepolizumab and reslizumab, and it is structurally related to mepolizumab. Structural modifications in depemokimab provide enhanced affinity for interleukin-5 together with a prolonged half-life. Its efficacy and safety were investigated in two replicate phase 3A placebo-controlled trials in which the drug was administered every six months. During the 52-week follow-up period, depemokimab significantly lowered exacerbation frequency in patients with severe eosinophilic asthma that remained uncontrolled despite medium- or high-dose inhaled corticosteroid therapy. However, its impact on symptom control and lung function outcomes remains unclear, and therefore its precise role in asthma management has yet to be fully established [74]. The results of studies in CRSwNP have been published more recently [75]. The ANCHOR-1 and ANCHOR-2 phase III trials investigated subcutaneous depemokimab 100 mg in patients with inadequately controlled CRSwNP, showing significant reductions in nasal polyp burden and nasal congestion compared with placebo [76]. In both asthma and nasal polyp studies, reductions in eosinophil levels were observed, and reported adverse events were generally comparable to those in the placebo groups [75]. Depemokimab is not yet widely available for clinical use. The key characteristics of currently available and investigational biologics in CRSwNP are summarized in **Table 2**.

Table 2. Characteristics of Approved and Investigational Biologics in CRSwNP.

Drug	Target	Route & Dosing	Key Phase 3 Trial	Biomarker Effects	Special Considerations	Other Approved Indications
Dupilumab	IL-4Rα (blocks IL-4/IL-13)	SC 600 mg loading, then 300 mg q2 weeks	SINUS-24/SINUS-52	↓ IgE, ↓ TARC, transient ↑ eosinophils	Strong effect on smell; useful in comorbid AD	Asthma, Atopic dermatitis,
Omalizumab	IgE	SC q2–4 weeks (weight and IgE based)	POLYP 1/POLYP 2	↓ free IgE	Effective irrespective of systemic atopy	Asthma, Chronic spontaneous urticaria
Mepolizumab	IL-5	SC 100 mg q4 weeks	SYNAPSE	↓ blood eosinophils	Particularly effective in high eosinophil phenotype	Asthma, EGPA, Hypereosinophilic syndrome
Reslizumab*	IL-5	IV 3 mg/kg q4 weeks	Phase 1/post-hoc	↓ eosinophils	Not approved for CRSwNP	Asthma (eosinophilic)
Benralizumab*	IL-5Rα (eosinophil depletion via ADCC)	SC 30 mg q4 weeks × 3, then q8 weeks	OSTRO	Near-complete ↓ blood & tissue eosinophils	Not approved for CRSwNP; ORCHID terminated	Asthma
Tezepelumab	TSLP	SC 210 mg q4 weeks	WAYPOINT	Broad upstream suppression	Targets early epithelial cytokine signaling	Asthma
Depemokimab	IL-5 (long-acting)	SC 100 mg q6 months	ANCHOR 1/2	↓ eosinophils	Ultra-long dosing interval	Not yet widely approved

Note: *Not currently approved for CRSwNP; ↓ reduced; ↑ increased.

5. Conclusions

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a heterogeneous inflammatory condition in which type 2 (T2) inflammation predominates in a substantial proportion of patients. The introduction of biologic therapies targeting key inflammatory mediators, including IgE, IL-5, IL-4/IL-13, and TSLP, has markedly changed the therapeutic landscape for patients with severe, uncontrolled disease. Evidence from phase 3 trials and real-world studies has consistently shown reductions in nasal polyp burden and symptom severity, along with decreased use of systemic corticosteroids and a lower need for revision surgery. From a clinical standpoint, the choice of biologic therapy should be individualized, taking into account factors such as inflammatory endotype, blood eosinophil levels, IgE

profile, the presence of comorbid asthma or atopic disease, prior surgical history, and patient-specific treatment goals.

In general, therapies targeting IL-5 may be more appropriate for patients with eosinophil-dominant disease, whereas approaches that act upstream—such as epithelial cytokine blockade or dual IL-4/IL-13 inhibition—may provide a broader suppression of T2 inflammation. Although omalizumab was widely used following its initial introduction as the first available biologic agent, accumulating real-world experience suggests that its relative efficacy may be less pronounced compared with newer agents such as mepolizumab and dupilumab. However, the lack of direct head-to-head comparisons and the absence of standardized switching strategies continue to make it difficult to clearly define the optimal positioning of these agents in clinical practice. In addition to clinical efficacy, treatment selection in CRSwNP is increasingly influenced by cost considerations and healthcare resource utilization, although robust head-to-head cost-effectiveness data remain scarce. It should also be noted that reimbursement policies and eligibility criteria for biologic therapies vary substantially between countries. Consequently, access to these agents may depend not only on disease severity and guideline recommendations, but also on national healthcare regulations and reimbursement policies.

Future research should aim to refine patient stratification through the identification of reliable biomarkers and to better define long-term treatment strategies. Additional studies are still required to clarify cost-effectiveness, optimal treatment duration, and appropriate discontinuation strategies. As clinical evidence continues to grow, biologic therapies are expected to assume an increasingly important role in the personalized management of CRSwNP.

Funding

This work received no external funding.

Institutional Review Board Statement

Ethical review and approval were waived for this study because this article is a review study based exclusively on previously published literature and does not involve human participants, animal subjects, or identifiable personal data.

Informed Consent Statement

Patient consent was waived because this study is a review article based exclusively on previously published literature and does not involve human participants or identifiable patient data.

Data Availability Statement

Data sharing is not applicable to this study because no new data were created or analyzed in this study. This review is based exclusively on previously published literature.

Conflicts of Interest

The authors declare no conflict of interest.

AI Use Statement

During the preparation of this manuscript, the authors used language editing tools (ChatGPT, OpenAI, San Francisco, CA, USA) solely for language refinement. No AI tools were used for data analysis, interpretation, or generation of scientific content. All outputs were critically reviewed and edited by the authors. The authors take full responsibility for the integrity and accuracy of the work.

References

1. Hirsch, A.G.; Stewart, W.F.; Sundaresan, A.S.; et al. Nasal and Sinus Symptoms and Chronic Rhinosinusitis in a Population-Based Sample. *Allergy* **2017**, *72*, 274–281. [[CrossRef](#)]
2. Chen, S.; Zhou, A.; Emmanuel, B.; et al. Systematic Literature Review of the Epidemiology and Clinical Burden of Chronic Rhinosinusitis with Nasal Polyposis. *Curr. Med. Res. Opin.* **2020**, *36*, 1897–1911. [[CrossRef](#)]

3. Khan, A.H.; Gouia, I.; Kamat, S.; et al. Prevalence and Severity Distribution of Type 2 Inflammation-Related Comorbidities Among Patients with Asthma, Chronic Rhinosinusitis with Nasal Polyps, and Atopic Dermatitis. *Lung* **2023**, *201*, 57–63. [[CrossRef](#)]
4. Wang, X.; Zhang, N.; Bo, M.; et al. Diversity of TH Cytokine Profiles in Patients with Chronic Rhinosinusitis: A Multicenter Study in Europe, Asia, and Oceania. *J. Allergy Clin. Immunol.* **2016**, *138*, 1344–1353. [[CrossRef](#)]
5. Peters, A.T.; Han, J.K.; Heffler, E.; et al. Thymic Stromal Lymphopoietin as a Therapeutic Target in Patients with Chronic Rhinosinusitis and Nasal Polyps. *Clin. Exp. Immunol.* **2025**, *219*, uxaf041. [[CrossRef](#)]
6. Bachert, C.; Hicks, A.; Gane, S.; et al. The Interleukin-4/Interleukin-13 Pathway in Type 2 Inflammation in Chronic Rhinosinusitis with Nasal Polyps. *Front. Immunol.* **2024**, *15*, 1356298. [[CrossRef](#)]
7. Matsunaga, K.; Katoh, N.; Fujieda, S.; et al. Dupilumab: Basic Aspects and Applications to Allergic Diseases. *Allergol. Int.* **2020**, *69*, 187–196. [[CrossRef](#)]
8. Luo, X.; Li, C.; Wang, Y.; et al. Interleukin-33 Promotes Th2/Th17 Response in Eosinophilic and Non-Eosinophilic Nasal Polyps. *ORL J. Otorhinolaryngol. Relat. Spec.* **2020**, *82*, 34–39. [[CrossRef](#)]
9. Liu, J.; Li, Y.Y.; Andiappan, A.K.; et al. Role of IL-13R α 2 in Modulating IL-13-Induced MUC5AC and Ciliary Changes in Healthy and CRSwNP Mucosa. *Allergy* **2018**, *73*, 1673–1685. [[CrossRef](#)]
10. Berni Canani, R.; Caminati, M.; Carucci, L.; et al. Skin, Gut, and Lung Barrier: Physiological Interface and Target of Intervention for Preventing and Treating Allergic Diseases. *Allergy* **2024**, *79*, 1485–1500. [[CrossRef](#)]
11. Kyriakopoulos, C.; Ntritsos, G.; Gogali, A.; et al. Efficacy of Biologic Agents in Patients with Comorbid Asthma and Chronic Rhinosinusitis with Nasal Polyps: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *Eur. Respir. Rev.* **2026**, *35*. [[CrossRef](#)]
12. Fokkens, W.J.; Viskens, A.S.; Backer, V.; et al. EPOS/EUFOREA Update on Indication and Evaluation of Biologics in Chronic Rhinosinusitis with Nasal Polyps 2023. *Rhinology* **2023**, *61*, 194–202. [[CrossRef](#)]
13. Snidvongs, K.; Kalish, L.; Sacks, R.; et al. Sinus Surgery and Delivery Method Influence the Effectiveness of Topical Corticosteroids for Chronic Rhinosinusitis: Systematic Review and Meta-Analysis. *Am. J. Rhinol. Allergy* **2013**, *27*, 221–233. [[CrossRef](#)]
14. Kariyawasam, H.H.; James, L.K. Chronic Rhinosinusitis with Nasal Polyps: Targeting IgE with Anti-IgE Omalizumab Therapy. *Drug Des. Devel. Ther.* **2020**, *14*, 5483–5494. [[CrossRef](#)]
15. Chhibba, K.D.; Patel, G.B.; Peters, A.T. Anti-IgE Therapy in Chronic Rhinosinusitis with Nasal Polyps. *J. Allergy Clin. Immunol.* **2025**, *155*, 24–30. [[CrossRef](#)]
16. Bai, J.; Tan, B.K. B Lineage Cells and IgE in Allergic Rhinitis and CRSwNP and the Role of Omalizumab Treatment. *Am. J. Rhinol. Allergy* **2023**, *37*, 182–192. [[CrossRef](#)]
17. Bachert, C.; Maurer, M.; Palomares, O.; et al. What Is the Contribution of IgE to Nasal Polyposis? *J. Allergy Clin. Immunol.* **2021**, *147*, 1997–2008. [[CrossRef](#)]
18. Gevaert, P.; Saenz, R.; Corren, J.; et al. Long-Term Efficacy and Safety of Omalizumab for Nasal Polyposis in an Open-Label Extension Study. *J. Allergy Clin. Immunol.* **2022**, *149*, 957–965. [[CrossRef](#)]
19. Gevaert, P.; Omachi, T.A.; Corren, J.; et al. Efficacy and Safety of Omalizumab in Nasal Polyposis: 2 Randomized Phase 3 Trials. *J. Allergy Clin. Immunol.* **2020**, *146*, 595–605. [[CrossRef](#)]
20. Geng, B.; Dilley, M.; Anterasian, C. Biologic Therapies for Allergic Rhinitis and Nasal Polyposis. *Curr. Allergy Asthma Rep.* **2021**, *21*, 36. [[CrossRef](#)]
21. Damask, C.; Chen, M.; Holweg, C.T.J.; et al. Defining the Efficacy of Omalizumab in Nasal Polyposis: A POLYP 1 and POLYP 2 Subgroup Analysis. *Am. J. Rhinol. Allergy* **2022**, *36*, 135–141. [[CrossRef](#)]
22. Gevaert, P. Omalizumab Improves Outcomes in Patients with Nasal Polyps Regardless of Their Asthma Status. *J. Allergy Clin. Immunol.* **2022**, *149*, AB64. [[CrossRef](#)]
23. Safia, A.; Khater, A.; Abd Elhadi, U.; et al. Optimizing Biologic Treatment Selection in Chronic Rhinosinusitis with Nasal Polyps: A Network Meta-Analysis of Efficacy and Safety Across 22 RCTs. *Pharmaceuticals* **2025**, *18*, 1455. [[CrossRef](#)]
24. Fang, X.; Zhou, T.; Ye, F. Analysis of Adverse Reaction Characteristics of Four Biologics for the Treatment of Chronic Sinusitis with Nasal Polyps: A Descriptive Analysis from WHO-VigiAccess. *Am. J. Otolaryngol.* **2025**, *46*, 104705. [[CrossRef](#)]
25. Bachert, C.; Han, J.K.; Desrosiers, M.; et al. Efficacy and Safety of Dupilumab in Patients with Severe Chronic Rhinosinusitis with Nasal Polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): Results from Two Multicentre, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Phase 3 Trials. *Lancet* **2019**, *394*, 1638–1650. [[CrossRef](#)]
26. Gandhi, N.A.; Pirozzi, G.; Graham, N.M.H. Commonality of the IL-4/IL-13 pathway in atopic diseases. *Expert Rev. Clin. Immunol.* **2017**, *13*, 425–437. [[CrossRef](#)]

27. Bachert, C.; Bhattacharyya, N.; Desrosiers, M.; et al. Burden of Disease in Chronic Rhinosinusitis with Nasal Polyps. *J. Asthma Allergy* **2021**, *14*, 127–134. [CrossRef]
28. Hara, Y.; Jha, M.K.; Mattoo, H.; et al. Interleukin 4 directly activates olfactory neurons and induces loss of smell in mice. *J. Allergy Clin. Immunol.* **2023**, *151*, AB128. [CrossRef]
29. Saraswathula, A.; Liu, M.M.; Kulaga, H.; et al. Chronic interleukin-13 expression in mouse olfactory mucosa results in regional aneuronal epithelium. *Int. Forum Allergy Rhinol.* **2023**, *13*, 230–241. [CrossRef]
30. Le Floc'h, A.; Allinne, J.; Nagashima, K.; et al. Dual blockade of IL-4 and IL-13 with dupilumab, an IL-4/IL-13 antibody, is required to broadly inhibit type 2 inflammation. *Allergy* **2020**, *75*, 1188–1204. [CrossRef]
31. Alobid, I.; Benitez, P.; Cardelus, S.; et al. Oral plus nasal corticosteroids improve smell, nasal congestion, and inflammation in sino-nasal polyposis. *Laryngoscope* **2014**, *124*, 50–56. [CrossRef]
32. DeConde, A.S.; Mace, J.C.; Levy, J.M.; et al. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *Laryngoscope* **2017**, *127*, 550–555. [CrossRef]
33. Rabe, K.F.; Nair, P.; Brusselle, G.; et al. Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. *N. Engl. J. Med.* **2018**, *378*, 2475–2485. [CrossRef]
34. Blauvelt, A.; de Bruin-Weller, M.; Gooderham, M.; et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet* **2017**, *389*, 2287–2303. [CrossRef]
35. Thaci, D.; Simpson, E.L.; Beck, L.A.; et al. Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomised, placebo-controlled, dose-ranging phase 2b trial. *Lancet* **2016**, *387*, 40–52. [CrossRef]
36. Mieli, O.M.; Valera, F.C.P.; Dinarte, V.R.P.; et al. One-year efficacy of Dupilumab in sense of smell, nasal polyp score and quality of life in CRSwNP patients: A real-world multicenter study in Brazil. *Braz. J. Otorhinolaryngol.* **2025**, *91*, 101704. [CrossRef]
37. Seys, S.F.; Schneider, S.; de Kinderen, J.; et al. Real-world effectiveness of dupilumab in a European cohort of chronic rhinosinusitis with nasal polyps (CHRINOSOR). *J. Allergy Clin. Immunol.* **2025**, *155*, 451–460. [Cross-Ref]
38. Hirschberg, A.; Matuz, M.; Kiricsi, A. Long-term experience with dupilumab treatment of chronic rhinosinusitis with nasal polyps. *Orv. Hetil.* **2025**, *166*, 1123–1131. [CrossRef] (in Hungarian)
39. Kemp, P.; van der Lans, R.J.L.; Otten, J.J.; et al. Hypereosinophilia during dupilumab treatment in patients with chronic rhinosinusitis with nasal polyps. *Rhinology* **2024**, *62*, 202–207. [CrossRef]
40. Wechsler, M.E.; Klion, A.D.; Paggiaro, P.; et al. Effect of Dupilumab on Blood Eosinophil Counts in Patients With Asthma, Chronic Rhinosinusitis With Nasal Polyps, Atopic Dermatitis, or Eosinophilic Esophagitis. *J. Allergy Clin. Immunol. Pract.* **2022**, *10*, 2695–2709. [CrossRef]
41. Di, Y.; Zeng, R.; Huang, L.; et al. Advance in biologics for chronic rhinosinusitis with nasal polyps. *Front. Allergy* **2026**, *7*, 1759649. [CrossRef]
42. Shen, S.; Yan, B.; Wang, M.; et al. Stapokibart for Severe Uncontrolled Chronic Rhinosinusitis With Nasal Polyps: The CROWNS-2 Randomized Clinical Trial. *JAMA* **2025**, *334*, 962–972. [CrossRef]
43. Liu, X.; Charn, T.C.; Wang, D.Y. Mepolizumab in chronic rhinosinusitis with nasal polyposis. *Immunotherapy* **2023**, *15*, 1105–1116. [CrossRef]
44. Brusselle, G.G.; Gevaert, P. Mepolizumab for chronic rhinosinusitis with nasal polyps. *Lancet Respir. Med.* **2021**, *9*, 1081–1082. [CrossRef]
45. Klimek, L.; Förster-Ruhrmann, U.; Beule, A.G.; et al. Indicating biologics for chronic rhinosinusitis with nasal polyps (CRSwNP). *Allergo J. Int.* **2022**, *31*, 149–160. [CrossRef]
46. Bachert, C.; Sousa, A.R.; Han, J.K.; et al. Mepolizumab for chronic rhinosinusitis with nasal polyps: Treatment efficacy by comorbidity and blood eosinophil count. *J. Allergy Clin. Immunol.* **2022**, *149*, 1711–1721. [Cross-Ref]
47. Han, J.K.; Bachert, C.; Fokkens, W.; et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Respir. Med.* **2021**, *9*, 1141–1153. [CrossRef]
48. Fokkens, W.; Trigg, A.; Lee, S.E.; et al. Mepolizumab improvements in health-related quality of life and disease symptoms in a patient population with very severe chronic rhinosinusitis with nasal polyps: psychometric and efficacy analyses from the SYNAPSE study. *J. Patient Rep. Outcomes* **2023**, *7*, 4. [CrossRef]
49. Mullol, J.; Lund, V.J.; Wagenmann, M.; et al. Mepolizumab improves sense of smell in severe chronic rhinosinusitis with nasal polyps: SYNAPSE. *Rhinology* **2024**, *62*, 320–329. [CrossRef]
50. Fujieda, S.; Wang, C.; Yoshikawa, M.; et al. Mepolizumab in CRSwNP/ECRS and NP: the phase III randomised

- MERIT trial in Japan, China, and Russia. *Rhinology* **2024**, *62*, 576–589. [CrossRef]
51. Gallo, S.; Castelnuovo, P.; Spirito, L.; et al. Mepolizumab Improves Outcomes of Chronic Rhinosinusitis with Nasal Polyps in Severe Asthmatic Patients: A Multicentric Real-Life Study. *J. Pers. Med.* **2022**, *12*, 1304. [Cross-Ref]
 52. Barroso, B.; Valverde-Monge, M.; Alobid, I.; 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.* **2023**, *33*, 37–44.
 53. Desrosiers, M.; Diamant, Z.; Castelnuovo, P.; et al. Sustained efficacy of mepolizumab in patients with severe chronic rhinosinusitis with nasal polyps: SYNAPSE 24-week treatment-free follow-up. *Int. Forum Allergy Rhinol.* **2024**, *14*, 18–31. [CrossRef]
 54. Chupp, G.; Alobid, I.; Lugogo, N.L.; et al. Mepolizumab Reduces Systemic Corticosteroid Use in Chronic Rhinosinusitis With Nasal Polyps. *J. Allergy Clin. Immunol. Pract.* **2023**, *11*, 3504–3512. [CrossRef]
 55. Pelaia, C.; Calabrese, C.; Vatrella, A.; et al. Benralizumab: From the Basic Mechanism of Action to the Potential Use in the Biological Therapy of Severe Eosinophilic Asthma. *Biomed Res. Int.* **2018**, *2018*, 4839230. [Cross-Ref]
 56. Dagher, R.; Kumar, V.; Copenhaver, A.M.; et al. Novel mechanisms of action contributing to benralizumab's potent anti-eosinophilic activity. *Eur. Respir. J.* **2022**, *59*, 2004306. [CrossRef]
 57. Emson, C.; Han, J.K.; Hopkins, C.; et al. Pharmacokinetics/pharmacodynamics of benralizumab in chronic rhinosinusitis with nasal polyps: Phase III, randomized, placebo-controlled OSTRO trial. *Br. J. Clin. Pharmacol.* **2024**, *90*, 1952–1963. [CrossRef]
 58. Bachert, C.; Han, J.K.; Desrosiers, M.Y.; et al. Efficacy and safety of benralizumab in chronic rhinosinusitis with nasal polyps: A randomized, placebo-controlled trial. *J. Allergy Clin. Immunol.* **2022**, *149*, 1309–1317. [CrossRef]
 59. Russo, D.; Di Filippo, P.; Di Pillo, S.; et al. New Indications of Biological Drugs in Allergic and Immunological Disorders: Beyond Asthma, Urticaria, and Atopic Dermatitis. *Biomedicines* **2023**, *11*, 236. [CrossRef]
 60. Almulhim, R.N.; Alsabhawi, A.H.; Alkhawajah, A.A.; et al. Efficacy of Benralizumab in Paediatric and Adult Populations with Chronic Rhinosinusitis with Nasal Polyps: A Systematic Review and Meta-analysis. *J. Adv. Trends Med. Res.* **2024**, *1*, 409–415.
 61. Tversky, J.; Lane, A.P.; Azar, A. Benralizumab effect on severe chronic rhinosinusitis with nasal polyps (CR-SwNP): A randomized double-blind placebo-controlled trial. *Clin. Exp. Allergy* **2021**, *51*, 836–844. [CrossRef]
 62. De Corso, E.; Mele, D.A.; Rizzi, A.; et al. Sinonasal Outcomes Obtained after 2 Years of Treatment with Benralizumab in Patients with Severe Eosinophilic Asthma and CRSwNP: A “Real-Life” Observational Study. *J. Pers. Med.* **2024**, *14*, 1014. [CrossRef]
 63. De Corso, E.; Bellocchi, G.; De Benedetto, M.; et al. Biologics for severe uncontrolled chronic rhinosinusitis with nasal polyps: a change management approach. Consensus of the Joint Committee of Italian Society of Otorhinolaryngology on biologics in rhinology. *Acta Otorhinolaryngol. Ital.* **2022**, *42*, 1–16. [CrossRef]
 64. ClinicalTrials.gov. Efficacy and Safety Study of Benralizumab in Patient With Eosinophilic Chronic Rhinosinusitis With Nasal Polyps (ORCHID). Available online: <https://clinicaltrials.gov/study/NCT04157335> (accessed on 19 February 2026).
 65. Maspero, J. Reslizumab in the treatment of inadequately controlled asthma in adults and adolescents with elevated blood eosinophils: clinical trial evidence and future prospects. *Ther. Adv. Respir. Dis.* **2017**, *11*, 311–325. [CrossRef]
 66. Gevaert, P.; Lang-Loidolt, D.; Lackner, A.; et al. Nasal IL-5 levels determine the response to anti-IL-5 treatment in patients with nasal polyps. *J. Allergy Clin. Immunol.* **2006**, *118*, 1133–1141. [CrossRef]
 67. Koski, R.R.; Hill, L.; Taavola, K. Efficacy and Safety of Biologics for Chronic Rhinosinusitis With Nasal Polyps. *J. Pharm. Technol.* **2022**, *38*, 289–296. [CrossRef]
 68. Weinstein, S.F.; Katial, R.K.; Bardin, P.; et al. Effects of Reslizumab on Asthma Outcomes in a Subgroup of Eosinophilic Asthma Patients with Self-Reported Chronic Rhinosinusitis with Nasal Polyps. *J. Allergy Clin. Immunol. Pract.* **2019**, *7*, 589–596. [CrossRef]
 69. Lombardi, C.; Comberiati, P.; Ridolo, E.; et al. Anti-IL-5 Pathway Agents in Eosinophilic-Associated Disorders Across the Lifespan. *Drugs* **2024**, *84*, 661–684. [CrossRef]
 70. Tiotiu, A. The current evidence regarding the efficacy of tezepelumab administered for asthma on T2-related comorbidities. *Expert Rev. Respir. Med.* **2026**, *20*, 5–11. [CrossRef]
 71. Pavord, I.D.; Hoyte, F.C.L.; Lindsley, A.W.; et al. Tezepelumab reduces exacerbations across all seasons in patients with severe, uncontrolled asthma (NAVIGATOR). *Ann. Allergy Asthma Immunol.* **2023**, *131*, 587–597.

[CrossRef]

72. Chen, L.; Fan, X.; Yang, L.; et al. Research progress of glucocorticoid resistance in chronic rhinosinusitis with nasal polyps: A review. *Medicine (Baltimore)* **2023**, *102*, e36024. [CrossRef]
73. Lipworth, B.J.; Han, J.K.; Desrosiers, M.; et al. Tezepelumab in Adults with Severe Chronic Rhinosinusitis with Nasal Polyps. *N. Engl. J. Med.* **2025**, *392*, 1178–1188. [CrossRef]
74. Jackson, D.J.; Wechsler, M.E.; Jackson, D.J.; et al. Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype. *N. Engl. J. Med.* **2024**, *391*, 2337–2349. [CrossRef]
75. Jackson, D.J.; Bourdin, A.; Blackorby, A.; et al. Safety and Tolerability of Twice-Yearly Depemokimab in Patients with Asthma and Chronic Rhinosinusitis with Nasal Polyps: Pooled Results from SWIFT-1/-2 and ANCHOR-1/-2. *Adv. Ther.* **2026**, *43*, 880–897. [CrossRef]
76. Gevaert, P.; Desrosiers, M.; Cornet, M.; et al. Efficacy and safety of twice per year depemokimab in chronic rhinosinusitis with nasal polyps (ANCHOR-1 and ANCHOR-2): phase 3, randomised, double-blind, parallel trials. *Lancet* **2025**, *405*, 911–926. [CrossRef]



Copyright © 2026 by the author(s). Published by UK Scientific Publishing Limited. This is an open access article under the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Publisher’s Note: The views, opinions, and information presented in all publications are the sole responsibility of the respective authors and contributors, and do not necessarily reflect the views of UK Scientific Publishing Limited and/or its editors. UK Scientific Publishing Limited and/or its editors hereby disclaim any liability for any harm or damage to individuals or property arising from the implementation of ideas, methods, instructions, or products mentioned in the content.