# Monoclonal Antibodies for the Treatment of Nasal Polyps

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**KEYWORDS**

• Biologics • Chronic rhinosinusitis • Asthma • Nasal polyps • Allergic rhinitis

**KEY POINTS**

- Biologics are emerging therapeutics that can target immunologic pathways significant in inflammatory disorders, such as nasal polyps and asthma.
- Targets currently under investigation include immunoglobulin E modulation; interleukin 4, 5, and 13; and sialic acid–binding immunoglobulin-type lectins.
- Chronic rhinosinusitis with nasal polyps is a multifactorial inflammatory disorder involving multiple cell signaling pathways and multiple endotypes. Biomarkers are needed to define patient selection and maximal impact.

## INTRODUCTION

With the advent of biological therapy, targeted disease and cell-specific therapy have become available for a variety of immune-mediated diseases. These therapeutics derive their utility from being able to intervene directly in dysfunctional immune pathways that remain inaccessible to small molecule–based therapies. Many of these biologics have been initially studied and developed for asthma. The upper airway is often also involved with the lower airway and demonstrates similar pathophysiologic mechanisms lending itself to study and possible concomitant treatment.

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Chronic rhinosinusitis (CRS) is a prevalent disease, affecting 12% to 15% of the general population in the United States.[1–3] Mucosal inflammation of the nasal cavity and paranasal sinuses is the hallmark of the disease, which may manifest in several ways. Symptoms include nasal obstruction, nasal discharge, facial pain/pressure, and reduced/lost smell. The most recent international consensus statement requires that 2 of these symptoms be present along with objective findings including a computed tomography (CT) or endoscopic examination with evidence of inflammation and/or purulence to make a diagnosis.[4] The mainstay of treatment consists of nasal saline irrigations in combination with topical intranasal corticosteroids, oral steroids, and surgery for those patients who fail medical therapy.[4,5] Antibiotic therapy in CRS is controversial; although commonly prescribed, the literature bears little substantive support for use in CRS with the exception of the macrolide class, which may have an antiinflammatory effect in certain populations.[4] A variety of preparations, including topical antibiotics, topical decongestants, and leukotriene receptors antagonists, have been trialed; but evidence to support these therapies to effectively treat CRS is scant.

CRS is commonly divided into 2 subsets, with (CRSsNP) and without (CRSwNP) polyps. Those who have polypoid disease (CRSwNP) with comorbid asthma represent a more severe disease variant.[5,6] When compared with the whole, a subset of CRSwNP demonstrate a poorer therapeutic response, with a higher rate of relapse or recurrence following surgical management and/or medical therapy. Based on a few select studies, the ability to control both subjective and objective outcome parameters in patients with CRS has been reported to range from 38% to 51%.[7,8] The mainstay of postsurgical medical therapy has long been a combination of intranasal topical corticosteroid therapy along with intermittent oral corticosteroid therapy based on examination and symptoms. Because of the inability of oral steroids to control the disease in refractory cases and the risks presented by chronic systemic steroid use, there is an increased need for novel therapies.

The most severe nasal polyp patients have comorbid asthma, which may be adult onset and nonatopic. Individuals with CRSwNP are estimated to have comorbid asthma ranging from 20% to 60%.[9–13] Within this subgroup is a unique subset of patients who exhibit exacerbation of respiratory symptoms in association with exposure to cyclooxygenase-1 inhibition. These patients with aspirin-exacerbated respiratory disease (AERD) comprise an important subset of CRSwNP who exhibit increased disease severity. Additional subgroups include allergic fungal rhinosinusitis and eosinophilic mucin rhinosinusitis (EMRS). The former is characterized by type I hypersensitivity, characteristic findings on CT scan, eosinophilic mucin without invasion, nasal polyposis, and a positive fungal stain.[14] This subtype may be found as a unilateral or bilateral process and generally exhibits fungal debris and polyps. Over time, the disease progression may cause bony remodeling and/or erosion. EMRS, on the other hand, is an inflammatory disease presenting with diffuse bilateral polyps, with the hallmark of thick and tenacious eosinophilic mucin, but without fungal elements on staining and no fungal hypersensitivity.[15]

## PATHOPHYSIOLOGY

CRS is conceptualized as a dysfunctional host response that elicits and propagates uncontrolled inflammation. The interplay between external triggers, modifiers, the innate and adaptive host immune system, anatomic and genetic predisposition likely contributes to the phenotype that is recognized as CRS. At present there is no singular theory that explains the entire range of CRS, which exists on a spectrum of many