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Omalizumab improves sinonasal outcomes in patients with chronic rhinosinusitis with nasal polyps regardless of allergic status

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ABSTRACT

Background: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) often have atopic comorbidities, including elevated IgE levels and comorbid asthma. Omalizumab, an IgE monoclonal antibody, is an effective treatment for CRSwNP, but the impact of allergy or asthma status on response to omalizumab in patients with CRSwNP has not been well studied.

Objective: To evaluate the impact of allergy and asthma status on omalizumab treatment in patients with CRSwNP, this posthoc exploratory analysis assessed sinonasal outcomes from subgroups of patients included in POLYP 1 and POLYP 2 and the open-label extension (OLE) trials.

Methods: Patients (N = 249) were grouped by the presence/absence of comorbid allergy (≥ 1 physician-reported allergic rhinitis, allergic sinusitis, food allergy, or atopic dermatitis), presence/absence of comorbid asthma, baseline serum total IgE (≥ 150 or <150 IU/mL), and baseline blood eosinophil levels (>300 or ≤ 300 cells/μL). Sinonasal outcomes were the nasal polyps score, nasal congestion score, and sino-nasal outcome test-22.

Results: During POLYP 1 and POLYP 2 and the OLE, omalizumab treatment improved the nasal polyps score, nasal congestion score, and sino-nasal outcome test-22 score in patients with/without physician-reported allergic comorbidities, with/without asthma, with higher/lower total IgE levels, and with higher/lower blood eosinophil counts. In the OLE, the pattern of improvement was similar in patients who continued or switched to omalizumab.

Conclusion: In patients with CRSwNP, omalizumab improved sinonasal outcomes independent of allergic status, which suggests that a wide range of patients with different endotypes and phenotypes of CRSwNP may benefit from omalizumab treatment.

Trial Registration: Clinicaltrials.gov Identifier: NCT03280550, NCT03280537, NCT03478930.

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a heterogenous inflammatory condition characterized by persistent sinonasal inflammation, with symptoms including anterior or posterior rhinorrhea, nasal congestion, hyposmia/anosmia, or facial pressure or pain.[1–3] CRSwNP imparts a significant burden on patients and has negative impacts on physical, emotional, and mental quality of life.[4,5] Several type 2 inflammatory mediators are thought to play key roles in the pathogenesis of CRSwNP, including functional specific and polyclonal IgE, eosinophils, and interleukin (IL)-5.[6,7] These pathogenic mechanisms are similar to asthma.[7,8] The frequent co-occurrence of CRSwNP with asthma, allergic rhinitis, food allergy, or atopic dermatitis[2,3,9] is associated with an increased disease burden on patients. For example, patients with allergy have a higher need for nasal polyp revision surgery,[10] and patients with nasal polyps and comorbid asthma have more severe disease, characterized by increased nasal polyp frequency[11] and recurrence,[8] greater rhinosinusitis symptom severity,[11] more poorly controlled asthma,[8] and higher rates of systemic corticosteroid dependence.[8,12]

Patients with CRSwNP may have increased levels of local IgE, IL-5, and eosinophils independent of their allergic status, suggesting that biologic therapies targeting type 2 inflammatory mediators may be effective in both patients with and without allergy. Omalizumab, an anti-IgE monoclonal antibody, is approved for use as an add-on treatment of CRSwNP in adults with inadequate response to nasal corticosteroids.[13,14] In the pivotal, phase 3, placebo-controlled clinical

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trials POLYP 1 and POLYP 2 and the subsequent open-label extension (OLE) trial, omalizumab was efficacious and well tolerated in patients with CRSwNP.[15,16] Although small trials (N = 24 and N = 17) suggest that patients with comorbid asthma gain similar benefits from omalizumab as patients without multimorbidities,[17,18] the impact of markers of allergy or asthma status on response to omalizumab in patients with CRSwNP has not been well studied. To evaluate the impact of allergic status and associated type 2 inflammation on omalizumab treatment in patients with CRSwNP, this posthoc exploratory analysis assessed sinonasal outcomes from subgroups of patients included in the POLYP 1 and POLYP 2 and OLE trials.

Methods

Study Design

The study designs of POLYP 1 (NCT03280550) and POLYP 2 (NCT03280537), replicate phase 3, randomized, multicenter, double-blind, placebo-controlled trials, and the associated OLE trial (NCT03478930), have been described in detail previously.[15,16] Briefly, adults were treated with omalizumab or placebo for 24 weeks followed by open-label omalizumab for an additional 28 weeks (from weeks 24 to 52; OLE omalizumab treatment period); omalizumab was withdrawn at week 52, and patients were observed for an additional 24 weeks (from weeks 52 to 76; OLE off-omalizumab treatment follow-up period). Omalizumab was administered by subcutaneous injection every 2 or 4 weeks, with dose (75-600 mg) determined by serum total IgE level (30-1500 IU/mL) and body weight (30-150 kg) before treatment initiation according to the omalizumab dosing table.[15] Study protocols were approved by the respective institutional review boards and ethics committees. All patients provided written informed consent. The study was conducted in accordance with the International Conference on Harmonization, Good Clinical Practice, the Declaration of Helsinki, and all applicable laws and regulations.

Study Population

Patients with CRSwNP aged 18 to 75 years with inadequate response to intranasal corticosteroids, a nasal polyps score (NPS) of greater than or equal to 5 (with a unilateral score of ≥ 2 for each nostril; score range, 0-4 for each nostril), a nasal congestion score (NCS) (score range, 0-3) of at least 2, and a sino-nasal outcome test-22 (SNOT-22) (score range, 0-110) score of 20 or more at screening were eligible to enroll in POLYP 1 or POLYP 2. Trial eligibility was independent of surgery and systemic corticosteroid treatment history. Patients from POLYP 1 and POLYP 2 (N = 265) were eligible for the OLE when they completed treatment and assessments through 24 weeks, completed daily eDiary assessments for at least 4 of 7 days in the week before the week 24 study visit, and did not experience severe adverse events because of the study drug. Most patients (N = 249) enrolled in the OLE and completed treatment (95.6%; reasons for discontinuation were n = 2 adverse events, n = 6 lack of efficacy, n = 3 withdrawal by the patient), and the treatment-free follow-up (92.8%; reasons for discontinuation were n = 1 lack of efficacy and n = 9 withdrawal by the patient).[16]

Analysis Populations

For this posthoc analysis, patients (N = 249) were grouped according to the treatment received in POLYP 1 and POLYP 2 and then the OLE and were then further divided as follows: (1) by the presence or absence of multimorbid allergy, (2) the presence or absence of comorbid asthma, (3) baseline serum total IgE, and (4) baseline blood eosinophil counts (BECs).

For the comparison of patients with allergy vs without allergy, allergy was defined as having 1 or more of the following physician-reported comorbidities at baseline: (1) allergic rhinitis (n = 104); (2) allergic sinusitis (n = 39); (3) food allergy (n = 11); or (4) atopic dermatitis (n = 1). The 4 groups analyzed were as follows: (1) patients with allergy who received placebo in POLYP 1 and POLYP 2 then omalizumab in the OLE (allergic PBO-OMA [n = 60]); (2) patients with allergy who received omalizumab in POLYP 1 and POLYP 2 and the OLE (allergic OMA-OMA [n = 49]); (3) patients without allergy who received placebo in POLYP 1 and POLYP 2 and omalizumab in the OLE (nonallergic PBO-OMA [n = 66]); and (4) patients without allergy who received omalizumab in POLYP 1 and POLYP 2 and the OLE (nonallergic OMA-OMA [n = 74]). Patients were designated as having asthma when they had a diagnosis of asthma recorded in their medical history; no data on whether diagnosis was allergic or nonallergic was captured. The 4 groups analyzed were the following: (1) asthma PBO-OMA (n = 69); (2) asthma OMA-OMA (n = 73); (3) nonasthmatic PBO-OMA (n = 57); and (4) nonasthmatic OMA-OMA (n = 50). The IgE subgroups were determined by baseline serum total IgE level (≥ 150 or < 150 IU/mL), and the 4 groups analyzed were as follows: (1) IgE greater than or equal to 150 PBO-OMA (n = 51); (2) IgE greater than or equal to 150 OMA-OMA (n = 44); (3) IgE less than 150 PBO-OMA (n = 75); and (4) IgE less than 150 OMA-OMA (n = 79). Eosinophil subgroups were determined by baseline BEC (> 300 or ≤ 300 cells/μL), and the 4 groups analyzed were as follows: (1) BEC greater than 300 PBO-OMA (n = 59); (2) BEC greater than 300 OMA-OMA (n = 53); (3) BEC less than or equal to 300 PBO-OMA (n = 67); and (4) BEC less than or equal to 300 OMA-OMA (n = 69).

Outcomes

The efficacy of omalizumab for CRSwNP in the pooled POLYP 1 and POLYP 2 OLE trial was assessed using 3 measures: (1) the NPS, a physician-scored endoscopic measurement of the number, size, and location of nasal polyps; (2) the NCS, a patient-reported outcome of nasal congestion; and (3) SNOT-22, a patient-reported health-related quality of life (HRQoL) measure that includes aspects of symptoms and treatment response. These end points in the POLYP 1 and POLYP 2 studies and the OLE have been described previously.[15,16]

Statistical Analysis

Adjusted mean change and 95% confidence intervals (CIs) from POLYP 1 and POLYP 2 baseline (randomization) in NPS, NCS, and SNOT-22 were estimated at weeks 4, 8, 16, 24, 36, 52, 64, and 76 on the basis of a mixed-effect model of repeated measures using an unstructured covariance matrix in patients who continued omalizumab and those previously on placebo who switched to omalizumab in the OLE omalizumab treatment period (from weeks 24 to 52). Intergroup *P* values are reported in eTable 1 (*P* values should be interpreted with caution as the study was not designed to test for these differences).

Results

Baseline Characteristics

Baseline patient characteristics were generally similar between the omalizumab and placebo arms for all subgroups of patients (Table 1). Patients with physician-reported allergic comorbidities or with asthma had higher BEC, a higher prevalence of previous sinonasal surgeries, and greater use of systemic corticosteroids. Patients with higher IgE levels had greater levels of eosinophils, and patients with higher BEC had a higher prevalence of systemic corticosteroid use (Table 1).

Table 1
Baseline Characteristics of Patients in the POLYP 1 and POLYP 2 Omalizumab and Placebo Treatment Arms

Characteristic	PBO-OMA Allergic (n = 60)	OMA-OMA Allergic (n = 49)	PBO-OMA Nonallergic (n = 66)	OMA-OMA Nonallergic (n = 74)
Age, mean (SD), y	51.9 (12.1)	47.8 (12.0)	51.4 (11.7)	51.2 (13.6)
Male sex, n (%)	35 (58.3)	32 (65.3)	47 (71.2)	46 (62.2)
Asthma, n (%)	44 (73.3)	36 (73.5)	25 (37.9)	37 (50.0)
Serum total IgE, mean (SD), IU/mL	176.4 (179.3)	191.5 (186.1)	179.6 (171.6)	156.3 (160.6)
Blood eosinophils, mean (SD), cells/μL	422.0 (312.8)	417.3 (294.0)	290.0 (178.9)	267.3 (146.3)
Previous sinonasal surgery, n (%)	44 (73.3)	32 (65.3)	34 (51.5)	37 (50.0)
Systemic corticosteroids past year, n (%)	12 (20.0)	18 (36.7)	11 (16.7)	14 (18.9)
	Asthma (n = 69)	**Asthma (n = 73)**	**Nonasthmatic (n = 57)**	**Nonasthmatic (n = 50)**
Age, mean (SD), y	51.6 (12.5)	48.7 (12.9)	51.7 (11.2)	51.6 (13.3)
Male sex, n (%)	38 (55.1)	39 (53.4)	44 (77.2)	39 (78.0)
Asthma, n (%)	69 (100)	73 (100)	0	0
Serum total IgE, mean (SD), IU/mL	184 (165.4)	186.3 (183.3)	170.5 (186.3)	147.0 (151.4)
Blood eosinophils, mean (SD), cells/μL	418.0 (300.6)	387.4 (239.0)	274.0 (169.4)	241.4 (184.3)
Previous sinonasal surgery, n (%)	52 (75.4)	50 (68.5)	26 (45.6)	19 (38.0)
Systemic corticosteroids past year, n (%)	16 (23.2)	21 (28.8)	7 (12.3)	11 (22.0)
	IgE ≥ 150 (n = 51)	**IgE ≥ 150 (n = 44)**	**IgE < 150 (n = 75)**	**IgE < 150 (n = 79)**
Age, mean (SD), y	52.6 (13.9)	49.1 (13.2)	51.0 (10.3)	50.3 (13.0)
Male sex, n (%)	36 (70.6)	24 (54.5)	46 (61.3)	54 (68.4)
Asthma, n (%)	32 (62.7)	31 (70.5)	37 (49.3)	42 (53.2)
Serum total IgE, mean (SD), IU/mL	332.1 (184.0)	341.5 (186.3)	73.4 (34.1)	75.0 (32.6)
Blood eosinophils, mean (SD), cells/μL	409.2 (327.3)	377.0 (265.5)	314.5 (193.5)	300.6 (203.4)
Previous sinonasal surgery, n (%)	30 (58.8)	23 (52.3)	48 (64.0)	46 (58.2)
Systemic corticosteroids past year, n (%)	9 (17.6)	11 (25.0)	14 (18.7)	21 (26.6)
	BEC > 300 (n = 59)	**BEC > 300 (n = 53)**	**BEC ≤ 300 (n = 67)**	**BEC ≤ 300 (n = 69)**
Age, mean (SD), y	51.4 (12.1)	46.3 (13.8)	51.8 (11.8)	52.6 (12.0)
Male sex, n (%)	35 (59.3)	30 (56.6)	47 (70.1)	48 (69.6)
Asthma, n (%)	42 (71.2)	41 (77.4)	27 (40.3)	31 (44.9)
Serum total IgE, mean (SD), IU/mL	184.5 (182.1)	196.2 (168.5)	172.5 (168.9)	150.0 (173.3)
Blood eosinophils, mean (SD), cells/μL	537.3 (270.5)	511.1 (233.1)	190.4 (76.0)	186.5 (73.2)
Previous sinonasal surgery, n (%)	44 (74.6)	31 (58.5)	34 (50.7)	37 (53.6)
Systemic corticosteroids past year, n (%)	16 (27.1)	19 (35.8)	7 (10.4)	13 (18.8)

Abbreviations: BEC, blood eosinophil count; OLE, open-label extension; OMA, omalizumab; PBO, placebo; POLYP, xxx.
NOTE. The initial treatment refers to the POLYP 1 and POLYP 2 treatment group (PBO or OMA), and the second treatment refers to the treatment in the OLE (all patients were on OMA). Patients were then further divided by (1) the presence or absence of multimorbid allergy (allergic or nonallergic), (2) the presence or absence of comorbid asthma (asthma or nonasthmatic), (3) baseline serum total IgE (IgE ≥150 IU/mL or IgE <150 IU/mL), and (4) baseline blood eosinophil counts (BEC >300 cells/μL or BEC ≤300 cells/μL).

Sinonasal Outcomes

In the POLYP 1 and POLYP 2 periods, all subgroups of patients receiving omalizumab had improvements in NPS, NCS, and SNOT-22 (Figs 1-4). Of note, patients in all omalizumab subgroups had better scores on all 3 measures from weeks 8 to 24 compared with those who received placebo. During the OLE period, omalizumab treatment improved NCS, NPS, and SNOT-22 in patients with or without physician-reported allergic comorbidities (Fig 1), with or without asthma (Fig 2), with higher or lower baseline total IgE levels (Fig 3), and with higher or lower BEC (Fig 4). For each subgroup, the pattern of improvement was similar in patients who continued or switched to omalizumab in the OLE. The change from baseline in the SNOT-22 score during the OLE period was greater than the minimal clinically important difference of 8.9 points in all subgroups.[19] During the follow-up period, improvements in NPS, NCS, and SNOT-22 scores declined but did not return to baseline (Figs 1-4).

Discussion

Given the potential link between CRSwNP, type 2 inflammatory mediators, and allergy-based conditions, it is important to understand how this complexity may impact treatment with omalizumab. In this posthoc analysis of data from the POLYP 1 and POLYP 2 trials and the OLE, omalizumab treatment improved disease burden, including endoscopic findings, a critical patient-reported sinonasal symptom (NCS), and HRQoL (SNOT-22, which includes symptoms and response) for patients with CRSwNP with and without physician-reported allergic comorbidities or asthma and irrespective of baseline total IgE or BEC. Safety results from the overall study populations included in these posthoc analyses have been published previously[15,16] (safety results from the subgroups presented were not evaluated). Therefore, in patients with CRSwNP, omalizumab improved sinonasal outcomes independent of markers of allergic or type 2 immunologic status, which is in line with initial small studies,[17,18] suggesting that anti-IgE treatment may be beneficial for a wide range of patients.

Other biologic treatments have been evaluated in similar subgroups of patients with CRSwNP. Consistent with the findings reported here, phase 3 studies of dupilumab, an antibody inhibitor of IL-4 and IL-13, and mepolizumab, an antibody inhibitor of IL-5, found that end points improved in a broad range of patients with CRSwNP, including those with comorbid allergic conditions and asthma.[20,21] In addition, a small retrospective study of dupilumab in patients with comorbid atopic dermatitis and CRSwNP found improvements in NPS, nasal congestion or obstruction score, SNOT-22, and markers for atopic dermatitis.[22] In contrast, in a phase 3 study of benralizumab, another antibody inhibitor of IL-5, in patients with CRSwNP and asthma, improvements in NPS favored patients with asthma.[23] Fewer studies have explored the effect of baseline IgE and eosinophil levels on response to biologic therapy, despite the recognition of these type 2 inflammatory indicators as potential biomarkers in CRSwNP.[24] In contrast to the results reported here, phase 3 studies of benralizumab and mepolizumab identified a trend toward greater improvements in

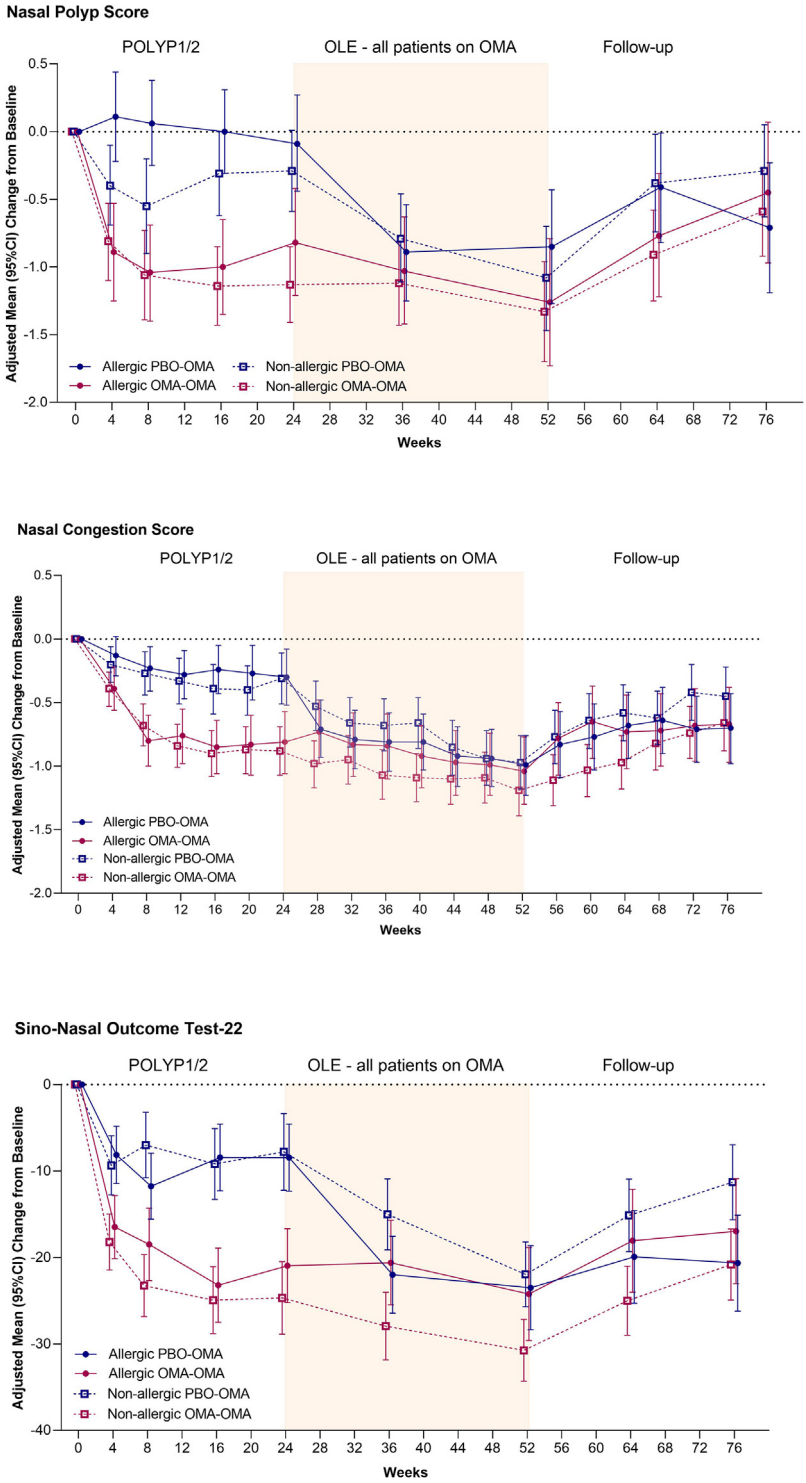

Figure 1. Change from baseline in key outcome measures for patients with allergy/without allergy enrolled in POLYP 1/2 and the OLE. In the POLYP 1 and POLYP 2 periods, all subgroups of patients on OMA had improvements in NPS, NCS, and SNOT-22 (with better scores from weeks 8 to 24 compared with those who received PBO). During the OLE period, OMA treatment improved NCS, NPS, and SNOT-22 in all subgroups of patients. For each subgroup, the pattern of improvement was similar in patients who continued or switched to omalizumab in the OLE. During the follow-up period, improvements in NPS, NCS, and SNOT-22 scores declined but did not return to baseline. Intergroup *P* values are reported in eTable 1. CI, confidence interval; NCS, nasal congestion score; NPS, nasal polyps score; OLE, open-label extension; OMA, omalizumab; PBO, placebo; SNOT-22, sino-nasal outcome test–22.

nasal outcomes relative to placebo in patients with higher eosinophil counts.[20,23]

The pathophysiology of CRSwNP is complex and involves several different pathways and mediators, as described by Gevaert et al.[6] Biologic therapies that interfere with the underlying pathogenic pathways and mediators of CRSwNP may prevent the development of symptoms. For example, omalizumab binds to free IgE, preventing the activation of mast cells and thereby interrupting the release of cytokines and inflammatory mediators.[25] In nasal polyps, the levels of specific and total IgE in the local tissue are associated with eosinophilic inflammation (which may be relevant to pathophysiology),[26] and elevated polyclonal IgE is present regardless of the presence of

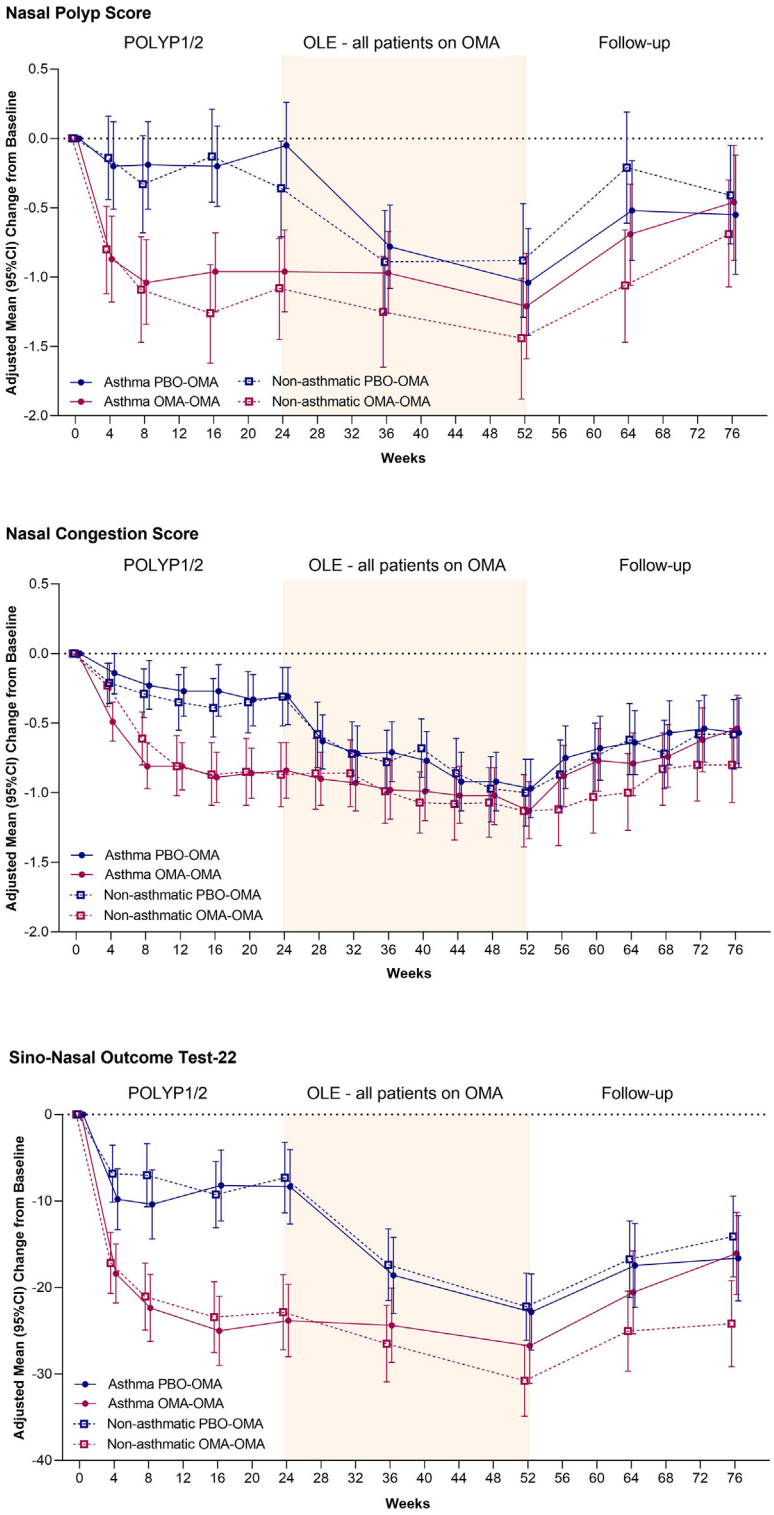

Figure 2. Change from baseline in key outcome measures for patients with and without asthma enrolled in POLYP 1/2 and the OLE. In the POLYP 1 and POLYP 2 periods, all subgroups of patients on OMA had improvements in NPS, NCS, and SNOT-22 (with better scores from weeks 8 to 24 compared with those who received PBO). During the OLE period, OMA treatment improved NCS, NPS, and SNOT-22 in all subgroups of patients. For each subgroup, the pattern of improvement was similar in patients who continued or switched to omalizumab in the OLE. During the follow-up period, improvements in NPS, NCS, and SNOT-22 scores declined but did not return to baseline. Intergroup *P* values are reported in eTable 1. CI, confidence interval; NCS, nasal congestion score; NPS, nasal polyps score; OLE, open-label extension; OMA, omalizumab; PBO, placebo; SNOT-22, sino-nasal outcome test−22.

allergy.[25] But, given that CRSwNP has a similar overall pathophysiology to other allergy-based conditions, treatment with biologics such as omalizumab that interrupt common disease mechanisms has the potential to improve multiple symptoms in people with asthma or comorbid allergic conditions, such as aspirin-exacerbated respiratory disease and atopic dermatitis. This is especially relevant as patients with allergic conditions often experience a high rate of comorbidities and a greater burden of disease.

This analysis has several limitations. In addition to being a posthoc analysis, patient numbers were relatively small, and the

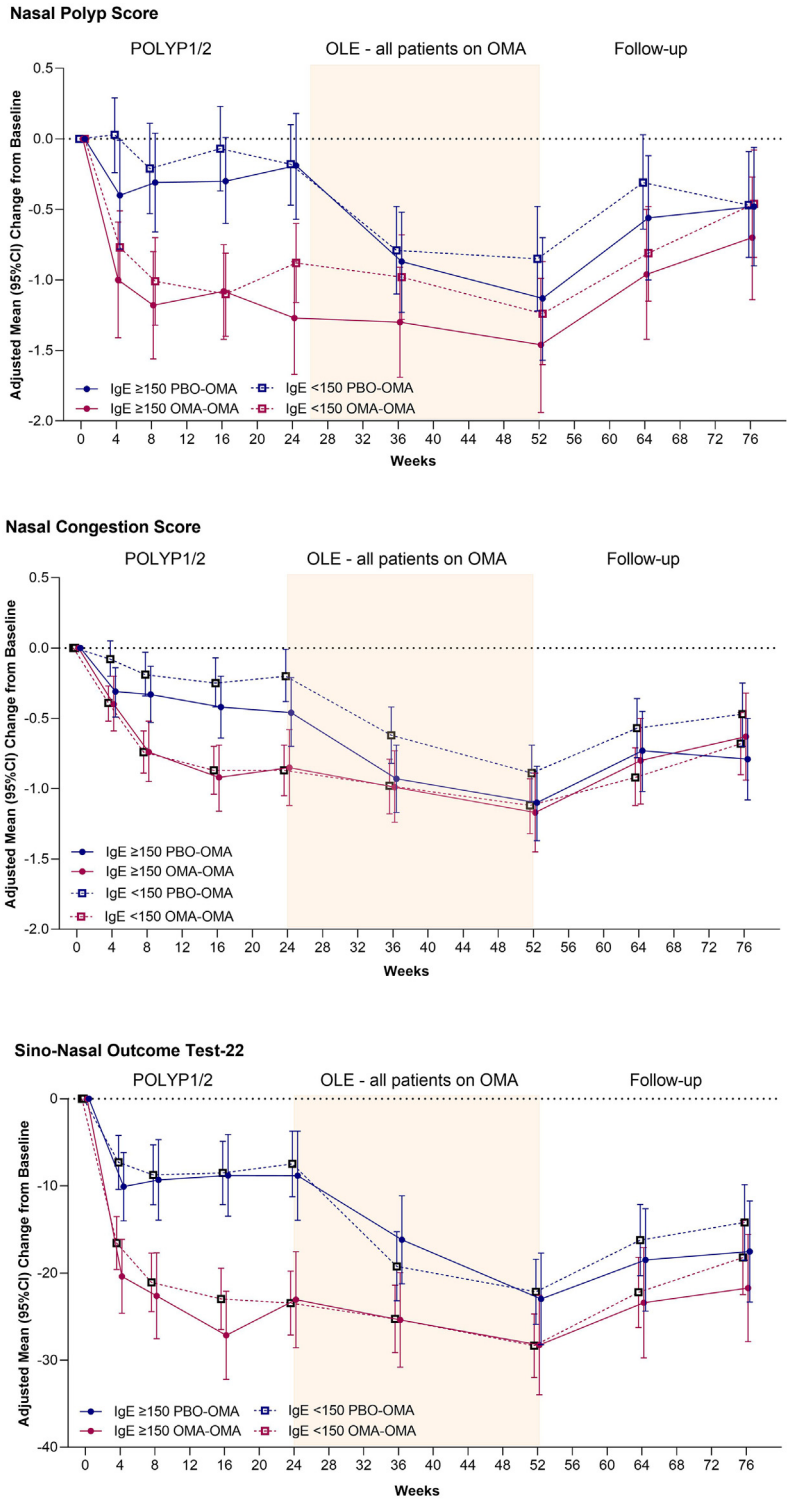

Figure 3. Change from baseline in key outcome measures for patients with baseline serum IgE levels less than 150 or greater than or equal to 150 IU/mL enrolled in POLYP 1/2 and the OLE. In the POLYP 1 and POLYP 2 periods, all subgroups of patients on OMA had improvements in NPS, NCS, and SNOT-22 (with better scores from weeks 8 to 24 compared with those who received PBO). During the OLE period, OMA treatment improved NCS, NPS, and SNOT-22 in all subgroups of patients. For each subgroup, the pattern of improvement was similar in patients who continued or switched to omalizumab in the OLE. During the follow-up period, improvements in NPS, NCS, and SNOT-22 scores declined but did not return to baseline. Intergroup *P* values are reported in eTable 1. CI, confidence interval; NCS, nasal congestion score; NPS, nasal polyps score; OLE, open-label extension; OMA, omalizumab; PBO, placebo; SNOT-22, sino-nasal outcome test–22.

ability to interpret subgroup data may be limited given that omalizumab dosing is on the basis of IgE levels, and the study included a specific population of patients with nasal polyps, but most patients completed the study. Finally, the classification of patients as having asthma or allergy relied on physician-reported diagnoses and were not confirmed clinically, and nor did the study capture whether asthma had an allergic or nonallergic diagnosis.

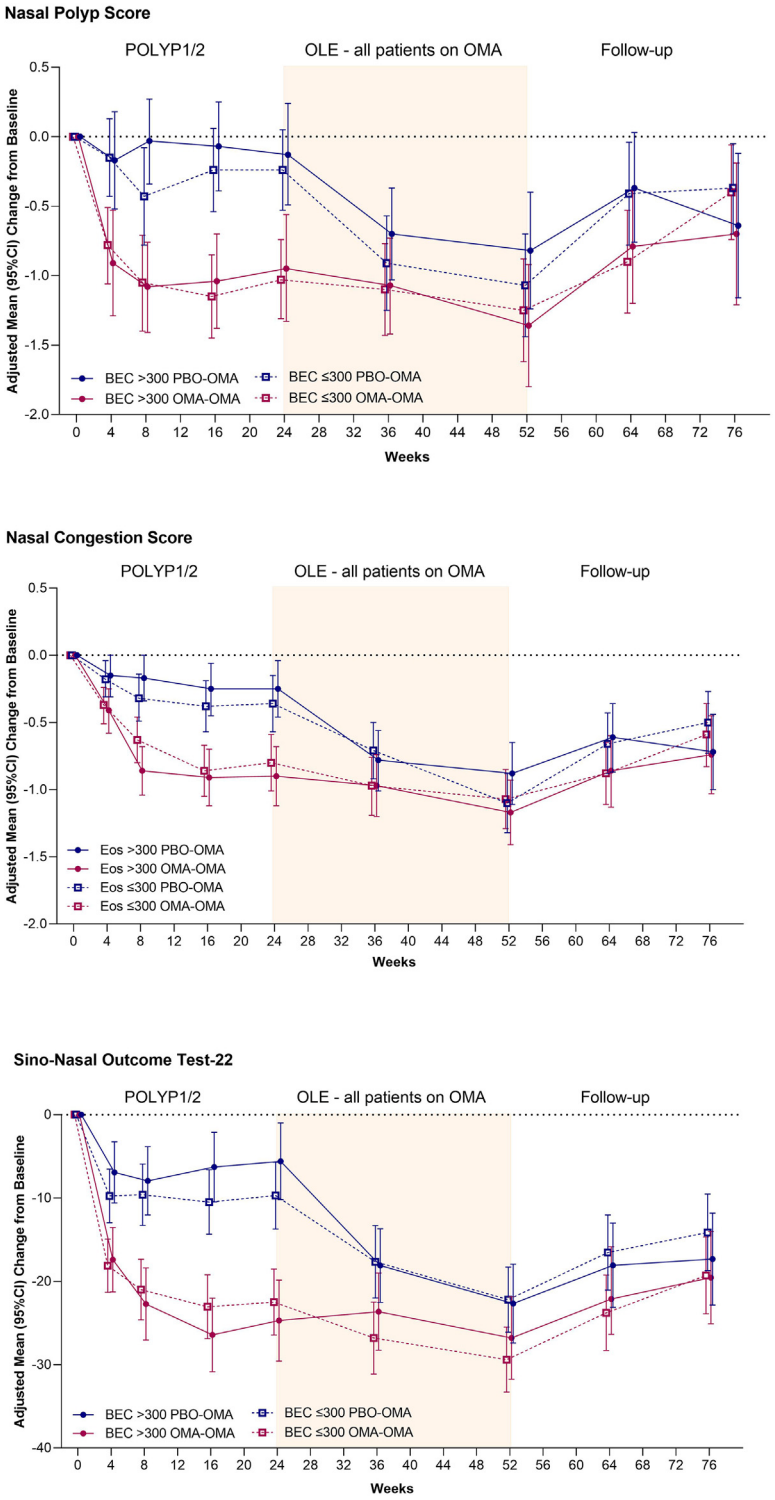

Figure 4. Change from baseline in key outcome measures for patients with BEC less than or equal to 300 or greater than 300 cells/μL enrolled in POLYP 1/2 and the OLE. In the POLYP 1 and POLYP 2 periods, all subgroups of patients on OMA had improvements in NPS, NCS, and SNOT-22 (with better scores from weeks 8 to 24 compared with those who received PBO). During the OLE period, OMA treatment improved NCS, NPS, and SNOT-22 in all subgroups of patients. For each subgroup, the pattern of improvement was similar in patients who continued or switched to omalizumab in the OLE. During the follow-up period, improvements in NPS, NCS, and SNOT-22 scores declined but did not return to baseline. Intergroup *P* values are reported in eTable 1. BEC, baseline serum eosinophils; CI, confidence interval; NCS, nasal congestion score; NPS, nasal polyps score; OLE, open-label extension; OMA, omalizumab; PBO, placebo; SNOT-22, sino-nasal outcome test–22.

In conclusion, long-term treatment with omalizumab improved chronic rhinosinusitis symptoms, nasal polyp outcomes, and sinonasal-related HRQoL for patients with nasal polyps independent of multimorbid allergies or asthma and IgE or BEC. Thus, a wider range of patients with different endotypes and phenotypes of CRSwNP may benefit from omalizumab treatment. Furthermore, given the common pathophysiology of CRSwNP and allergy-based diseases, omalizumab may not only improve sinonasal symptoms but also improve the symptoms of comorbid conditions.

Data availability

Qualified researchers may request access to individual patient-level data through the clinical study data request platform (https://vivli.org/). Further details on Roche's criteria for eligible studies are available here (https://vivli.org/members/ourmembers/). For further details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here (https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm).

Disclosures

Dr Gevaert is a speaker and advisory board member for ALK-Abello, Argenx, AstraZeneca, Genentech, Inc, Hal Allergy, Novartis, Regeneron, Roche, Sanofi, and Stallergenes. Dr Mullol has received research grants from AstraZeneca, Genentech, Inc, GlaxoSmithKline, NOUCOR/Uriach Group, Novartis, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, and Viatris; has received consulting fees from NOUCOR/Uriach Group and Sanofi Genzyme; and has attended speaker bureaus and/or advisory boards for AstraZeneca, Genentech, Inc, GlaxoSmithKline, Glenmark, Menarini, Mitsubishi-Tanabe, Merck Sharp & Dohme, NOUCOR/Uriach Group, Novartis, Procter & Gamble, Regeneron, Sanofi Genzyme, UCB Pharma, and Viatris. Dr Saenz, Dr Ko, Dr Steinke, and Dr Milllette are employees of Genentech, Inc, and stockholders in Roche. Dr Meltzer is a consultant/advisory board member for ALK-Abello, AstraZeneca, Axdev, Bristol Myers Squibb, Church & Dwight, Genentech, Inc, GlaxoSmithKline, Glenmark, Gossamer Bio, Hikma, Merck, Novartis, Principia, and Regeneron/Sanofi Genzyme and a speaker for ALK-Abello, GlaxoSmithKline, Glenmark, Merck, Optinose, and Regeneron/Sanofi Genzyme.

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.anai.2023.11.001.

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Supplementary Data

eTable 1
Intergroup *P* Values, Omalizumab Vs Placebo

Nasal Congestion Score		
Week	**Allergic**	**Nonallergic**
Week 4	0.0313	0.0591
Week 8	<0.0001	0.0010
Week 16	<0.0001	0.0003
Week 24	0.0026	0.0001
Week 36	0.8337	0.0071
Week 52	0.8167	0.1369
Week 64	0.7956	0.0112
Week 76	0.8935	0.1822
	Asthma	**Nonasthmatic**
Week 4	0.0007	0.8961
Week 8	<0.0001	0.0144
Week 16	<0.0001	0.0028
Week 24	0.0004	0.0006
Week 36	0.0733	0.2091
Week 52	0.2914	0.4720
Week 64	0.3395	0.0479
Week 76	0.8556	0.2384
	IgE ≥ 150	**IgE < 150**
Week 4	0.5426	0.0006
Week 8	0.0092	<0.0001
Week 16	0.0027	<0.0001
Week 24	0.0354	<0.0001
Week 36	0.7481	0.0115
Week 52	0.7384	0.1044
Week 64	0.7415	0.0223
Week 76	0.4723	0.2022
	BEC > 300	**BEC ≤ 300**
Week 4	0.0255	0.0483
Week 8	<0.0001	0.0134
Week 16	<0.0001	0.0006
Week 24	<0.0001	0.0039
Week 36	0.2530	0.0876
Week 52	0.0876	0.8744
Week 64	0.1858	0.1699
Week 76	0.9383	0.5862

Nasal Polyp Score		
Week	**Allergic**	**Nonallergic**
Week 4	<0.0001	0.0474
Week 8	<0.0001	0.0357
Week 16	<0.0001	0.0002
Week 24	0.0080	<0.0001
Week 36	0.6277	0.1439
Week 52	0.1972	0.3615
Week 64	0.2526	0.0350
Week 76	0.4743	0.2030
	Asthma	**Nonasthmatic**
Week 4	0.0032	0.0030
Week 8	0.0002	0.0047
Week 16	0.0003	<0.0001
Week 24	<0.0001	0.0052
Week 36	0.3865	0.1888
Week 52	0.5218	0.0661
Week 64	0.5044	0.0036
Week 76	0.7748	0.2926
	IgE ≥ 150	**IgE < 150**
Week 4	0.0379	<0.0001
Week 8	0.0013	0.0005
Week 16	0.0009	<0.0001
Week 24	0.0002	0.0007
Week 36	0.1147	0.3835
Week 52	0.3133	0.1480
Week 64	0.2128	0.0364
Week 76	0.4584	0.9806
	BEC > 300	**BEC ≤ 300**
Week 4	0.0054	0.0017
Week 8	<0.0001	0.0143
Week 16	<0.0001	<0.0001
Week 24	0.0027	0.0002
Week 36	0.1252	0.4336
Week 52	0.0845	0.5049
Week 64	0.1375	0.0620
Week 76	0.8749	0.9002

SNOT-22		
Week	**Allergic**	**Nonallergic**
Week 4	0.0012	0.0003
Week 8	0.0208	<0.0001
Week 16	<0.0001	<0.0001
Week 24	<0.0001	<0.0001
Week 36	0.6771	<0.0001
Week 52	0.8415	0.0011
Week 64	0.6466	0.0010
Week 76	0.3775	0.0020
	Asthma	**Nonasthmatic**
Week 4	0.0007	<0.0001
Week 8	<0.0001	<0.0001
Week 16	<0.0001	<0.0001
Week 24	<0.0001	<0.0001
Week 36	0.0666	0.0036
Week 52	0.2149	0.0035
Week 64	0.3707	0.0118
Week 76	0.8713	0.0044
	IgE ≥ 150	**IgE < 150**
Week 4	0.0007	<0.0001
Week 8	0.0002	<0.0001
Week 16	<0.0001	<0.0001
Week 24	0.0004	<0.0001
Week 36	0.0168	0.0336
Week 52	0.1829	0.0209
Week 64	0.2665	0.0417
Week 76	0.3327	0.1941
	BEC > 300	**BEC ≤ 300**
Week 4	0.0002	0.0004
Week 8	<0.0001	<0.0001
Week 16	<0.0001	<0.0001
Week 24	<0.0001	<0.0001
Week 36	0.0904	0.0038
Week 52	0.2358	0.0113
Week 64	0.4131	0.0275
Week 76	0.5750	0.1197

Abbreviations: BEC, blood eosinophil count; SNOT-22, sino-nasal outcome test−22.
NOTE. that *P* values should be interpreted with caution as the study was not designed to test for these differences. In addition, please note that the omalizumab vs placebo comparison is most appropriate from week 0 to week 24, when patients were in these treatment arms. From after week 24 all patients were on omalizumab: comparison between omalizumab and placebo refers to their original treatment arm and has been included to reveal any potential carry-over effects.