Omalizumab Improves Outcomes in Patients With Chronic Rhinosinusitis With Nasal Polyps Irrespective of Asthma Status

Claus Bachert,[1,2] Philippe Gevaert,[1] Jonathan Corren,[3] Joaquim Mullol,[4] Joseph K. Han,[5] Randall Ow,[6] Sanna Toppila-Salmi,[7,8] Isam Alobid,[4,9] Bongin Yoo,[10] Monet Howard,[10] Rui Zhu,[10] Monica Ligueros-Saylan,[11] Kit Wong,[10] Lutaf Islam,[12] Theodore A. Omachi[10]

[1]Upper Airway Research Laboratory, Department of Otorhinolaryngology, Ghent University Hospital, Ghent, Belgium; [2]Division of ENT Diseases, CLINTEC, Karolinska Institute, University of Stockholm, Sweden; [3]Departments of Medicine and Pediatrics, David Geffen School of Medicine at the University of California Los Angeles, Los Angeles, CA, USA; [4]Hospital Clinic, IDIBAPS, Universitat de Barcelona, CIBERES, Barcelona, Catalonia, Spain; [5]Eastern Virginia Medical School, Norfolk, VA, USA; [6]Sacramento Ear, Nose and Throat Surgical and Medical Group, Inc, Sacramento, CA, USA; [7]Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland; [8]Haartman Institute, University of Helsinki, Helsinki, Finland; [9]Centro Medico Teknon, Barcelona, Spain; [10]Genentech, Inc., South San Francisco, CA, USA; [11]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [12]Roche, Welwyn Garden City, UK

Background

- Chronic rhinosinusitis with nasal polyps (CRSwNP) and asthma share underlying T2 inflammation involving immunoglobulin E (IgE) antibody production.[1]
- Due to this shared etiology, CRSwNP and asthma frequently coexist and present with a more severe, treatment-resistant phenotype.[2,3]
- Although the anti-IgE monoclonal antibody, omalizumab, has demonstrated efficacy in patients with CRSwNP with comorbid asthma,[4] whether there is a difference between patients with and without comorbid asthma is an important remaining question.

Objective

- To determine if there is a difference in response to omalizumab in patients with severe CRSwNP with and without comorbid asthma.

Methods

- Subgroup analysis of pooled data from Phase III, placebo-controlled, 24-week trials of omalizumab (POLYP 1 [NCT03280550] and POLYP 2 [NCT03280537]) in patients with CRSwNP with and without comorbid asthma.
- POLYP 1 and POLYP 2 consisted of a 5-week run-in period, followed by a 24-week treatment period and a 4-week safety follow-up period.
  - During the run-in period, all patients were treated with intranasal mometasone (200 µg twice daily [BID], or once daily [QD] in patients unable to tolerate higher doses).
- Adult patients with corticosteroid-refractory CRSwNP were enrolled in POLYP 1 and POLYP 2 if they had:
  - Severe nasal polyps, ie, Nasal Polyp Score (NPS) ≥5 (NPS ≥2 for each nostril) at screening and end of run-in, and Nasal Congestion Score (NCS) ≥2 at first screening visit and weekly average NCS >1 at randomization
  - Sino-Nasal Outcome Test-22 (SNOT-22) score ≥20 at baseline
  - Body weight between 30 and 150 kg and serum IgE level between 30 and 1,500 IU/mL for omalizumab dosing of 75–600 mg every 2 weeks or every 4 weeks.
- Patients receiving background intranasal mometasone (≥200 µg QD [or equivalent] for ≥1 month before screening and ≥200 µg BID or QD during run-in) were randomized 1:1 to omalizumab or placebo for the 24-week double-blind treatment period.

Endpoint Assessments

- NPS was determined by nasal endoscopy at screening and randomization and at Weeks 4, 8, 16, and 24 (score range, 0 [no nasal polyps] to 4 [large nasal polyps reaching the floor of the nasal cavity]; total NPS=0–8).
- Daily NCS was calculated as a 7-day prior average of NCS daily scores. Patients completed an NCS assessment every morning (on a daily basis) via an eDiary throughout the study (score range, 0 [not at all] to 3 [severe congestion]).
- SNOT-22 was determined as the total score of 22 CRSwNP-related symptoms at screening and baseline (randomization) and at Weeks 4, 8, 16, and 24 (score range, 1–5 for each symptom; higher scores indicate worse CRSwNP-related quality of life; total SNOT-22 score=0–110).

Statistical Analyses

- A mixed-effect model for repeated measurement with unstructured covariance matrix was used to estimate the placebo-adjusted change from baseline at Week 24 and its associated 95% CI and *P* value for NPS, NCS, and SNOT-22.
- Placebo-adjusted changes were calculated from baseline at Week 24 for NPS, NCS, and SNOT-22 scores among patients with CRSwNP with and without comorbid asthma, and the pooled population.
- Corrections for multiple comparisons were not made.

Results

Baseline Demographics and Clinical Characteristics

- Demographic and NP severity factors were generally similar when comparing populations with versus without asthma, although a greater percentage of patients with asthma than without asthma were female (**Table**).
- Blood eosinophils, prior systemic steroid usage, and prior NP surgery were numerically higher in patients with asthma than without asthma.

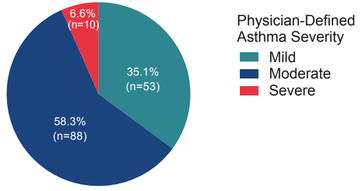
Table. Baseline Demographics and Clinical Characteristics in Patients With CRSwNP With and Without Comorbid Asthma From the Pooled Population of POLYP 1 and POLYP 2

Characteristic	With Comorbid Asthma n=151 (57.0%)	Without Comorbid Asthma n=114 (43.0%)
Age, y, mean (SD)	49.6 (12.9)	51.9 (12.0)
Female, n (%)	69 (45.7)	25 (21.9)
NPS (score, 0–8), mean (SD)	6.1 (1.0)	6.4 (0.9)
NCS (score, 0–3), mean (SD)	2.4 (0.7)	2.3 (0.6)
SNOT-22 (score, 0–110), mean (SD)	61.9 (17.6)	57.1 (19.2)
AQLQ (score, 0–6), mean (SD)	4.9 (1.3)	NA
UPSIT (score, 0–40), mean (SD)	11.7 (5.8)	15.0 (9.0)
IgE, IU/mL, mean (SD)	186.8 (173.7)	159.2 (168.8)
Blood eosinophils, cells/µL, mean (SD)	399.7 (268.6)	262.8 (174.9)
Patients with systemic steroid use in past year, n (%)	40 (26.5)	19 (16.7)
Patients with prior NP surgery, n (%)	109 (72.2)	49 (43.0)
Patients with planned dose Q4W, n (%)	135 (89.4)	100 (87.7)
Physician-assessed asthma severity, n (%)		
Mild	53 (35.1)	NA
Moderate	88 (58.3)	NA
Severe	10 (6.6)	NA

AQLQ, Asthma Quality of Life Questionnaire; CRSwNP, chronic rhinosinusitis with nasal polyps; IgE, immunoglobulin E; NA, not applicable; NCS, Nasal Congestion Score; NP, nasal polyps; NPS, Nasal Polyp Score; Q4W, every 4 weeks; SNOT-22, Sino-Nasal Outcome Test-22; UPSIT, University of Pennsylvania Smell Identification Test.

- 57.0% (151/265) of patients in the pooled population from POLYP 1 and POLYP 2 had comorbid asthma.
- Physician-assessed asthma severity was typically mild or moderate (**Figure 1**).

Figure 1. Physician-Defined Asthma Severity in Patients With CRSwNP With Comorbid Asthma



CRSwNP, chronic rhinosinusitis with nasal polyps.

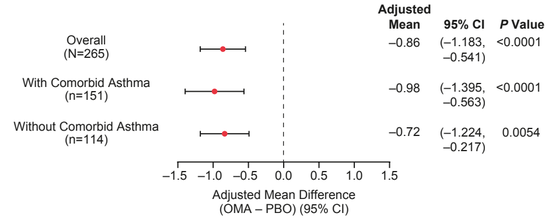
Improvements in Nasal Polyps Following Omalizumab Initiation

- Improvements from baseline at Week 24 were significantly greater for omalizumab- versus placebo-treated patients across all 3 endpoints in the pooled population (**Figures 2–4**).

Nasal Polyp Score

- In the pooled population, improvements in NPS from baseline at Week 24 were greater for omalizumab- versus placebo-treated patients.
- Improvements in NPS were similar in patients with CRSwNP with versus without comorbid asthma (**Figure 2**).

Figure 2. Placebo-Adjusted Effect of Omalizumab on Change From Baseline at Week 24 in NPS in Patients With CRSwNP With and Without Comorbid Asthma

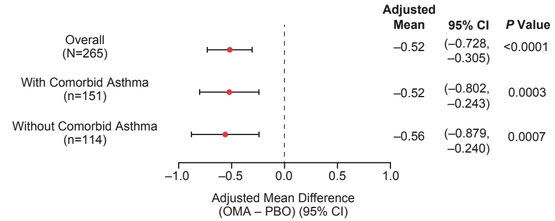


CRSwNP, chronic rhinosinusitis with nasal polyps; NPS, Nasal Polyp Score; OMA, omalizumab; PBO, placebo.

Nasal Congestion Score

- In the pooled population, improvements in NCS from baseline at Week 24 were greater for omalizumab- versus placebo-treated patients.
- Improvements in NCS were similar in patients with CRSwNP with versus without comorbid asthma (**Figure 3**).

Figure 3. Placebo-Adjusted Effect of Omalizumab on Change From Baseline at Week 24 in NCS in Patients With CRSwNP With and Without Comorbid Asthma

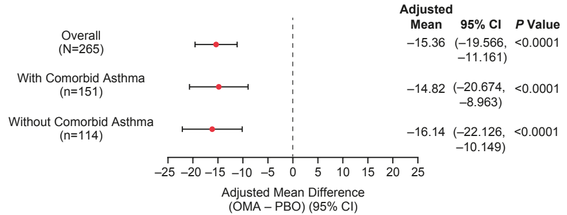


CRSwNP, chronic rhinosinusitis with nasal polyps; NCS, Nasal Congestion Score; OMA, omalizumab; PBO, placebo.

SNOT-22 Score

- In the pooled population, improvements in SNOT-22 score from baseline at Week 24 were greater for omalizumab- versus placebo-treated patients.
- Improvements in SNOT-22 score were similar in patients with CRSwNP with versus without comorbid asthma (**Figure 4**).

Figure 4. Placebo-Adjusted Effect of Omalizumab on Change From Baseline at Week 24 in SNOT-22 Score in Patients With CRSwNP With and Without Comorbid Asthma



CRSwNP, chronic rhinosinusitis with nasal polyps; SNOT-22, Sino-Nasal Outcome Test-22; OMA, omalizumab; PBO, placebo.

Safety

- Safety results from the overall study population have been presented previously in Gevaert et al (2019).[5] No new safety signals were identified.

Limitations

- As most patients had mild-to-moderate asthma, it is unclear whether these results extend to the more severe asthma population.

Conclusions

- Omalizumab improved NPS, NCS, and SNOT-22 scores above placebo in patients with CRSwNP with and without comorbid asthma.
- There were no marked differences in response between patients with CRSwNP with asthma and those without comorbid asthma.
- Mean improvements in SNOT-22 score in the overall population and in patients with CRSwNP with and without comorbid asthma exceeded the minimal clinically important difference of 8.9 points,[6] indicating a clinically relevant response.

References 1. Humbert M, et al. *J Allergy Clin Immunol Pract.* 2019;7:1418–29. 2. Ceylan E, et al. *Respirology.* 2007;12:272–6. 3. Ryu G, et al. *Allergy Asthma Immunol Res.* 2019;11:664–76. 4. Bidder T, et al. *Rhinology.* 2018;56:42–5. 5. Gevaert P, et al. *Ann Allergy Asthma Immunol.* 2019;123:S17. 6. Chowdhury NI, et al. *Int Forum Allergy Rhinol.* 2017;7:1149–55.

Disclosures **CB:** speaker and advisory board member for ALK, ASIT Biotech, AstraZeneca, GlaxoSmithKline, Mylan, Novartis, Sanofi, and Stallergenes. **PG:** speaker and advisory board member for Ablynx, ALK, Argenx, Genentech, Inc., Hal Allergy, Novartis, Regeneron, Roche, Sanofi, and Stallergenes. **JC:** consultant for AstraZeneca, Genentech, Inc., Novartis, Regeneron, and Sanofi; speaker bureau for AstraZeneca and Genentech, Inc.; grants to institution from Genentech, Inc., Regeneron, and Sanofi. **JM:** speaker, advisory board member, and research grants from ALK-Abelló, AstraZeneca, Genentech, Inc., GlaxoSmithKline, Menarini, Mitsubishi-Tanabe, MSD, Mylan, Novartis, Sanofi-Genzyme/Regeneron, and Uriach Group. **JKH:** advisory board for Sanofi-Genzyme/Regeneron; investigator for Amgen, AstraZeneca, GlaxoSmithKline, Novartis, and Sanofi-Genzyme/Regeneron. **RO:** speaker/consultant for Optinose; consultant for Stryker, Tusker Medical, and Vigilant Technologies; advisory board for AstraZeneca and Genentech, Inc. **ST-S:** consultant for ERT, Novartis, and Sanofi; grants from GlaxoSmithKline. **IA:** speaker and advisory board member for GlaxoSmithKline, Menarini, MSD, Mylan, and Novartis. **BY, RZ, KW:** employees of Genentech, Inc. **MH, LI:** employees of Roche. **ML-S:** employee of Novartis.

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