PRS2

Proportion of Patients With Nasal Polyposis Achieving Clinically Important Improvements in Quality of Life With Omalizumab Treatment

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Background

- Chronic rhinosinusitis with nasal polyps (CRSwNP) is associated with adult-onset asthma, significant morbidity, and substantial quality of life (QoL) impairment.[1-5]
- Nasal polyps are benign lesions of the nasal mucosa that affect ~4% of the population and have been associated with nasal obstruction, loss of smell, rhinorrhea, postnasal drip, and facial pain.[6]
- The Sino-Nasal Outcome Test-22 (SNOT-22) questionnaire is a validated, self-administered instrument used to evaluate the impact of rhinologic disease, including CRSwNP, on QoL over 4 domains (nasal, otological, sleep, psychological).[7,8]
  - Each of the 22 items on the questionnaire is scored from 0 (no problem) to 5 (problem as bad as it can be), with higher scores indicating greater impairment, for a maximum total score of 110.[7]
  - The previously validated minimal clinically important difference (MCID) for the SNOT-22 questionnaire is an ≥8.9-point reduction.[9]

Objective

- To examine the effect on QoL, according to SNOT-22 total score, in patients with CRSwNP receiving omalizumab versus placebo in 2 replicate Phase III, randomized, placebo-controlled omalizumab studies, POLYP 1 (NCT03280550) and POLYP 2 (NCT03280537).

Methods

- Post hoc analyses of data from POLYP 1 (n=138) and POLYP 2 (n=127) were performed.
  - Patient data from POLYP 1 and POLYP 2 were pooled for analysis, as similar trends were observed in unpooled data.
- Outcome measures included:
  - The adjusted mean change in SNOT-22 total score from baseline (95% CI) at Weeks 4, 8, 16, and 24
  - The proportion of patients achieving the MCID of ≥8.9-point reduction in SNOT-22 total score.[9]
- The change from baseline SNOT-22 repeated outcome was analyzed using a mixed-effect model with repeated measures (MMRM) approach, with Weeks 4, 8, 16, and 24 as response variables with an unstructured covariance matrix.
- The SNOT-22 MCID repeated binary outcome was analyzed using a generalized binary regression (using generalized estimating equations), which included the odds of achieving SNOT-22 MCID at Weeks 4, 8, 16, and 24 as response variables with an unstructured working correlation matrix.
- Model-based mean difference from MMRM (95% CI) and model-based odds ratios (95% CI) at each study week were estimated after adjusting for study (POLYP 1/POLYP 2), baseline SNOT-22 total score, geographic region, and asthma/aspirin sensitivity.

Results

Baseline Characteristics

- Baseline demographic and clinical characteristics for the pooled population from POLYP 1 and POLYP 2 are outlined in the **Table**.
  - Baseline mean (SD) SNOT-22 total scores were similar for omalizumab-treated (59.5 [20.0]; n=134) and placebo-treated (60.1 [16.7]; n=131) patients.

Efficacy

- Omalizumab-treated patients observed clinically meaningful improvement in adjusted mean SNOT-22 total score from baseline as early as 4 weeks after initiating therapy (all *P*<0.0001; **Figure 1**).
- Omalizumab-treated patients were more likely than placebo-treated patients to achieve MCID in SNOT-22 at all time points; **Figure 2**).
- A greater percentage of patients who received omalizumab achieved the MCID in SNOT-22 total score compared with those who received placebo at all time points (**Figure 2**).

Safety

- The safety profile was consistent with the known safety profile of omalizumab; no new safety signals were identified.
- Safety results have been presented previously.[10]

Limitations

- The present analysis was post hoc in nature and is subject to all inherent limitations.

Conclusions

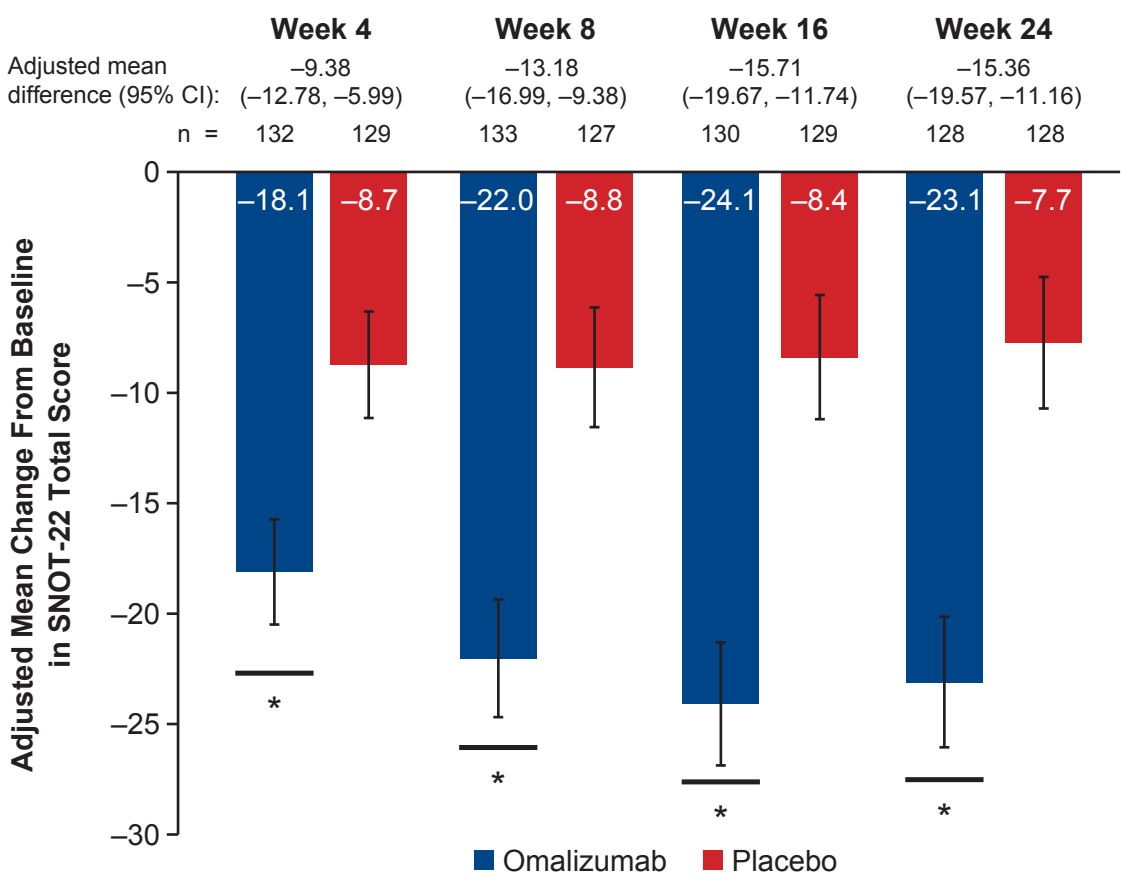
- Pooled patients from the replicate Phase III, randomized, placebo-controlled omalizumab studies, POLYP 1 and POLYP 2, who received omalizumab therapy for CRSwNP achieved clinically meaningful improvements in mean SNOT-22 total scores at all assessment time points of this post hoc analysis.
  - At each time point, the MCID of a ≥8.9-point reduction in average SNOT-22 score was reached by the omalizumab group, but not by the placebo group.
- A greater proportion of patients receiving omalizumab met the MCID compared with those in the placebo group at all time points.
- Together, these results indicate that omalizumab therapy is capable of providing meaningful improvements in QoL for patients with CRSwNP after as little as 4 weeks of therapy, with lasting improvements up to the final measurement at 24 weeks.

Table. Baseline Demographics and Clinical Characteristics

Characteristic	Placebo n=131	Omalizumab n=134
Age, y, mean (SD)	51.6 (11.8)	49.6 (13.3)
Male, n (%)	85 (64.9)	86 (64.2)
Race, n (%)		
White	131 (100)	126 (94.0)
Black or African American	0 (0.0)	2 (1.5)
Other/unknown	0 (0.0)	6 (4.5)
BMI, kg/m^2, mean (SD)	27.9 (5.1)	27.1 (4.4)
NPS, mean (SD)	6.2 (0.9)	6.3 (1.0)
7-day average NCS, mean (SD)	2.4 (0.6)	2.3 (0.7)
SNOT-22 score, mean (SD)	60.1 (16.7)	59.5 (20.0)
SCS in 12 months before screening, n (%)	23 (17.6)	36 (26.9)

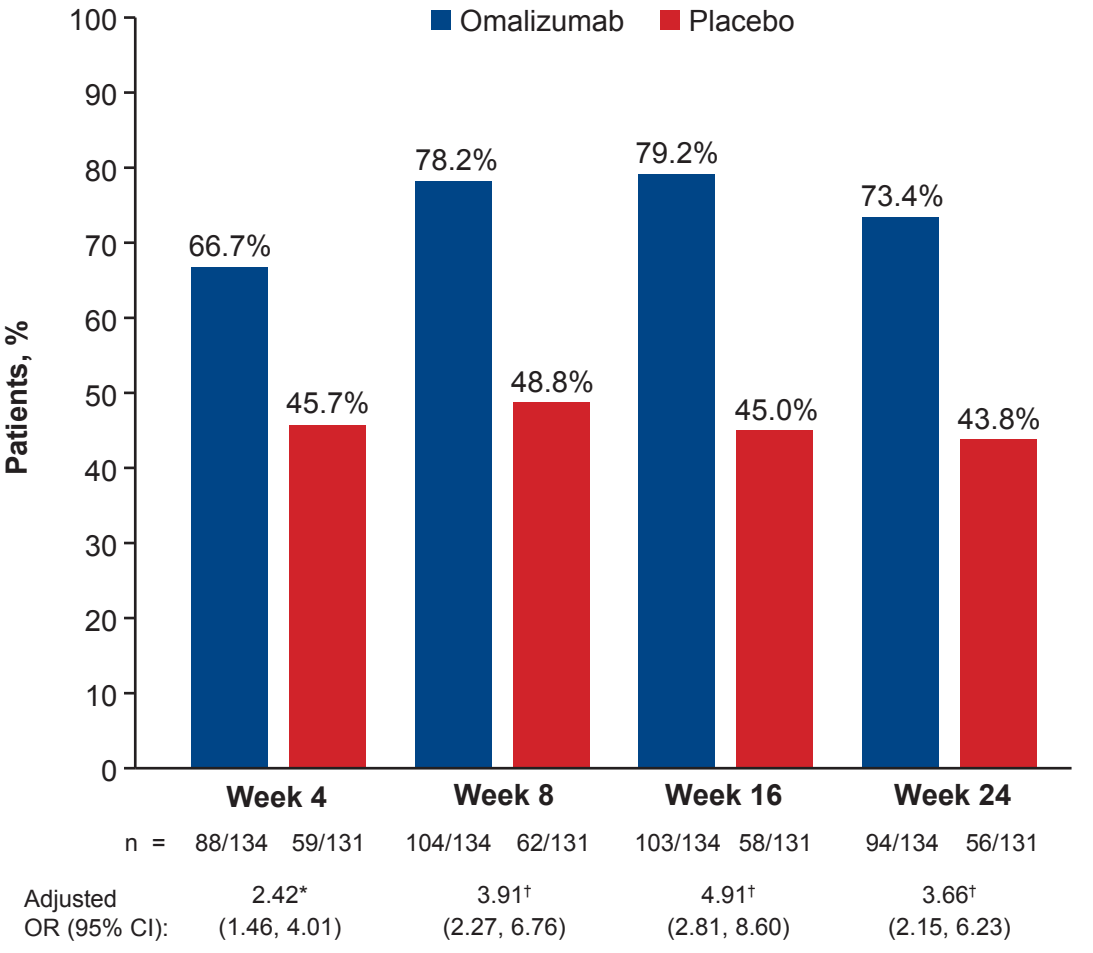
BMI, body mass index; NCS, Nasal Congestion Score; NPS, Nasal Polyp Score; SCS, systemic corticosteroids; SNOT-22, Sino-Nasal Outcome Test-22.

Figure 1. Adjusted Mean Change From Baseline in SNOT-22 Total Score in Patients Receiving Omalizumab Versus Placebo



SNOT-22, Sino-Nasal Outcome Test-22.
**P*<0.0001. Error bars represent 95% CI.

Figure 2. Percentage of Patients Achieving MCID (≥8.9-Point Reduction in SNOT-22 Total Score)



MCID, minimal clinically important difference; OR, odds ratio; SNOT-22, Sino-Nasal Outcome Test-22.
**P*=0.0006.
†*P*<0.0001.

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Disclosures **SEL:** investigator and advisory board for AstraZeneca, Genentech, Inc., GlaxoSmithKline, Regeneron, and Sanofi; **BY, RS, LAM, YR:** employees of Genentech, Inc.; **JB:** employee of Roche.

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