The Impact of Omalizumab Therapy on Sleep in Patients With Nasal Polyps

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Introduction

- Chronic rhinosinusitis with nasal polyps (CRSwNP), sometimes referred to as nasal polyposis, is a common condition affecting up to 4% of the US population in which patients exhibit anterior and posterior rhinorrhea, nasal obstruction, loss of smell, and facial pain/pressure lasting for ≥12 weeks.[1,2]
- According to patients, symptoms vary throughout the day, frequently worsening at night.[3]
- Patients with nasal polyposis exhibit a 2-fold higher risk of sleep disturbance compared with healthy controls.[4]
  - Sleep disturbance, a common complaint in patients with CRSwNP, often drives patients to seek more intense disease management.
- The anti–immunoglobulin E (IgE), omalizumab, has demonstrated efficacy in patients with CRSwNP in the POLYP 1 and POLYP 2 trials, though its specific impact on sleep outcomes is not well described.[5]

Objective

- To examine the impact of omalizumab on sleep in patients with CRSwNP and understand the benefits beyond rhinological symptoms.

Methods

- The randomized, placebo-controlled POLYP 1 and POLYP 2 trials examined the efficacy of omalizumab plus background intranasal corticosteroids in patients with CRSwNP through 24 weeks.
- This prespecified exploratory analysis evaluated patient-reported sleep outcomes from the POLYP 1 and POLYP 2 open-label extension (OLE; NCT03478930).
- In the OLE, patients in the placebo arm of the original studies switched to omalizumab (n=126), while those in the omalizumab arm continued therapy from Weeks 24 through 52 (n=123). At Week 52, treatment for all patients was discontinued through Week 76.
- Efficacy was assessed using the Medical Outcomes Study (MOS) Sleep Scale and the sleep subdomain of the Sino-Nasal Outcome Test-22 (SNOT-22).
- The sleep subdomain of SNOT-22 is composed of questions 11–18 of the SNOT-22 questionnaire, which examine the ability to fall asleep and stay asleep throughout the night, morning/daytime fatigue, and reduced concentration and productivity, and frustration, with a score range of 0–40.[6] For SNOT-22 subdomains, higher scores indicate greater disease severity.
  - SNOT-22 sleep subdomain data were collected for both the placebo and omalizumab arms from screening through POLYP 1 and POLYP 2 and the OLE.
  - Mean change from baseline (randomization) was estimated based on a mixed-effect model of repeated measures using an unstructured covariance matrix.
- The MOS Sleep Scale, which was not assessed in POLYP 1 and POLYP 2, examined patient-reported symptoms over the previous 4 weeks, including sleep disturbance (score range, 0–100), snoring (0–100), shortness of breath (0–100), somnolence (0–100), sleep adequacy (0–100), and sleep quantity (0–24).
  - Higher scores indicated better sleep adequacy and quantity, and lower scores showed better outcomes for other elements of the MOS.
  - Sleep Problems Index I/II are abbreviated indices of 6/9 distinct aspects of sleep quality, respectively, including sleep disturbance, somnolence, adequacy, and awakening with shortness of breath.
  - Change from Week 24 (baseline) at Weeks 36, 52, 64, and 76 was analyzed for omalizumab-naïve patients who switched from placebo to omalizumab for the OLE.
- Due to the exploratory nature of these endpoints, formal statistical testing was not performed.

Results

- Baseline characteristics of the patients who completed the OLE were generally comparable between omalizumab and placebo arms of POLYP 1 and POLYP 2 (**Table 1**).

Table 1. Baseline Demographics and Characteristics

Characteristic	POLYP 1 and POLYP 2 Treatment: Placebo n=126	POLYP 1 and POLYP 2 Treatment: Omalizumab n=123
Age, y, mean (SD)	51.6 (11.9)	49.9 (13.1)
Male, n (%)	82 (65.1)	78 (63.4)
Patients with asthma, n (%)	69 (54.8)	73 (59.3)
Previous sinonasal surgery, n (%)	78 (61.9)	69 (56.1)
SCS use in past year, n (%)	23 (18.3)	32 (26.0)
SNOT-22 sleep subdomain (range, 0–40), mean (SD)	21.13 (8.28)	21.31 (9.51)
MOS Sleep Scale, mean (SD)*		
Sleep disturbance	36.81 (22.15)	—
Snoring	47.25 (32.19)	—
Shortness of breath	25.97 (25.88)	—
Sleep Problems Index I	37.12 (18.23)	—
Sleep Problems Index II	37.83 (18.06)	—
Somnolence	30.81 (19.60)	—
Sleep adequacy	49.35 (23.92)	—
Sleep quantity	6.67 (1.17)	—

MOS, Medical Outcomes Study; OLE, open-label extension; SCS, systemic corticosteroids; SNOT-22, Sino-Nasal Outcome Test-22. *MOS Sleep Scale was not collected during POLYP 1 and POLYP 2. Baseline data reflect Week 24 (OLE baseline) scores of patients who previously received placebo.

- In POLYP 1 and POLYP 2 (pooled for analysis), significant improvements in the SNOT-22 sleep subdomain were observed in patients who received omalizumab versus placebo from baseline through Week 24 (**Table 2; Figure 1**).
- At Week 24, all patients received omalizumab therapy through Week 52 during the POLYP 1 and POLYP 2 OLE. Patients who previously received placebo demonstrated rapid mean improvements in the SNOT-22 sleep subdomain while receiving omalizumab. Patients who received omalizumab during POLYP 1 and POLYP 2 showed continued improvement through Week 52.
- At Week 52, all patients discontinued omalizumab therapy through Week 76 of the POLYP 1 and POLYP 2 OLE. Improvements in the SNOT-22 sleep subdomain waned, though benefits over baseline remained at final follow-up.
- Mean (95% CI) improvements in MOS from Weeks 24–52 were observed in sleep disturbance, snoring, sleep adequacy, and Sleep Problems Index I/II, with the greatest improvements in shortness of breath. Minimal to no improvements were observed in somnolence and sleep quantity (**Table 3**).
- Beneficial effects in MOS waned upon therapy discontinuation after Week 52, but remained over baseline and Week 76 of the OLE (**Figure 2**).

Safety

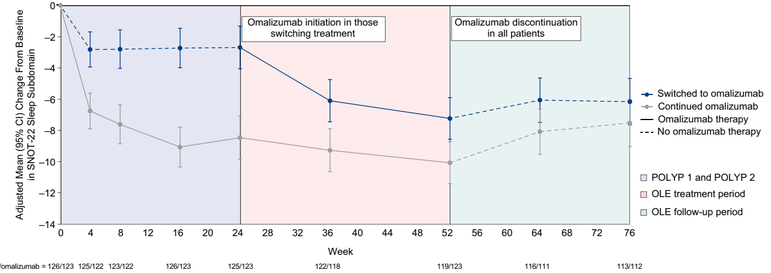
- Overall safety data on the POLYP 1 and POLYP 2 studies have been previously reported.[5] Safety findings from the OLE have also been previously presented[7] and were consistent with the original POLYP 1 and POLYP 2 studies.

Table 2. Adjusted Mean (95% CI) Change From POLYP 1 and POLYP 2 Baseline in SNOT-22 Sleep Subdomain Scores (Score Range, 0–40) in Omalizumab vs Placebo Arms From POLYP 1 and POLYP 2

		Placebo n=126	Omalizumab n=123
POLYP 1 and POLYP 2 Studies	Week 4	−3.33 (−4.38, −2.29)	−7.08 (−8.14, −6.02)
	Week 8	−3.37 (−4.54, −2.20)	−8.26 (−9.44, −7.08)
	Week 16	−3.48 (−4.70, −2.25)	−9.73 (−10.97, −8.49)
OLE Treatment Period	Week 24	−3.49 (−4.82, −2.16)	−9.31 (−10.65, −7.96)
	Week 36	−7.08 (−8.38, −5.79)	−9.81 (−11.12, −8.49)
	Week 52	−8.19 (−9.45, −6.92)	−10.54 (−11.83, −9.24)
OLE Follow-up Period	Week 64	−6.61 (−7.97, −5.26)	−8.60 (−9.98, −7.22)
	Week 76	−6.78 (−8.17, −5.38)	−7.98 (−9.38, −6.57)

OLE, open-label extension; SNOT-22, Sino-Nasal Outcome Test-22.

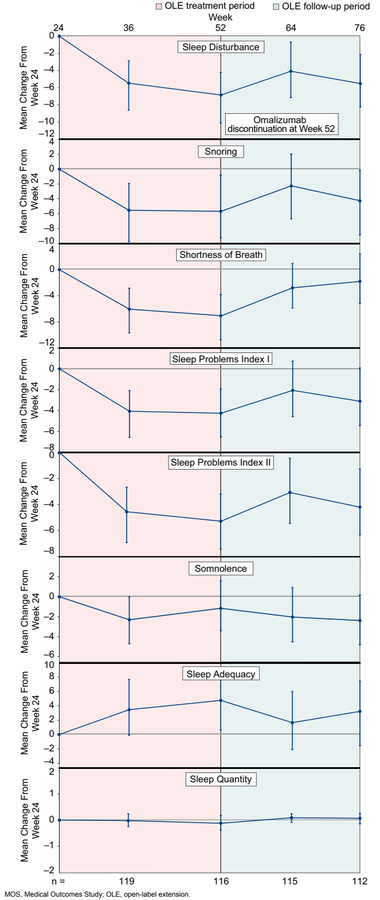
Figure 1. Mean Change From POLYP 1 and POLYP 2 Baseline in SNOT-22 Sleep Subdomain Scores in Omalizumab (n=123) vs Placebo (n=126) Arms From POLYP 1 and POLYP 2



n placebo/omalizumab = 126/123 125/122 123/122 126/123 125/123 122/118 119/123 116/111 113/112

OLE, open-label extension; SNOT-22, Sino-Nasal Outcome Test-22.

Figure 2. Mean (95% CI) Change From Week 24 (OLE Baseline) in MOS Sleep Scale Factors in Omalizumab-Naïve Patients (n=126)



MOS, Medical Outcomes Study; OLE, open-label extension.

Table 3. Mean (95% CI) Change From Week 24 (OLE Baseline) in MOS Sleep Scale Factors in Omalizumab-Naïve Patients

Mean (95% CI) Change From Week 24	OLE Treatment Period: Week 36 n=119	OLE Treatment Period: Week 52 n=116	OLE Follow-up Period: Week 64 n=115	OLE Follow-up Period: Week 76 n=112
Sleep Disturbance (Score Range, 0–100)	−5.47 (−8.62, −2.88)	−6.85 (−10.11, −4.24)	−4.08 (−7.15, −0.70)	−5.52 (−8.25, −2.14)
Snoring (Score Range, 0–100)	−5.55 (−9.77, −1.92)	−5.69 (−9.26, −0.82)	−2.26 (−6.70, 2.04)	−4.29 (−8.87, −0.18)
Shortness of Breath (Score Range, 0–100)	−6.05 (−9.69, −2.83)	−7.07 (−10.74, −3.82)	−2.78 (−5.88, 0.95)	−1.79 (−5.17, 2.41)
Sleep Problems Index I (Score Range, 0–100)	−4.06 (−6.56, −2.08)	−4.25 (−6.51, −1.92)	−2.06 (−4.59, 0.73)	−3.10 (−5.42, 0.08)
Sleep Problems Index II (Score Range, 0–100)	−4.56 (−6.95, −2.66)	−5.29 (−7.45, −3.19)	−3.07 (−5.47, −0.41)	−4.20 (−6.34, −1.26)
Somnolence (Score Range, 0–100)	−2.30 (−4.71, −0.01)	−1.15 (−3.39, 1.61)	−2.03 (−4.53, 0.92)	−2.38 (−4.79, 0.18)
Sleep Adequacy* (Score Range, 0–100)	3.45 (−0.10, 7.67)	4.74 (0.63, 8.19)	1.65 (−2.08, 5.97)	3.21 (−1.53, 7.42)
Sleep Quantity* (Score Range, 0–24)	−0.02 (−0.25, 0.24)	−0.12 (−0.38, 0.18)	0.09 (−0.09, 0.24)	0.07 (−0.14, 0.25)

MOS, Medical Outcomes Study; OLE, open-label extension. *Lower scores indicate a greater disease severity for sleep adequacy and quantity.

Conclusions

- Sleep improvements were observed in patients with CRSwNP following omalizumab therapy, as measured by both the SNOT-22 sleep subdomain and MOS Sleep Scale.
- Improvements were generally maintained throughout treatment, and waned following omalizumab discontinuation, though improvements from pretreatment levels remained at Week 76.
- Patients who received omalizumab in POLYP 1 and POLYP 2 and the OLE experienced sleep improvements across multiple measures, suggesting that omalizumab can provide value beyond rhinological symptoms in patients with CRSwNP.
- The present study suggests that omalizumab offers benefit for sleep disturbance for nasal polyposis, which is one of the most bothersome patient-reported symptoms of the disease.[4]

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