# Sustained Clinical Benefits in Patients With Chronic Rhinosinusitis With Nasal Polyps 24 Weeks Post-mepolizumab Treatment

**Poster No. P213**

Desrosiers M[1], Diamant Z[2], Castelnuovo P[3], Hellings PW[2], Han JK[4], Silver J[5], Gevaert P[6], Peters AT[7]

[1]Faculté de Médecine, Université de Montréal, Montreal, Canada; [2]Department of Microbiology Immunology & Transplantation, KU Leuven, Catholic University of Leuven, Leuven, Belgium; [3]Department of Otolaryngology Head & Neck Surgery, Ospedale di Circolo ASST Settelaghi Varese, Italy; [4]Division of Rhinology and Endoscopic Sinus-Skull Base Surgery & Division of Allergy, Eastern Virginia Medical School, VA, USA; [5]US Medical Affairs Respiratory, GSK, Research Triangle Park, NC, USA; [6]Upper Airways Research Laboratory, Department of Otorhinolaryngology, Ghent University, Ghent, Belgium; [7]Division of Allergy-Immunology, Northwestern University, Chicago, Illinois, USA

## Introduction

- Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) experience a range of symptoms including nasal blockage, facial pain/pressure, and loss of smell, which negatively affect health-related quality of life.[1]
- Standard of care treatment for CRSwNP includes intranasal corticosteroids, short courses of systemic corticosteroids, and sinus surgery; patients with severe CRSwNP frequently need repeat surgeries.[1,2]
- Mepolizumab, a humanized monoclonal antibody that targets interleukin-5, is approved for the treatment of several eosinophil-driven diseases, including CRSwNP, in multiple regions worldwide.[3–5]
- SYNAPSE, a Phase III study in patients with severe CRSwNP, demonstrated significantly improved NP size, sinonasal symptoms, and disease-specific quality of life with 52 weeks of 4-weekly mepolizumab 100 mg treatment compared with placebo. Reductions in sinus surgery and SCS use were also observed with mepolizumab versus placebo. However, the durability of clinical improvements following mepolizumab treatment cessation has not yet been reported.[6]
- Here, we present outcomes during the 24-week treatment-free follow-up period in patients who continued in the SYNAPSE study following the 52-week treatment period.

## Methods

### Study design (GSK ID: 205687/NCT03085797)

Randomized
Double-blind
Placebo-controlled
Parallel-group
Phase III study

**Patient eligibility criteria**

- ≥18 years of age
- ≥1 prior* surgery†
- Need for surgery‡
- Bilateral NP diagnosis
- Nasal obstruction VAS score >5
- No current or former smokers (>6 months)
- No SCS use <4 weeks before screening
- No biologic/immunosuppressant treatment
- No pre-existing clinically significant conditions that are uncontrolled with standard treatment


**Assessments**

**Total NP score**
Assessed endoscopically; blinded and centrally read
Scored using a 0–8 scale (score of 0–4 per nostril)
Larger score indicates greater disease severity

**VAS score**
Patients completed six individual VAS questions using a daily eDiary, with a 24-hour recall period
Scored using a 0–10 scale. Meaningful within-patient changes:
- ≥3-point decrease in nasal obstruction and loss of smell[7]
- ≥2.5-point decrease[7] in overall sinonasal symptoms

Larger scores indicate greater symptom severity

**SNOT-22 score**
Patients completed 22 questions every 4 weeks, with a 2-week recall period
Scored overall using a 0–110 scale (score of 0–5 per question)
MCID: 8.9 points[8]
Larger scores indicate worse HRQoL

**Sinus surgery**
At each visit, it was recorded whether the patient had undergone sinus surgery‡

**SCS use**
At each visit, it was recorded whether the patient had required a course of SCS

**Blood eosinophil count**
Absolute blood eosinophil count was determined from peripheral blood samples

**Analyses in the follow-up population**

- **Mean change from baseline to Week 76 in total endoscopic NP score**
- **Mean change from baseline to Weeks 73–76 in nasal obstruction VAS score**
- **Mean change from baseline to Week 76 in SNOT-22 total score**
- **Time to first sinus surgery up to Week 76**
- **Time to first SCS use up to Week 76 (post hoc)**
- **Blood eosinophil count up to Week 76**

*Within the last 10 years; †defined as any incision of the paranasal sinuses and removal of polyp tissue from the nasal cavity and sinuses; ‡defined as overall VAS symptom score >7 and an endoscopic bilateral NP score ≥5 (with a minimum score of 2 per nasal cavity).

## Results

### Figure 1. Patients included in the follow-up analysis (Weeks 52–76)

From the ITT population of 407 patients:

**134 patients**
entered follow-up after Week 52
(placebo: N=65; mepolizumab: N=69)

Mean (SD) time in follow-up after Week 52: **5.40 (0.5) months**

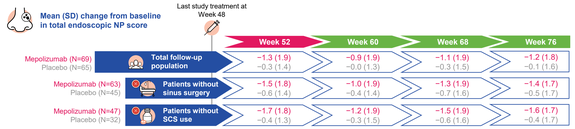
Post hoc subgroup analyses of NP and VAS scores:

**108 patients with no sinus surgeries*** during SYNAPSE
(placebo: n=45; mepolizumab: n=63)

**79 patients with no SCS use for NP†** during SYNAPSE
(placebo: n=32; mepolizumab: n=47)

*Since methodology dictated that patients with sinus surgery during SYNAPSE had their worst observed total endoscopic NP and VAS scores carried forward; †to assess the impact of mepolizumab in the absence of SCS.

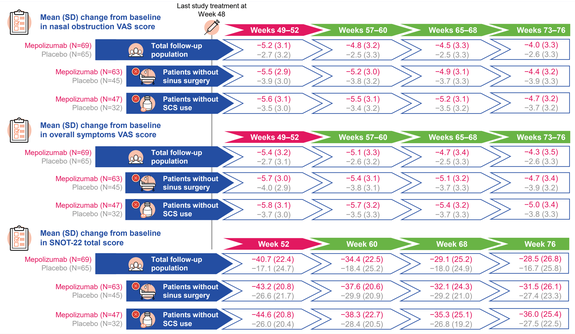
### Figure 2. Larger improvements from baseline in nasal polyp size persisted throughout the off-treatment follow-up period with mepolizumab versus placebo




| | | Week 52 | Week 60 | Week 68 | Week 76 |
|---|---|---|---|---|---|
| Mepolizumab (N=69) | Total follow-up population | −1.3 (1.9) | −0.9 (1.9) | −1.1 (1.9) | −1.2 (1.8) |
| Placebo (N=65) | | −0.3 (1.4) | −0.0 (1.3) | −0.3 (1.5) | −0.1 (1.6) |
| Mepolizumab (N=63) | Patients without sinus surgery | −1.5 (1.8) | −1.0 (1.9) | −1.3 (1.9) | −1.4 (1.7) |
| Placebo (N=45) | | −0.6 (1.4) | −0.4 (1.4) | −0.7 (1.6) | −0.5 (1.7) |
| Mepolizumab (N=47) | Patients without SCS use | −1.7 (1.8) | −1.2 (1.9) | −1.5 (1.9) | −1.6 (1.7) |
| Placebo (N=32) | | −0.4 (1.3) | −0.3 (1.5) | −0.6 (1.6) | −0.4 (1.7) |

Larger decreases in NP score indicate larger improvements in disease severity. Patients who withdrew from the study or had missing visit data were assigned their worst observed score prior to the missing visit.

### Figure 3. Larger improvements from baseline in patient-reported sinonasal symptoms and quality of life persisted throughout the off-treatment follow-up period with mepolizumab versus placebo



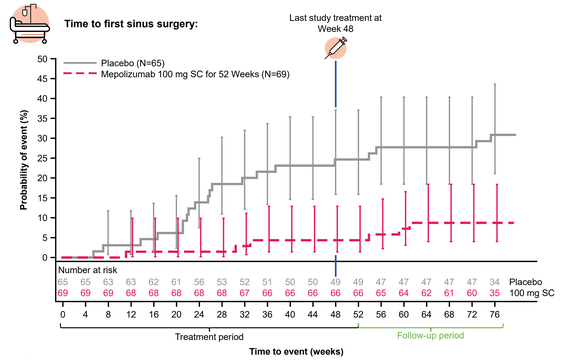

| | | Weeks 49–52 | Weeks 57–60 | Weeks 65–68 | Weeks 73–76 |
|---|---|---|---|---|---|
| Mepolizumab (N=69) | Total follow-up population | −5.2 (3.1) | −4.8 (3.2) | −4.5 (3.3) | −4.0 (3.3) |
| Placebo (N=65) | | −2.7 (3.2) | −2.5 (3.3) | −2.5 (3.3) | −2.6 (3.3) |
| Mepolizumab (N=63) | Patients without sinus surgery | −5.5 (2.9) | −5.2 (3.0) | −4.9 (3.1) | −4.4 (3.2) |
| Placebo (N=45) | | −3.9 (3.0) | −3.8 (3.2) | −3.7 (3.3) | −3.9 (3.3) |
| Mepolizumab (N=47) | Patients without SCS use | −5.6 (3.1) | −5.5 (3.1) | −5.2 (3.1) | −4.7 (3.2) |
| Placebo (N=32) | | −3.5 (3.0) | −3.4 (3.2) | −3.5 (3.2) | −3.7 (3.2) |

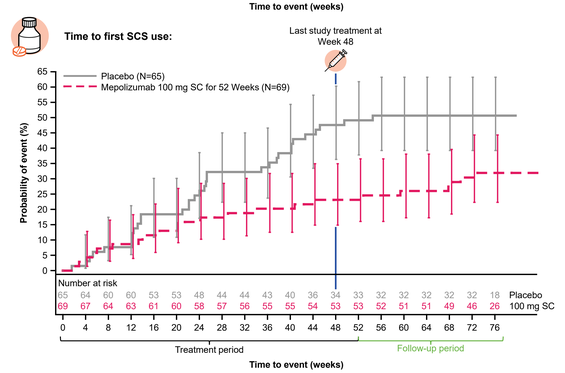
| | | Weeks 49–52 | Weeks 57–60 | Weeks 65–68 | Weeks 73–76 |
|---|---|---|---|---|---|
| Mepolizumab (N=69) | Total follow-up population | −5.4 (3.2) | −5.1 (3.3) | −4.7 (3.4) | −4.3 (3.5) |
| Placebo (N=65) | | −2.7 (3.1) | −2.6 (3.2) | −2.5 (3.3) | −2.6 (3.3) |
| Mepolizumab (N=63) | Patients without sinus surgery | −5.7 (3.0) | −5.4 (3.1) | −5.1 (3.2) | −4.7 (3.4) |
| Placebo (N=45) | | −4.0 (2.9) | −3.8 (3.1) | −3.7 (3.3) | −3.9 (3.2) |
| Mepolizumab (N=47) | Patients without SCS use | −5.8 (3.1) | −5.7 (3.2) | −5.4 (3.2) | −5.0 (3.4) |
| Placebo (N=32) | | −3.7 (3.0) | −3.5 (3.3) | −3.7 (3.3) | −3.8 (3.3) |

| | | Week 52 | Week 60 | Week 68 | Week 76 |
|---|---|---|---|---|---|
| Mepolizumab (N=69) | Total follow-up population | −40.7 (22.4) | −34.4 (22.5) | −29.1 (25.2) | −28.5 (26.8) |
| Placebo (N=65) | | −17.1 (24.7) | −18.4 (25.2) | −18.0 (24.9) | −16.7 (25.8) |
| Mepolizumab (N=63) | Patients without sinus surgery | −43.2 (20.8) | −37.6 (20.6) | −32.1 (24.3) | −31.5 (26.1) |
| Placebo (N=45) | | −26.6 (21.7) | −29.9 (20.9) | −29.2 (21.0) | −27.4 (23.3) |
| Mepolizumab (N=47) | Patients without SCS use | −44.6 (20.8) | −38.3 (22.7) | −35.3 (25.1) | −36.0 (25.4) |
| Placebo (N=32) | | −26.0 (20.4) | −28.4 (20.5) | −26.8 (19.2) | −27.5 (22.5) |

Larger reductions in VAS/SNOT-22 score indicate larger improvements in disease severity/disease-specific quality of life. Patients who withdrew from the study or had missing visit data were assigned their worst observed score prior to the missing visit.

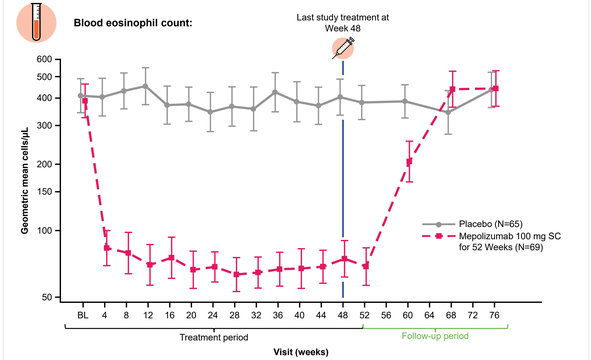
### Figure 4. The risk of sinus surgery and SCS use remained lower with mepolizumab versus placebo throughout the follow-up period




Kaplan-Meier estimates of time-to-first sinus surgery and SCS use up to Week 76. Vertical bars represent 95% CIs.

### Figure 5. In mepolizumab-treated patients, blood eosinophil counts returned to baseline levels by Week 68 (16 weeks after treatment cessation)




For blood eosinophil counts of 0, the log transformation was based on a value of 0.005. Vertical bars represent 95% CIs.

## Conclusions

- Although clinical improvements with mepolizumab versus placebo were most notable with continuous treatment, several important clinical benefits persisted in patients with severe CRSwNP 24 weeks after mepolizumab cessation, despite blood eosinophil counts returning to baseline levels. These included:
  - Reduced NP size and nasal obstruction
  - Improved overall sinonasal symptoms and disease-specific quality of life
  - A reduced risk of sinus surgery and SCS use
- Patients who did not require SCS during SYNAPSE had the most durable clinical response to mepolizumab in the follow-up population; this may be indicative of less severe disease or a unique disease phenotype
- The observation of a sustained clinical response despite a return to baseline blood eosinophil counts is suggestive of disease modification and warrants further research
- These findings suggest that mepolizumab has a durable positive impact in patients with severe CRSwNP and should be considered by clinicians when addressing real-world challenges with their patients, such as determining an appropriate biologic therapy/treatment schedule and assessing treatment adherence


### References

1. Fokkens WJ, et al. *Rhinology* 2020;58(Suppl S29):1–464.
2. DeConde AS, et al. *Laryngoscope* 2017;127:550–5.
3. EMA. Mepolizumab summary of product characteristics. 2020. Available from: https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf [last accessed September 2022].
4. FDA. Mepolizumab prescribing information. 2022. Available from: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL-IFU-COMBINED.PDF [last accessed September 2022].
5. GSK. Mepolizumab prescribing information, Japan. 2022. Available from: https://gskpro.com/ja-jp/products-info/nucala/index/ [last accessed September 2022].
6. Han JK, et al. *Lancet Respir Med* 2021;9(10):1141–53.
7. Tabberer M, et al. *JACI* 2021;147(2, Supplement):AB126.
8. Hopkins C, et al. *Clin Otolaryngol* 2009;34(5):447–54.


### Abbreviations

BL, baseline; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; HRQoL, health-related quality of life; ITT, intention-to-treat; log, logarithmic; MCID, meaningful clinically important difference; MF, mometasone furoate; NP, nasal polyps; SC, subcutaneous; SCS, systemic corticosteroids; SD, standard deviation; SNOT, Sino-Nasal Outcome Test; VAS, visual analog scale.


### Disclosures

This study was funded by GSK (GSK ID: 205687).

On behalf of all authors, and with their permission, an audio recording of this poster was prepared by Martin Desrosiers, who did not receive any payment for this recording.

**JS** is an employee of GSK and holds stocks/shares; **MD** has received clinical trial funding from AstraZeneca, GSK, Probionase Therapies, and Sanofi, has participated in advisory boards for Regeneron Pharmaceuticals, Inc., Sanofi, and holds equity in Probionase Therapies; **ZD** has received honoraria or speaker fees serving on advisory boards or as a consultant from ALK, AstraZeneca, Antabio, Boehringer Ingelheim, GSK, HAL Allergy, Merck Sharp & Dohme, QPS-Netherlands, and Sanofi-Genzyme-Regeneron, all outside the submitted work; **PC** has participated in advisory board and received speaker fees from AstraZeneca, GSK, Novartis, Regeneron, and Sanofi Genzyme; **PWH** is a speaker and/or recipient of research grant by Sanofi, Regeneron, Novartis, GSK, Stallergenes, ALK and Viatris; **JKH** has received consultancy fees from Sanofi Genzyme, Regeneron, Genentech, AstraZeneca, GSK, and Gossamer Bio; **ATP** has received personal fees from Sanofi Regeneron, grants from Sanofi Regeneron, Optinose, and AstraZeneca and has participated in advisory boards for Sanofi Regeneron, Optinose, AstraZeneca, and GSK; **PG** has participated in advisory boards and received speaker fees from ALK-Abelló, Argenx, AstraZeneca, Genentech, GSK, Novartis, Regeneron, Roche, Sanofi Genzyme, and Stallergenes-Greer.

Editorial support (in the form of writing assistance, including preparation of the draft poster under the direction and guidance of the authors, collating and incorporating authors' comments for each draft, assembling tables and figures, grammatical editing and referencing) was provided by Bianca Paris, PhD, at Fishawack Indicia Ltd, UK, part of Fishawack Health, and was funded by GSK.


Scan the QR codes to access a PDF version of this poster and the associated audio recording

SCAN ME

Audio File

Presented at the American College of Allergy, Asthma & Immunology, Louisville, Kentucky, November 10–14, 2022