# Mepolizumab improves outcomes in patients with CRSwNP with one or more prior nasal polyp surgeries

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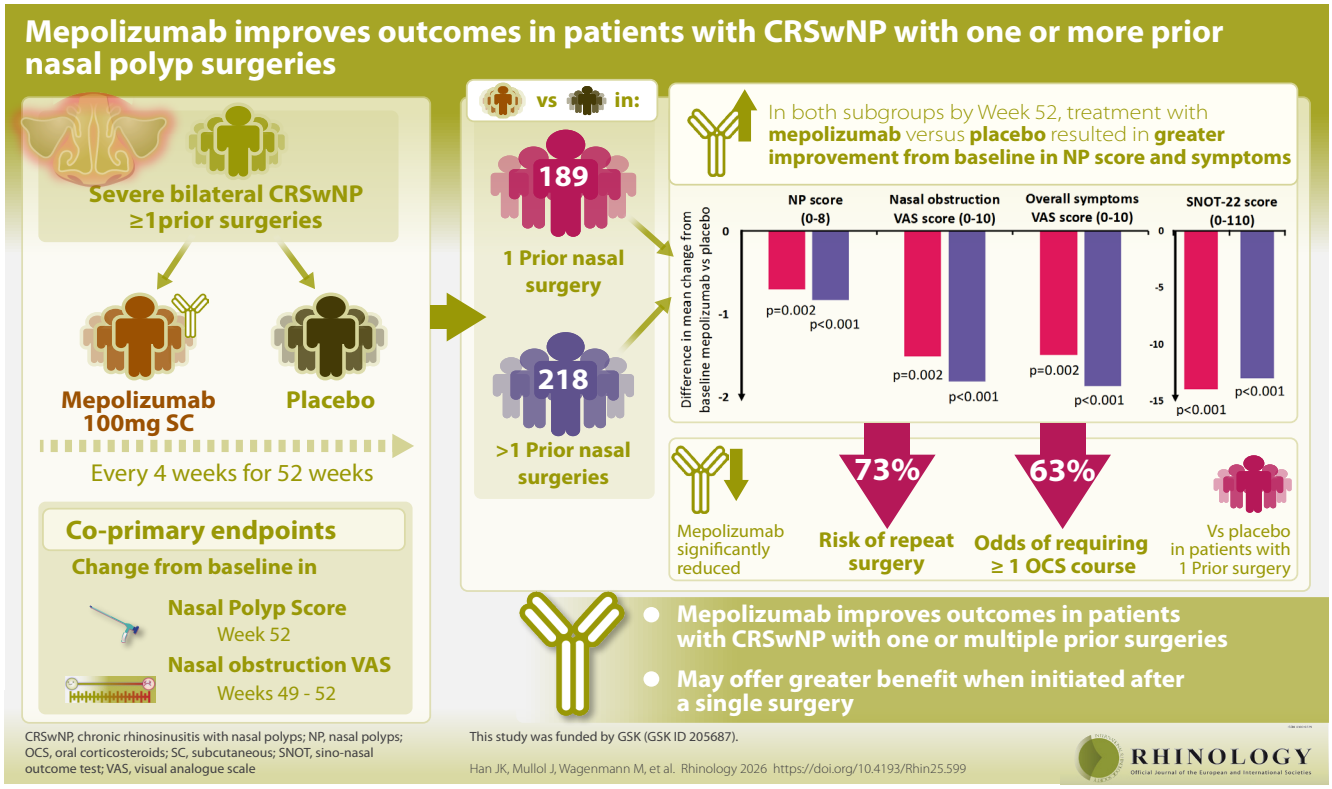


## Abstract

**Background**: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) often undergo multiple nasal surgeries. The Phase III SYNAPSE study (GSK ID:205687; NCT0308579) demonstrated that mepolizumab reduces the need for repeat surgery. We explored whether outcomes differed based on the number of prior surgeries.

**Methodology**: This post hoc analysis of SYNAPSE stratified patients by history of 1 or >1 prior surgery. Patients were randomised to receive mepolizumab or placebo every 4 weeks, alongside standard of care, for 52 weeks. Outcomes included change from baseline in endoscopic nasal polyp (NP) score, visual analogue scale (VAS) scores for nasal obstruction, loss of smell and overall symptoms, Sino-Nasal Outcome Test-22 (SNOT-22), and time to repeat surgery and/or oral corticosteroid (OCS) use.

**Results**: 189 patients had 1 prior surgery (108 mepolizumab; 81 placebo) and 218 had >1 prior surgery (98; 120). In both sub-groups, mepolizumab significantly improved mean changes versus placebo in NP, nasal obstruction, loss of smell VAS, overall symptom VAS, and SNOT-22. Significant reductions in risk of repeat surgery and requiring OCS were observed with mepolizumab versus placebo in patients with 1 prior surgery.

**Conclusions**: Mepolizumab improves outcomes in patients with CRSwNP with one or multiple prior surgeries; however, may offer greater benefit when initiated after a single surgery.

**Key words**: biological treatment, chronic rhinosinusitis, interleukin-5, nasal polyps, nasal surgical procedures

## Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic type 2 (T2) inflammatory condition of the sinonasal mucosa [1-3]. Symptoms include nasal congestion/obstruction, reduction/loss of smell, anterior/posterior rhinorrhoea, and facial pain/pressure, often significantly impairing health-related quality of life (HRQoL) [4-6].

Standard of care includes intranasal corticosteroids (INCS), oral corticosteroids (OCS), and nasal surgery [7,8]. Up to half of patients with CRSwNP eventually undergo nasal surgeries such as endoscopic sinus surgery (ESS) to remove NP and CRS sinus tissue, improve sinus ventilation, enhance topical drug delivery, and promote mucosal preservation and healing [1,9-11]. However, surgery is not curative and does not address underlying drivers of inflammation [10]. Recurrence following nasal surgery is common, as around 40% of patients will experience recurrence of CRSwNP within 18 months, and approximately 20% of patients require revision surgery within 5 years [1,12]. Surgery is also associated with risk of scarring, mucosal damage, perioperative complications, and patient discomfort, particularly in cases of revision surgery [7,11,13]. While some targeted therapies are now approved, there remains a need to optimise treatment selection by addressing underlying inflammatory mechanisms [7].

Biologic therapies targeting drivers of T2 inflammation have emerged as adjunctive options for patients with CRSwNP who remain uncontrolled despite standard of care [8,14-16]. CRSwNP is characterised by T2 inflammation, of which interleukin-5 (IL-5) is a central cytokine and, playing a pivotal role in disease pathogenesis [7,14,17]. IL-5 signalling orchestrates effects on a wide range of immune and structural cells involved in lower airway, sinus and nasal tissue inflammation, including epithelial cells, mast cells, plasma cells, eosinophils, basophils, smooth muscle cells, neutrophils, fibroblasts, T regulatory cells, and ILC2 cells [17]. Mepolizumab is a humanised monoclonal antibody that targets IL-5 and is approved as add-on therapy to INCS in adults with severe CRSwNP inadequately controlled with systemic corticosteroids and/or surgery [14]. In the pivotal Phase III SYNAPSE study, mepolizumab reduced the need for repeat nasal surgery and improved clinical outcomes and HRQoL in patients with severe CRSwNP with a history of prior nasal surgery, with an acceptable safety profile [7].

Over 45% of patients in SYNAPSE had undergone 2 or more prior nasal surgeries, reflecting a population with high disease and surgical burden [7]. While other recent biologic trials in CRSwNP have included subgroup analyses based on prior ESS, these typically compare outcomes in patients with or without any prior surgery [18]. In contrast, all patients in SYNAPSE had undergone at least 1 prior nasal surgery, allowing evaluation of whether the number of surgeries, and potentially earlier biologic intervention, may influence treatment outcome. This post hoc analysis of SYNAPSE aimed to evaluate the efficacy of mepolizumab compared with placebo in patients with recurrent, refractory severe bilateral CRSwNP stratified by 1 versus >1 prior nasal surgery.

## Materials and methods

### SYNAPSE study design and patient population

SYNAPSE (GSK ID: 205687; NCT03085797) was a randomised, double-blind, placebo-controlled, parallel-group, multicentre, Phase III study conducted across 93 sites in 11 countries to evaluate the efficacy and safety of mepolizumab in patients with severe CRSwNP eligible for repeat nasal surgery despite medical standard of care. Patients were randomised 1:1 to receive subcutaneous mepolizumab 100 mg or placebo every 4 weeks for 52 weeks, in addition to standard of care therapies, including daily INCS (mometasone furoate) and, as needed, saline irrigations, OCS and/or antibiotics. Full details of the SYNAPSE study design and procedures have been published previously [7].

Patients enrolled in SYNAPSE were aged ≥18 years with recurrent, refractory, severe bilateral CRSwNP, characterised by persistent symptoms despite standard of care and an indication for repeat nasal surgery. All included patients had undergone ≥1 prior nasal surgery within the past 10 years. Key inclusion criteria included an endoscopic NP score ≥5 out of 8 (with ≥2 in each nostril) and a visual analogue scale (VAS) score ≥5 for nasal obstruction. Key exclusion criteria included nasal conditions other than CRSwNP that could confound assessment, recent nasal surgery (within 6 months), or use of other biologics for treatment of CRSwNP.

This manuscript presents a post hoc analysis of SYNAPSE data, stratifying patients by history of 1 versus >1 prior nasal surgery to explore whether the number of prior surgical interventions influenced treatment outcomes with mepolizumab.

### Outcomes and assessments

This analysis evaluated key clinical and patient-reported outcomes (PROs) from the SYNAPSE study stratified by post hoc subgroups of 1 versus >1 prior nasal surgeries. Outcomes included change from baseline to Week 52 in NP score and total Sino-Nasal Outcome Test-22 (SNOT-22) score, change from baseline to average of Weeks 49–52 in VAS scores for nasal obstruction, loss of smell, and overall symptoms (disease severity), incidence and risk of repeat nasal surgery up to Week 52 and proportion of patients requiring ≥1 course of OCS and total course of OCS up to Week 52. Higher NP, VAS, and SNOT-22 scores, as well as incidence of repeat nasal surgery, and the use of ≥1 course of OCS reflect increased severity of symptoms. Reduced time to repeat surgery also reflects increased severity of symptoms. Responder analyses included a change of ≥3 points for nasal obstruction VAS, ≥3 for loss of smell VAS, and ≥3 and ≥5 points for overall symptom VAS (CRS severity) [19], as well as a SNOT-22 total score

Table 1. Baseline characteristics by number of prior nasal surgeries.

| | 1 prior nasal surgery | | >1 prior nasal surgery | |
|---|---|---|---|---|
| | Placebo (n=81) | Mepolizumab (n=108) | Placebo (n=120) | Mepolizumab (n=98) |
| Age, years, mean (SD) | 48.3 (13.11) | 46.8 (14.10) | 49.3 (12.05) | 50.6 (12.69) |
| Sex, female, n (%) | 34 (42) | 33 (31) | 42 (35) | 34 (35) |
| Body mass index, kg/m$^2$, mean (SD) | 27.9 (5.58) | 27.9 (4.92) | 28.3 (5.39) | 28.4 (5.63) |
| Concurrent diagnosis of asthma, n (%) | 54 (67) | 69 (64) | 95 (79) | 71 (72) |
| Concurrent diagnosis of AERD/N-ERD, n (%) | 19 (23) | 21 (19) | 44 (37) | 24 (24) |
| Nasal polyp score (0–8), mean (SD) | 5.5 (1.3) | 5.4 (1.2) | 5.6 (1.5) | 5.4 (1.1) |
| Nasal obstruction VAS score (0–10), mean (SD) | 8.9 (0.8) | 9.0 (0.8) | 9.1 (0.8) | 8.9 (0.9) |
| Loss of smell VAS score (0–10), mean (SD) | 9.5 (0.7) | 9.5 (1.0) | 9.8 (0.5) | 9.8 (0.5) |
| Overall symptom VAS score (0–10), mean (SD) | 9.0 (0.7) | 9.1 (0.7) | 9.2 (0.7) | 9.0 (0.8) |
| SNOT-22 total score (0–110), mean (SD) | 63.3 (19.4) | 62.0 (15.8) | 65.2 (18.9) | 65.6 (19.3) |

threshold of ≥8.9, ≥12.0, and ≥28.0, which aligns with the previously established minimal clinically important difference (MCID) of 8.9 for SNOT-22 scores [20]. The additional SNOT 22 thresholds of ≥12.0 and ≥28.0 have been included as previously proposed as appropriate in medically managed patients with CRS [22], and patients with higher severity of CRSwNP, respectively [21,23].

### Statistical analysis

All analyses were conducted in the intent-to-treat population. As a post hoc analysis, all statistical tests were exploratory and descriptive in nature. Nominal p-values are reported with no adjustments made for multiple comparisons. Treatment differences for continuous outcomes such as NP score, VAS, and SNOT-22 were analysed using mixed model repeated measures with covariates of treatment group, region, baseline score, and loge blood eosinophil count. Binary outcomes such as responder proportions and OCS use were assessed using logistic regression and adjusted for treatment group, baseline score, prior OCS use (where relevant), and region. Time to repeat nasal surgery was analysed using a Cox proportional hazards model and adjusted for treatment group, region, baseline NP score, nasal obstruction VAS, eosinophil count, and number of prior nasal surgeries. The hazard ratio (HR), representing risk, generated from this analysis is presented alongside the incidence of repeat nasal surgery occurring by Week 52. Patients who had nasal surgery before Week 52 were assigned their worst observed pre-surgical score, as pre-specified in the SYNAPSE protocol [7].

## Results

### Patient population

Among 407 patients from 93 sites across 11 countries, 189 patients had only 1 prior nasal surgery, with 108 receiving mepolizumab and 81 receiving placebo, and 218 patients had >1 prior nasal surgery, with 98 receiving mepolizumab and 120 receiving placebo. Baseline characteristics were generally similar between treatment groups within each subgroup (Table 1). Across the total population, most patients were male, with a mean age of 48.8 years (standard deviation [SD] 13.01) and a mean body mass index of 28.2 kg/m$^2$ (SD 5.4). Notably, a lower proportion of patients with >1 prior nasal surgery at baseline received mepolizumab (44%) compared with placebo (55%) [7].

A greater number of prior nasal surgeries was associated with a higher prevalence of comorbid T2 inflammatory conditions at baseline. When both treatment groups are combined, the association between number of prior nasal surgeries and presence of comorbid asthma or aspirin/non-steroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease (aspirin-exacerbated respiratory disease/NSAID-exacerbated respiratory disease [AERD/N-ERD] was statistically significant. Asthma was present in 65% of patients with 1 prior surgery compared with 76% of patients with >1 prior surgery (odds ratio [OR] 1.71 [95% confidence interval {CI}: 1.11–2.64]; p=0.015). Similarly, AERD/N-ERD was present in 21% of patients with 1 prior surgery and 31% of patients with >1 prior surgery (OR 1.69 [95% CI: 1.08–2.65]; p=0.023).

In the placebo group, patients with >1 prior nasal surgery, compared with the 1 prior nasal surgery group, were significantly more likely to have asthma (79% vs 67%; OR 1.90 [95% CI: 1.00–3.60]; p=0.049) and AERD/N-ERD; 37% vs 23%; OR 1.89 [95% CI: 1.00–3.56]; p=0.049). The mepolizumab group had similar but not statistically significant trends, with asthma present in 72% versus 64% of patients (OR 1.49 [95% CI: 0.82–2.69]; p=0.190) and AERD/N-ERD in 24% versus 19% of patients (OR 1.34 [95% CI: 0.69–2.61]; p=0.382).

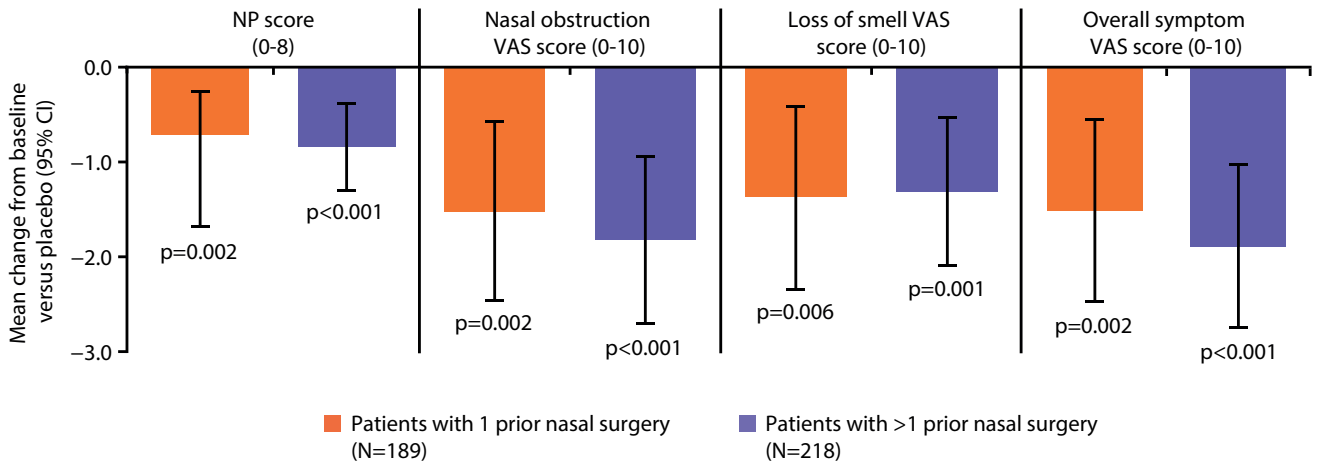


Figure 1. Mean change from baseline in NP score, nasal obstruction, loss of smell and overall symptoms VAS (mepolizumab vs placebo).

### Mean change from baseline in NP score and VAS scores

In both prior surgery subgroups (1 or >1), mepolizumab resulted in greater mean improvements from baseline compared with placebo in nasal obstruction VAS (–1.52 and –1.82), loss of smell VAS (–1.37 and –1.31), and overall symptom VAS (–1.50 and –1.88) scores (all nominal p≤0.006). It also led to greater reductions in NP score (–0.71 and –0.84; nominal p=0.002 and p<0.001, respectively) (Figure 1).

### Mean change from baseline in SNOT-22 total score

Mepolizumab led to significantly greater mean reductions in SNOT-22 total score at Week 52 compared with placebo in both surgery subgroups, with consistent treatment effects across subgroups and similar magnitudes of improvement (Figure 2). In the 1 prior surgery and >1 prior surgery subgroups, the mean reduction from baseline with mepolizumab versus placebo was -14.00 (p<0.001) and -13.01 (p<0.001), respectively.

### Incidence and risk of repeat nasal surgery

Time to repeat nasal surgery in the study was delayed with mepolizumab compared with placebo among both subgroups (Table 2), representing a decreased risk of repeat surgery over time as all patients received prior nasal surgery within the past 10 years. The incidence of repeat surgery by the end of the study period was numerically reduced in both subgroups with mepolizumab versus placebo (Table 2).

Among patients with 1 prior surgery, 6% of those receiving mepolizumab underwent an additional nasal surgery by the end of the 52-week study period compared with 20% with placebo. This reflects a significantly reduced risk (-73%) of repeat surgery with mepolizumab versus placebo over a 52-week treatment period (HR 0.27; 95% CI: 0.10–0.69; p=0.006). Among patients with >1 prior surgery, 12% of those receiving mepolizumab underwent repeat surgery compared with 25% with placebo by the end of the 52-week study period. This reflects a reduced risk (-39%) of repeat surgery with mepolizumab versus placebo, although not statistically significant (HR 0.61; 95% CI: 0.30–1.23; p=0.168).

Patients were additionally analysed by those who had undergone 2 nasal surgeries prior to study and ≥3 nasal surgeries

Table 2. Incidence of and time to repeat nasal surgery and odds of requiring ≥1 course of OCS with mepolizumab versus placebo, stratified by number of prior nasal surgeries (1 and >1 prior nasal surgery).

| | 1 prior nasal surgery | | >1 prior nasal surgery | |
|---|---|---|---|---|
| | Placebo (n=81) | Mepolizumab (n=108) | Placebo (n=120) | Mepolizumab (n=98) |
| Patients requiring further surgery by Week 52, n (%) | 16 (20) | 6 (6) | 30 (25) | 12 (12) |
| HR (95% CI)* | 0.27 (0.10–0.69); p=0.006 | | 0.61 (0.30–1.23); p=0.168 | |
| Patients requiring ≥1 course OCS, n (%) | 29 (36) | 20 (19) | 45 (38) | 32 (33) |
| OR (95% CI) | 0.37 (0.18–0.76); p=0.007 | | 0.94 (0.49–1.79); p=0.841 | |
| Total courses of OCS by Week 52 (n) | 40 | 35 | 84 | 47 |

*HR is derived from time to repeat surgery data, representing risk of repeat surgery over time.

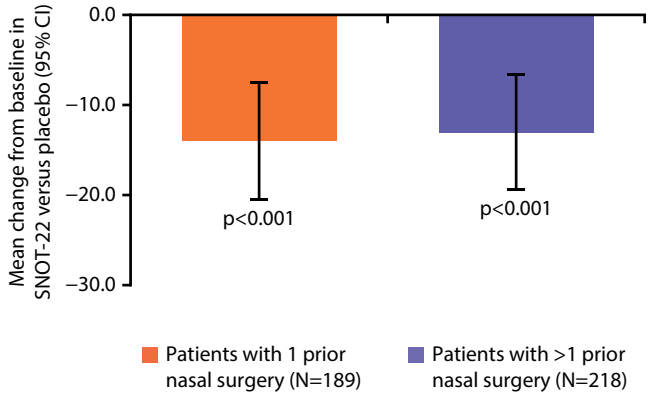


Figure 2. Mean change from baseline in SNOT-22 score (0-110) (mepolizumab vs placebo).

prior to study subgroups (Table 3). Among patients with 2 prior surgeries, mepolizumab resulted in a 21% reduction in the risk of repeat surgery, and in patients with ≥3 prior surgeries this reduction in risk was 52%, although in both cases the differences were not statistically significant.

### Odds of requiring ≥1 course of OCS

The need for OCS was also reduced with mepolizumab treatment, particularly in the 1 prior surgery subgroup (Table 2), 19% of patients receiving mepolizumab required ≥1 OCS course compared with 36% of those receiving placebo, corresponding to a statistically significant 63% reduction in the odds of requiring OCS (OR 0.37; 95% CI: 0.18–0.76; p=0.007). Patients receiving mepolizumab were prescribed a total of 35 courses of OCS, compared with a total of 40 OCS courses prescribed in those receiving placebo.

In the >1 prior surgery group, 33% of patients receiving mepolizumab required ≥1 OCS course compared with 35% of those receiving placebo, corresponding to a 6% reduction in the odds of requiring OCS (OR 0.94; 95% CI: 0.49–1.79; p=0.841). This reduction in need for OCS during the 52-week study period was not statistically significant (Table 2).

Among patients with 2 prior surgeries, there was a non-significant increase in the odds of requiring OCS whereas in patients with ≥3 prior surgeries there was a 45% non-significant reduction in the odds of requiring OCS in mepolizumab versus placebo (Table 3).

Among the patients with >1 prior surgery, a total of 47 courses of OCS were prescribed in patients receiving mepolizumab, compared with 84 courses of OCS in patients receiving placebo (Tables 2 and 3).

### Responder analyses

At Weeks 49–52, significantly higher proportions of patients receiving mepolizumab achieved clinically meaningful improvements in symptom VAS scores and SNOT-22 total scores compared with those receiving placebo, in both prior surgery subgroups. Improvements were observed across all thresholds assessed, including ≥3 and ≥5-point improvements in overall symptom VAS and ≥8.9, ≥12, and ≥28-point improvements in SNOT-22. ORs for response consistently favoured mepolizumab and reached statistical significance in both subgroups for all endpoints (Table 4).

## Discussion

The SYNAPSE study addressed an unmet need in the CRSwNP landscape as the first large, multinational, Phase III study to show the safety and efficacy of an anti-IL-5 biologic in patients with recurrent, refractory, severe CRSwNP who were eligible for repeat nasal surgery [7]. This post hoc analysis of SYNAPSE demonstrated that mepolizumab significantly improved symptom burden and HRQoL compared with placebo in patients with 1 and >1 prior nasal surgeries. Thus, mepolizumab demonstrates broad effectiveness across different levels of surgical history and disease burden.

The improvement in patient outcomes, as shown in NP score, nasal obstruction VAS, and overall symptom VAS score in both 1

Table 3. Incidence of, and time to repeat nasal surgery, and odds of requiring ≥1 course of OCS with mepolizumab versus placebo, stratified by number of prior surgeries, in patients with >1 prior nasal surgery (2 and ≥3 prior nasal surgery).

| | 2 prior nasal surgery | | ≥3 prior nasal surgery | |
|---|---|---|---|---|
| | Placebo (n=47) | Mepolizumab (n=47) | Placebo (n=73) | Mepolizumab (n=51) |
| Patients requiring further surgery by Week 52, n (%) | 9 (19) | 5 (11) | 21 (29) | 7 (14) |
| HR (95% CI)* | 0.79 (0.24–2.61) | | 0.48 (0.20–1.16) | |
| Patients requiring ≥1 course OCS, n (%) | 14 (30) | 14 (30) | 31 (42) | 18 (35) |
| OR (95% CI) | 1.77 (0.60–5.19) | | 0.55 (0.22–1.37) | |
| Total courses of OCS by Week 52 (n) | 28 | 18 | 56 | 29 |

*HR is derived from time to repeat surgery data, representing risk of repeat surgery over time.

Table 4. Proportion of Responders at Week 49–52 by endpoint and number of prior nasal surgeries.

| | 1 prior nasal surgery | | >1 prior nasal surgery | |
|---|---|---|---|---|
| | Placebo (n=81) | Mepolizumab (n=108) | Placebo (n=120) | Mepolizumab (n=98) |
| **Nasal Obstruction VAS** | | | | |
| ≥3-point improvement | 44% | 64% | 31% | 56% |
| OR (95% CI) | 2.25 (1.24–4.08); p=0.008 | | 2.90 (1.65–5.12); p<0.001 | |
| **Loss of Smell VAS** | | | | |
| ≥3-point improvement | 23% | 43% | 17% | 29% |
| OR (95% CI) | 2.45 (1.28–4.68); p=0.007 | | 2.01 (1.04–3.88); p=0.037 | |
| **Overall Symptom VAS** | | | | |
| ≥3-point improvement | 46% | 66% | 33% | 58% |
| OR (95% CI) | 2.35 (1.29–4.29); p=0.005 | | 2.79 (1.59–4.91); p<0.001 | |
| ≥5-point improvement | 26% | 50% | 20% | 44% |
| OR (95% CI) | 2.96 (1.56–5.61); p<0.001 | | 3.28 (1.77–6.07); p<0.001 | |
| **SNOT-22** | | | | |
| ≥8.9-point improvement | 55% | 75% | 53% | 71% |
| OR (95% CI) | 2.46 (1.31–4.61); p=0.005 | | 2.37 (1.33–4.24); p=0.003 | |
| ≥12.0-point improvement | 54% | 75% | 50% | 69% |
| OR (95% CI) | 2.61 (1.39–4.90); p=0.003 | | 2.39 (1.35–4.25); p=0.003 | |
| ≥28.0-point improvement | 33% | 55% | 31% | 52% |
| OR (95% CI) | 2.74 (1.47–5.09); p=0.001 | | 2.52 (1.42–4.46); p=0.002 | |

prior surgery and >1 prior surgery groups, may reflect mepolizumab's efficacy at improving symptom burden even in those with higher inflammation at baseline with limited response to conventional therapies.

Treatment with mepolizumab led to similar magnitudes of improvement in mean change from baseline in SNOT-22 scores across both surgery subgroups, as well as significantly higher and clinically meaningful responder rates compared with placebo across all SNOT-22 improvement thresholds (≥8.9-, ≥12.0-, and ≥28.0-point improvement). These SNOT-22 thresholds reflect clinically meaningful within-patient improvements in HR-QoL as previously established and utilised for SNOT-22 assessment [20-23]. Even at the most stringent threshold of a ≥28-point improvement, over half of patients treated with mepolizumab in both the 1 and >1 prior surgery groups achieved this response. Treatment with mepolizumab also led to significantly greater improvements in key VAS symptom scores including nasal obstruction, loss of smell, and overall symptoms, across both subgroups.

These findings reinforce the clinical relevance of mepolizumab's benefits, reflecting meaningful improvements in daily functioning and HRQoL for a broad range of patients with CRSwNP. Responder analyses demonstrated consistent and statistically significant benefits across all assessed thresholds, reinforcing the robustness of treatment effects with mepolizumab. Patients who received mepolizumab after just 1 prior surgery experienced significant reduction in the risk over time and overall incidence of repeat surgery, as well as need for ≥1 OCS course compared with placebo. This may suggest a therapeutic window in which early intervention with mepolizumab (just after 1 nasal surgery as recommended in European position paper on rhinosinusitis and nasal polyps/European Forum for Research and Education in Allergy and Airway Diseases [EPOS/EUFOREA] guidelines) offers advantages in reducing long-term burden of disease and healthcare resource utilisation by preventing disease progression [8,24].

The use of mepolizumab versus placebo led to some improvements with regards to reducing surgery and OCS use in the >1 prior surgery group, although these were not statistically significant. The proportion of patients treated with mepolizumab requiring further surgery by Week 52 was higher in the cohort of patients with >1 prior surgery compared with 1 prior surgery group (12% vs 6%), as were their odds of requiring more than 1 course of OCS (33% vs 19%). This further supports the suggestion that earlier interventions with mepolizumab offers more significant advantages to patient outcomes. However, this needs to be interpreted with caution due to a variety of possible confounding factors. Beyond the history of multiple recurrences reflected by the greater number of prior surgeries, the increased disease burden in patients with >1 prior surgery is further

evidenced by the higher baseline rates of comorbid asthma and AERD/N-ERD, as shown in Table 1. This implied higher severity of T2 inflammation may mean this population may be harder to treat, with a higher treatment requirement [6]. As demonstrated in previous subgroup analyses of SYNPASE, mepolizumab reduced the risk of surgery versus placebo to a greater extent in patients without asthma compared with patients with comorbid asthma; however, the reductions in the risk of surgery with mepolizumab was similar in patients with and without a diagnosis of AERD/N-ERD [25]. Furthermore, subdividing the >1 prior surgery into patients who had 2 prior surgery and ≥3 prior surgeries, showed that outcomes for the >1 prior surgery group are mainly driven by those with exactly 2 prior surgeries, as patients with ≥3 prior surgeries had relatively better outcomes. Additionally, a lower proportion of these patients received mepolizumab versus placebo. This, alongside small patient numbers in subgroups makes interpretation difficult.

These findings are particularly relevant within the evolving CRSwNP treatment landscape. Biologics, including mepolizumab, dupilumab, omalizumab, depemokimab, and tezepelumab have reported benefits in reducing surgical need in various patient groups [7,16,26-31]. By stratifying outcomes by number of prior nasal surgeries, this analysis further supports the role of biologics in the management of CRSwNP, demonstrating that mepolizumab can lead to sustained improvements in symptoms and CRSwNP burden. This may help optimise clinical decision making, especially surrounding the optimal timing of biologic therapy initiation, and helps provide a better understanding of the value of mepolizumab across the spectrum of disease severity. By interrupting the cycle of chronic inflammation, biologic therapies like mepolizumab offer the potential for disease modification, going beyond symptomatic relief to address the underlying drivers of the condition. This has been demonstrated by sustained clinical benefits of mepolizumab treatment even after treatment cessation, in outcomes such as NP size and risk of further surgery [32]. Future prospective studies should explore long-term outcomes of early mepolizumab use.

Limitations of this study should be considered. The study was not powered to detect differences between the 1 versus >1 prior nasal surgery subgroups. The higher baseline rates of asthma and AERD/N-ERD in the >1 prior surgery group may have contributed to higher rates of revision surgery and OCS use seen in this subgroup. These covariates were not statistically adjusted for, and represents a main limitation of this analysis. Additionally, there is large variability in the outcomes for the patients in the >1 prior surgery subgroup. This, alongside the small patient numbers in each prior surgery subgroup, limits the interpretability of the result. The findings were exploratory and descriptive in nature, with nominal p-values reported with no adjustments made for multiple comparisons. In addition, the cut-off used to categorise prior nasal surgery subgroups by 1 versus >1 is clinically pragmatic, and assumes that surgical type heterogeneity is similar between both cohorts given the randomisation of treatment during the trial. Differences in response according to time since last surgery (<3 or ≥3 years) has been analysed previously [31]; however, key factors affecting patient outcomes such as the extent and timing of previous procedures, response to previous procedures, or type of prior nasal surgeries (e.g., nasal polypectomy, functional ESS and limited, comprehensive or extended ESS) were not accounted for in the current analysis. Previous studies have shown variance in the long-term outcomes, and need for revision surgery for patients with CRSwNP depending on the type of nasal surgery they have received [33], and this would be of clinical interest for future analyses.

## Conclusion

Mepolizumab significantly improved key clinical and PROs in patients with CRSwNP, regardless of prior surgical history, specifically NP score, VAS scores for nasal obstruction, loss of smell, overall symptoms, and SNOT-22 total score. Significant reductions in the incidence and need for future surgery over time, and OCS treatment were observed in patients with 1 prior nasal surgery. These findings support a proactive approach to medical treatment, suggesting that earlier initiation of mepolizumab after a single nasal surgery, as recommended by international guidelines (i.e., EPOS-EUFOREA) [24], would offer benefit without the need for multiple, invasive nasal surgeries. Benefits in patient outcomes are still observed following multiple nasal surgeries; however, patients in this group showed a marginally smaller response, possibly impacted by greater cumulative damage from multiple recurrences and surgeries and a potentially higher T2 inflammatory burden. Overall, this study provides further support for the clinical value of mepolizumab in managing severe, recurrent, refractory CRSwNP, and support its use without waiting for multiple surgical interventions.

## Abbreviations

AERD, aspirin-exacerbated respiratory disease; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; EPOS, European position paper on rhinosinusitis and nasal polyp; ESS, endoscopic sinus surgery; EUFOREA, European Forum for Research and Education in Allergy and Airway Diseases; HR, hazard ratio; HRQoL, health-related quality of life; IL-5, interleukin-5; INCS, inhaled corticosteroid; MCID, minimal clinically important difference; N-ERD, NSAID-exacerbated respiratory disease; NP, nasal polyps; NSAID, non-steroidal anti-inflammatory drug; OCS, oral corticosteroid; OR, odds ratio; PRO, patient-reported outcome; SD, standard deviation; SNOT-22, Sino-Nasal Outcome Test-22; T2, type 2 ; VAS, visual analogue scale.

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## Author contributions

JKH, MW, and CH contributed to data acquisition and interpretation; JM, ARS, and PH to data interpretation; LZ to data analysis and interpretation; and LW to study concept and design and data interpretation. All authors reviewed and revised the manuscript critically for important intellectual content, agreed to submit to the current journal, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

## Conflict of interest

JKH has received consultancy fees from Sanofi Genzyme, Regeneron, Genentech, Novartis, AstraZeneca, and GSK. JM has received research grants from and attended speaker bureaus and/or advisory boards for Almirall, AstraZeneca, Glenmark, GSK, Lilly, Menarini, Mitsubishi-Tanabe Pharma, MSD, Noucor/Uriach, Novartis, Regeneron Pharmaceuticals Inc., Sanofi-Genzyme, and Viatris/MEDA Pharma. MW has received personal fees from ALK-Abelló, AstraZeneca, Genzyme, GSK, HAL-Allergy, InfectoPharm, LETI Pharma, Med update, Novartis, Regeneron, Sanofi, and Stallergenes, and is a member of the executive committee of the German Society of Allergology and Clinical Immunology (DGAKI). His institution has received payments from ALK-Abelló, AstraZeneca, GSK, Novartis, Regeneron, Sanofi-Aventis, and Takeda. LW, LZ, ARS, and PH are employed by GSK and hold financial equities in GSK. CH has received advisory board fees from Sanofi, AstraZeneca, Olympus, and GSK, and lecture fees from Mylan.

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## Data sharing statement

Please refer to GSK weblink to access GSK's data sharing policies and as applicable seek anonymised subject level data via the link https://www.gsk-studyregister.com/en/.

## References

1. Fieux M, Rumeau C, De Bonnecaze G, Papon JF, Mortuaire G. Surgery for chronic rhinosinusitis with nasal polyps: An update. Eur Ann Otorhinolaryngol Head Neck Dis 2023; 140: 297-304.
2. Stevens WW, Schleimer RP, Kern RC. Chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol Pract 2016; 4: 565-572.
3. Gevaert P, Han JK, Smith SG, et al. The roles of eosinophils and interleukin-5 in the pathophysiology of chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol 2022; 12: 1413-1423.
4. Hall R, Trennery C, Chan R, et al. Understanding the patient experience of severe, recurrent, bilateral nasal polyps: a qualitative interview study in the United States and Germany. Value Health 2020; 23: 632-641.
5. Mullol J, Azar A, Buchheit KM, Hopkins C, Bernstein JA. Chronic rhinosinusitis with nasal polyps: quality of life in the biologics era. J Allergy Clin Immunol Pract 2022; 10: 1434-1453. e1439.
6. Bachert C, Bhattacharyya N, Desrosiers M, Khan AH. Burden of disease in chronic rhinosinusitis with nasal polyps. J Asthma Allergy 2021; 14: 127-134.
7. Han JK, Bachert C, Fokkens WJ, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med 2021; 9: 1141-1153.
8. Fokkens WJ, Lund VJ, Hopkins C, et al. Executive summary of EPOS 2020 including integrated care pathways. Rhinology 2020; 58: 82-111.
9. Cherian LM, Bright RR, Varghese L, Rupa V, Kurien R. Characteristics of chronic rhinosinusitis with nasal polyps based on allergic mucin and fungal elements in patients undergoing revision endoscopic sinus surgery. Indian J Otolaryngol Head Neck Surg 2022; 74: 108-115.
10. Huvenne W, Zhang N, Tijsma E, et al. Pilot study using doxycycline-releasing stents to ameliorate postoperative healing quality after sinus surgery. Wound Repair Regen 2008; 16: 757-767.
11. Selvarajah J, Saim AB, Bt Hj Idrus R, Lokanathan Y. Current and alternative therapies for nasal mucosa injury: a review. Int J Mol Sci 2020; 21.
12. DeConde AS, Mace JC, Levy JM, Rudmik L, Alt JA, Smith TL. Prevalence of polyp recurrence after endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. Laryngoscope 2017; 127: 550-555.
13. Hellings PW, Alobid I, Anselmo-Lima WT, et al. EUFOREA/EPOS2020 statement on the clinical considerations for chronic rhinosinusitis with nasal polyps care. Allergy 2024; 79: 1123-1133.
14. GSK. Nucala EU summary of product characteristics. Updated 2024. Available from: https://www.ema.europa.eu/en/documents/product-information/nucala-epar-product-information_en.pdf [Accessed 30 October 2025].
15. Novartis. Xolair EU summary of product characteristics. Updated 2025. Available from: https://www.ema.europa.eu/en/documents/product-information/xolair-epar-product-information_en.pdf [Accessed 30 October 2025].
16. Sanofi. Dupixent EU summary of product characteristics. Updated 2025. Available from: https://www.ema.europa.eu/en/documents/product-information/dupixent-epar-product-information_en.pdf [Accessed 30 October 2025].
17. Buchheit KM, Shaw D, Chupp G, et al. Interleukin-5 as a pleiotropic cytokine orchestrating airway type 2 inflammation: Effects on and beyond eosinophils. Allergy 2024; 79: 2662-2679.
18. Lee SE, Hopkins C, Mullol J, et al. Dupilumab improves health related quality of life: results from the phase 3 SINUS studies. Allergy 2022; 77: 2211-2221.
19. Hopkins C, Han JK, Lund VJ, et al. Evaluating treatment response to mepolizumab in

patients with severe CRSwNP. Rhinology 2023; 61: 108-117.
20. Hopkins C, Gillett S, Slack R, Lund V, Browne J. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol 2009; 34: 447-454.
21. Mullol J, Backer V, Constantinidis J, et al. Global airway disease: mepolizumab simultaneously improves outcomes in severe CRSwNP and asthma. Rhinology 2025; 63: 113-115.
22. Phillips KM, Hoehle LP, Caradonna DS, Gray ST, Sedaghat AR. Minimal clinically important difference for the 22-item Sinonasal Outcome Test in medically managed patients with chronic rhinosinusitis. Clin Otolaryngol 2018; 43: 1328-1334.
23. Fokkens WJ, Trigg A, Lee SE, et al. Mepolizumab improvements in health-related quality of life and disease symptoms in a patient population with very severe chronic rhinosinusitis with nasal polyps: psychometric and efficacy analyses from the SYNAPSE study. J Patient Rep Outcomes 2023; 7: 4.
24. Fokkens WJ, Viskens AS, Backer V, et al. EPOS/EUFOREA update on indication and evaluation of biologics in chronic rhinosinusitis with nasal polyps 2023. Rhinology 2023; 61: 194-202.
25. Bachert C, Sousa AR, Han JK, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps: Treatment efficacy by comorbidity and blood eosinophil count. J Allergy Clin Immunol 2022; 149: 1711-1721.e1716.
26. Gevaert P, Saenz R, Corren J, et al. Long-term efficacy and safety of omalizumab for nasal polyposis in an open-label extension study. J Allergy Clin Immunol 2022; 149: 957-965 e953.
27. Gevaert P, Desrosiers M, Cornet M, et al. Efficacy and safety of twice per year depemokimab in chronic rhinosinusitis with nasal polyps (ANCHOR-1 and ANCHOR-2): phase 3, randomised, double-blind, parallel trials. Lancet 2025; 405: 911-926.
28. Han J, Lipworth B, Desrosiers M, et al. efficacy and safety of tezepelumab in adults with severe chronic rhinosinusitis with nasal polyps: results from the phase 3 WAYPOINT study. J Allergy Clin Immunol 2025; 155: AB442.
29. Lipworth BJ, Han JK, Desrosiers M, et al. Tezepelumab in adults with severe chronic rhinosinusitis with nasal polyps. N Engl J Med 2025; 392: 1178-1188.
30. Bachert C, Han JK, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet 2019; 394: 1638-1650.
31. Fokkens WJ, Mullol J, Kennedy D, et al. Mepolizumab for chronic rhinosinusitis with nasal polyps (SYNAPSE): in-depth sinus surgery analysis. Allergy 2023; 78: 812-821.
32. Desrosiers M, Diamant Z, Castelnuovo P, et al. Sustained efficacy of mepolizumab in patients with severe chronic rhinosinusitis with nasal polyps: SYNAPSE 24-week treatment-free follow-up. Int Forum Allergy Rhinol 2024; 14: 18-31.
33. Rodriguez-Van Strahlen C, Arancibia C, Calvo-Henriquez C, Mullol J, Alobid I. systematic review of long term sinonasal outcomes in CRSwNP after endoscopic sinus surgery: a call for unified and standardized criteria and terms. Curr Allergy Asthma Rep 2024; 24: 443-456.

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**SUPPLEMENTARY MATERIAL**

## Plain Language Summary

**Why was this study done?**

Chronic rhinosinusitis with nasal polyps is an inflammatory disease of the nose and sinuses. Symptoms include a blocked nose, facial pain or pressure and loss of smell, which can greatly affect quality of life. Many people need several sinus operations and repeated courses of steroid tablets to manage their symptoms. Mepolizumab is a medicine that targets inflammation in the immune system and may help improve symptoms and reduce the need for surgery.

**What did the researchers do and find?**

The study looked at whether the effect of mepolizumab depended on how many surgeries a patient had already had. People in this study were divided into two groups: those with one prior nasal surgery, and those with two or more. For 52 weeks, participants received either mepolizumab or a placebo (inactive treatment), alongside their usual care.

The results showed that mepolizumab improved symptoms compared with placebo, regardless of the number of previous nasal surgeries. In people who had only one prior surgery, mepolizumab also reduced the need for further surgery and steroid tablets during the study.

**What do these findings mean?**

Mepolizumab can improve symptoms in people with chronic rhinosinusitis with nasal polyps whether they have had one, or several, surgeries in the past. Starting mepolizumab earlier in a patient's treatment journey may give greater benefits by reducing the need for additional surgery and steroid tablets.