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Global airway disease: mepolizumab simultaneously improves outcomes in severe CRSwNP and asthma

Joaquim Mullol[1], Vibeke Backer[2], Jannis Constantinidis[3], Ibon Eguíluz-Gracia[4], Abraham L. Moure[5], Rafael Cuervo-Pinto[5], Lingjiao Zhang[6], Palvi Shah[7], William Kerr[8], Peter Hellings[9]

[1] Rhinology Unit & Smell Clinic, ENT Department, Hospital Clinic Barcelona, IDIBAPS, CIBERES, Barcelona, Catalonia, Spain
[2] Department of Otorhinolaryngology Head & Neck Surgery and Audiology, Rigshospitalet, Copenhagen, Denmark
[3] Department of ORL, AHEPA University Hospital, Thessaloniki, Greece
[4] Allergy Unit, Hospital Regional Universitario de Málaga. Allergy group, IBIMA-Plataforma BIONAND. RICORS Inflammatory Diseases. Málaga, Spain
[5] Specialty Care Unit, Medical Affairs, GSK, Madrid, Spain
[6] Respiratory Biostatistics, GSK, Warren, NJ, USA
[7] Data Analysis Statistics, GSK, UK
[8] Global Specialty Care, GSK, UK
[9] Otorhinolaryngology, Catholic University of Leuven, and Upper Airways Research Laboratory, University of Ghent, Belgium

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Dear Editor:

Chronic rhinosinusitis with nasal polyps (CRSwNP) often co-exists with asthma and non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD), creating a more severe phenotype and an additional burden compared with CRSwNP disease alone [1-3]. The relationship between these diseases in terms of shared immunological disbalance has been coined in the literature as 'global airway disease' or 'unified airway disease' and requires integrated treatment strategies [4-6]. Our post hoc analysis of the Phase III randomised, double-blind, placebo-controlled, multicentre SYNAPSE study (GSK ID: 205687; NCT03085797 [7]) assessed the efficacy of mepolizumab, an anti-interleukin-5 monoclonal antibody, in simultaneously improving both CRSwNP and asthma outcomes versus placebo. By utilising a combined measure that accounts for quality of life, sinonasal symptoms and asthma control, we aimed to validate the potential of mepolizumab as an effective therapeutic option for global airway disease.

Full study design and eligibility criteria have been previously published [7]. This post hoc analysis focused on patients from SYNAPSE with severe CRSwNP and concomitant asthma or N-ERD who were treated with mepolizumab or placebo and assessed simultaneous improvement in both CRSwNP and asthma outcomes. Odds ratios were calculated for patients achieving a minimal clinically important difference (MCID) in both the Sino-Nasal Outcome Test (SNOT-22) or the visual analogue scale (VAS) for CRSwNP symptoms and the Asthma Control Questionnaire (ACQ-5) at Weeks 4, 24 and 52 (Supplementary Methods).

Of the 407 patients with severe CRSwNP enrolled in SYNAPSE, 289 (71%) had a clinical record of asthma at baseline and 108 (27%) had N-ERD [8]. In patients with severe CRSwNP and asthma, treatment with mepolizumab consistently favoured the likelihood of achieving simultaneous improvements above MCID in SNOT-22 and ACQ-5 versus placebo as early as 4 weeks after the first mepolizumab dose. Odds ratios favouring mepolizumab were statistically significant across any of the composite endpoints of SNOT-22 MCID ≥8.9, ≥12 and ≥28 plus ACQ-5 MCID ≥0.5 at Weeks 24 and 52 (Figure 1). When considering patients achieving an ACQ-5 of ≤1 combined with a MCID in SNOT-22 (≥8.9, ≥12 or ≥28) at Week 52, statistically this was also more likely to be achieved with mepolizumab than placebo (Supplementary results). For patients with severe CRSwNP with N-ERD receiving mepolizumab, the proportions who achieved a MCID in both SNOT-22 (thresholds of ≥8.9, ≥12 and 2≥8) and ACQ-5 (≥0.5) compared with placebo at Week 52 were similar to the proportions observed in the asthma population and in those with multimorbid asthma without N-ERD (Figure 2). Approximately twice as many patients treated with mepolizumab achieved a simultaneous MCID≥28 in SNOT-22 and MCID≥0.5 in ACQ-5 compared with placebo regardless of the presence or absence of N-ERD. Patients were more likely to achieve simultaneous and clinically meaningful improvement (above the MCID defined thresholds) for overall VAS score and ACQ-5 when treated with mepolizumab versus placebo (Supplementary Figure 1). This was also true for each of the individual VAS symptoms, including nasal obstruction, loss of smell, nasal discharge, mucus in the throat and facial pain. Baseline disease characteristics were

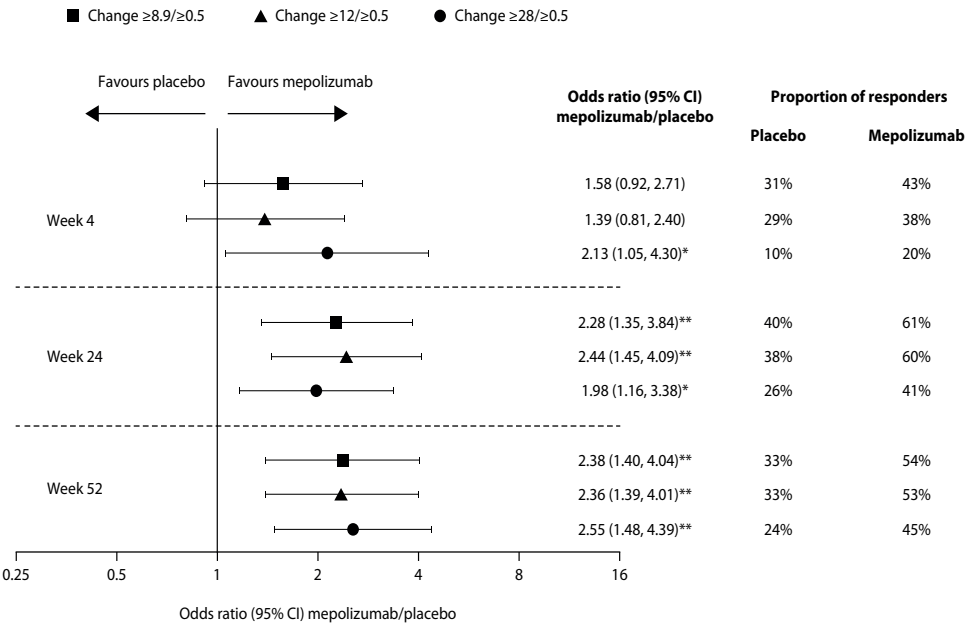

Figure 1. Odds ratios for patients with severe CRSwNP and asthma simultaneously achieving a MCID in SNOT-22 (≥8.9, ≥12 or ≥28) and ACQ-5 (≥0.5) at Weeks 4, 24 and 52. *p<0.05; **p≤0.002. Placebo: n=144; mepolizumab: n=138. ACQ-5, Asthma Control Questionnaire-5 items; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; MCID, minimal clinically important difference; SNOT-22, Sino-Nasal Outcomes Test-22 items.

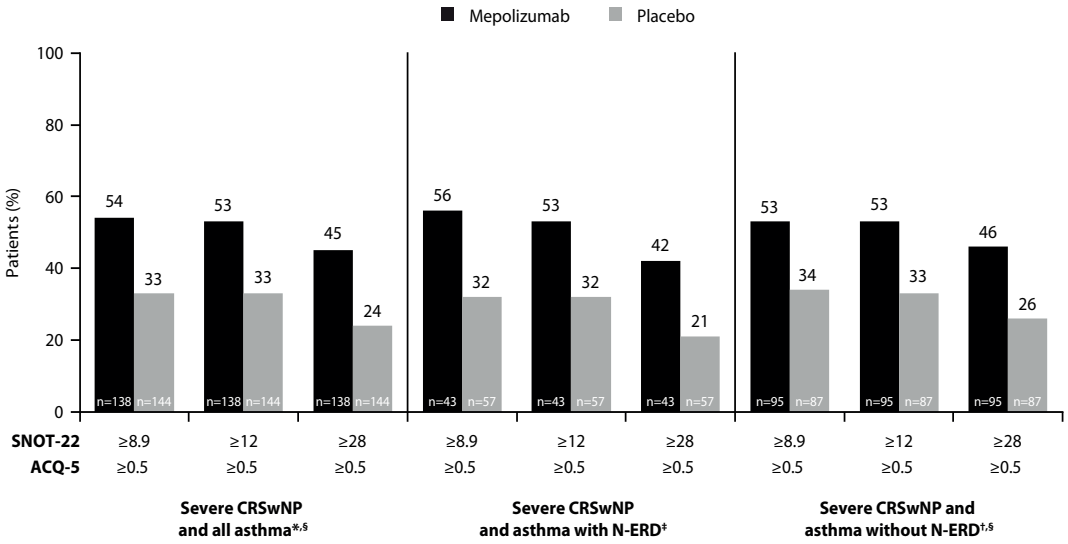

Figure 2. Proportion of patients with severe CRSwNP and asthma, and severe CRSwNP and asthma with or without N-ERD, who simultaneously achieved a MCID in SNOT-22 (≥8.9, ≥12 or ≥28) and ACQ-5 (≥0.5) at Week 52. * Excludes six patients (placebo, 5; mepolizumab, 1) with missing SNOT-22 and/or ACQ-5 scores at baseline; † excludes three patients (placebo, 2; mepolizumab, 1) with missing SNOT-22 and/or ACQ-5 scores at baseline; ‡ excludes three patients (placebo, 3; mepolizumab, 0) with missing SNOT-22 and/or ACQ-5 scores at baseline; § excludes one additional mepolizumab-treated patient with no ACQ-5 records. ACQ-5, Asthma Control Questionnaire-5 items; CRSwNP, chronic rhinosinusitis with nasal polyps; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; SNOT-22, Sino-Nasal Outcomes Test-22 items.

similar between responders and non-responders (Supplementary Tables 1 and 2).

Conclusion

Our findings demonstrate that mepolizumab showed a statistically significant, clinically meaningful, patient-reported, simultaneous improvement in sinonasal and asthma outcomes in patients with severe CRSwNP and asthma/N-ERD versus placebo. These positive effects on multimorbid disease became evident as early as 4 weeks after the first dose and were sustained for

52 weeks. These results highlight the potential for mepolizumab to swiftly provide, and sustain, a simultaneous clinical benefit in both upper and lower respiratory diseases within the framework of global airway disease.

List of abbreviations

ACQ-5, Asthma Control Questionnaire-5 items; CRSwNP, chronic rhinosinusitis with nasal polyps; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; SNOT-22, Sino-Nasal Outcome Test-22 items; VAS, visual analogue scale.

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Authorship contribution

ALM, RC-P, LZ and PS were involved in the conception or design of the study. All authors contributed to data analysis or interpretation, and to critically reviewing the manuscript and approving the final version for submission.

Conflict of interest

JM has received funding from research grants/clinical trials from AstraZeneca, GSK, Viatris, Optinose, Novartis, Regeneron, Sanofi-Genzyme and Noucor/Uriach Group; consulting fees from Sanofi-Genzyme and Noucor/Uriach Group; and attended speaker bureaus and/or advisory boards for Almirall, AstraZeneca, Genentech, GSK, Glenmark, Lilly, Menarini, Mitsubishi-Tanabe, MSD, Noucor/Uriach Group, Novartis, Procter & Gamble, Regeneron, Sanofi-Genzyme, UCB Pharma and Viatris. VB has received research grants, participated in advisory boards, and developed pharmaceutical studies for GSK, AstraZeneca, Sanofi, Novartis, MSD, Pharmaxis, Birk NPC and Chiesi. JC has received honoraria for consultancy from GSK. IE-G has no conflicts of interest to declare. PH has received grants or contracts, consulting fees, and payment or honoraria from GSK, Sanofi, Regeneron, Novartis, Viatris and AstraZeneca. ALM, RC-P, LZ, PS and WK are employed by GSK and hold financial equities in GSK.

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Data sharing

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/.

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Joaquim Mullol
Department of Otorhinolaryngology
Hospital Clínic Barcelona
FRCB-IDIBAPS
Villarroel 170
08036, Barcelona
Catalonia
Spain

Tel: +34 932 279 872
E-mail: JMULLOL@clinic.cat

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SUPPLEMENTARY MATERIAL

Materials and methods

Study population (patients)

Adults with recurrent, refractory, severe and symptomatic chronic rhinosinusitis with bilateral nasal polyps (CRSwNP) were included in SYNAPSE [1]. Scores of >5 for nasal obstruction and >7 for overall sinonasal symptoms (severe) using visual analogue scale (VAS, 0–10) were required, along with a score ≥5/8 for endoscopic bilateral nasal polyp size (NPS; with a minimum score of 2 in each nasal cavity). Patients were also required to have had ≥1 endoscopic sinus surgery in the last 10 years, and stable maintenance therapy with intranasal corticosteroid (mometasone furoate) spray for ≥8 weeks prior to screening. In this post hoc analysis, patients in SYNAPSE who had a clinical history of asthma or non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD) according to their medical history were included.

Assessments and endpoints

Patients completed the Sino-Nasal Outcome Test (SNOT-22) using an electronic diary (eDiary) at randomisation and every 4 weeks thereafter. SNOT-22 measures symptoms and impacts related to severe CRSwNP in the last 2 weeks. Patients with an improvement of an ≥8.9 decrease in overall score (0–110) from baseline to Week 52 were considered responders (minimal clinically important difference; MCID) [2]. Two additional, more stringent, criteria for SNOT-22 MCIDs of ≥12 and ≥28 were also used and assessed. These additional MCIDs were used as it has been suggested that using a value of 8.9 for medically managed patients might not accurately address clinically meaningful differences, and the alternative MCID of ≥12 has previously been proposed for this population [3]. A previous post hoc analysis of SYNAPSE data suggested that a ≥28-point improvement in SNOT-22 was an appropriate threshold for meaningful within-patient improvement for the very severe population evaluated in SYNAPSE [4].

Patients also completed a daily symptom VAS (0–10) throughout the study using an eDiary, to indicate the severity of overall symptoms and individual symptoms of nasal obstruction, nasal discharge, mucus in the throat, reduction/loss of smell and facial pain/pressure. The MCID for within-patient improvement was a change of −2.5 points for overall symptoms, nasal discharge and facial pain/pressure, and −3.0 points for nasal obstruction, loss of smell and mucus in the throat [4].

Eligible patients with a clinical diagnosis of asthma also completed the Asthma Control Questionnaire (ACQ-5) at randomisation and every 4 weeks using the eDiary. The most recent guidelines from the Global Strategy for Asthma Management and Prevention state that an improvement of ≥0.5 in total score ACQ is considered as the MCID for this endpoint and so an improvement of ≥0.5 in total score was considered the MCID in this study [5]. In addition, GINA guidelines state that the crossover between poorly- and well-controlled asthma has been shown to be close to an ACQ-5 score of 1.00, and therefore a score of ≥1 was determined the threshold for poorly-controlled asthma, with a score <1 more likely indicating well-controlled asthma [6-7].

This post hoc analysis utilised composite endpoints to evaluate the effects of mepolizumab versus placebo on patients with multimorbid severe CRSwNP and asthma/N-ERD (defined as CRSwNP with comorbid asthma and N-ERD, or CRSwNP with comorbid asthma without N-ERD), to determine whether simultaneous improvements in both conditions were achieved. Odds ratios (OR) for patients with multimorbid asthma or N-ERD simultaneously achieving a MCID in both SNOT-22 (thresholds of 8.9, 12 and 28) and ACQ-5 (threshold of 0.5) were calculated for treatment with mepolizumab versus placebo at Weeks 4, 24 and 52. An additional analysis of patients who had an ACQ-5 score of ≤1 at Week 52, plus an MCID in SNOT-22 (all thresholds) was also completed. Baseline demographics (sex, age and body mass index), clinical characteristics (time since diagnosis of CRSwNP, number of previous sinus surgeries, number of oral corticosteroid courses for severe CRSwNP in the previous 12 months, NPS score, nasal obstruction [VAS score], overall sinonasal symptoms [VAS score], quality of life [SNOT-22] score, and clinical history of N-ERD) and blood eosinophil count (cells/μL) were compared between those who achieved a MCID in both SNOT-22 (8.9 and 28 threshold only) and ACQ-5 (0.5) at Week 52 (responders), and those who did not (non-responders).

The proportions of patients with multimorbid asthma and N-ERD at baseline who simultaneously achieved a MCID in both SNOT-22 (thresholds of 8.9, 12 and 28) and ACQ-5 (threshold of 0.5) at Week 52 were calculated. Patients with severe CRSwNP and multimorbid asthma but without N-ERD were also analysed. ORs for patients with multimorbid asthma simultaneously achieving an MCID in overall and specific symptoms VAS (using various thresholds as described earlier (4)) and ACQ-5 (threshold of 0.5) were calculated for treatment with mepolizumab versus placebo at Weeks 49–52.

Statistical analysis

All analyses were performed on the intent-to-treat population but in a subset of patients with asthma or N-ERD. Patients were classified as responders or non-responders at each visit up to and including Week 52, for various endpoints based on the MCID of the endpoint of interest. Patients with nasal surgery/sinuplasty prior to visit, patients who withdrew from study with no surgery/sinuplasty and patients with missing visit data were

assigned their worst observed score prior to nasal surgery/sinuplasty or study withdrawal or the missing visit, respectively. The proportion of responders was analysed at each visit separately using a logistic regression model with covariates of treatment group, geographic region, baseline score and log(e) baseline blood eosinophil count. The likelihood of patients achieving a response with mepolizumab versus placebo were calculated as ORs with corresponding 95% confidence interval and p-value.

Supplementary results

When considering patients achieving an ACQ-5 of ≤1 combined with a MCID in SNOT-22 (8.9, 12 or 28) at Week 52, statistically this was also more likely to be achieved in those receiving mepolizumab than placebo. A similar magnitude of effect was observed across SNOT-22 MCIDs of 8.9 (OR 2.17 [95% CI 1.31, 3.59], p=0.003), 12 (2.22 [95% CI 1.34, 3.68], p=0.002), and 28 (3.08 [95% CI 1.81, 5.24] p<0.001).

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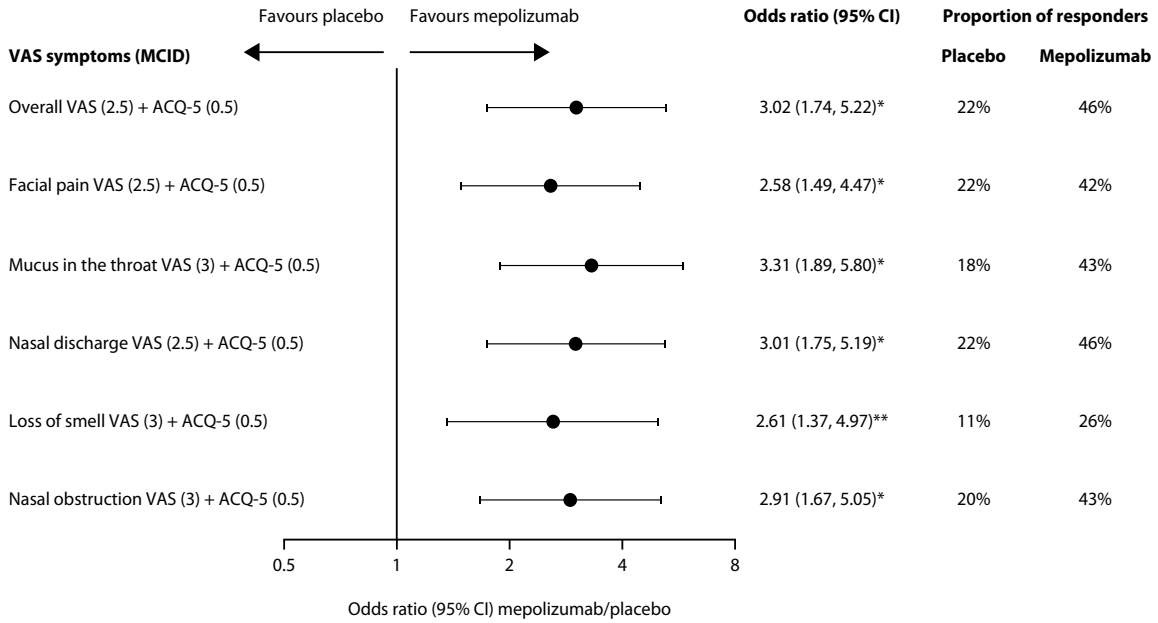

Supplementary Figure 1. Odds ratios for patients with severe CRSwNP and asthma simultaneously achieving a MCID in specific symptoms of VAS and ACQ-5 (0.5) at Week 52. *p<0.01; **p=0.003. Placebo: n=144; mepolizumab: n=138. ACQ-5, Asthma Control Questionnaire-5 items; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; MCID, minimal clinically important difference; VAS, visual analogue scale.

Supplementary Table 1. Baseline disease characteristics of patients with severe CRSwNP and asthma who simultaneously achieved a MCID in SNOT-22 (≥8.9) and ACQ-5 (≥0.5) at Week 52 (responders) and those who did not (non-responders).

	Responders			Non-responders		
Characteristics	**Placebo (N=48)**	**Mepolizumab (N=74)**	**Total (N=122)**	**Placebo (N=96)**	**Mepolizumab (N=64)**	**Total (N=160)**
Female, n (%)	23 (48)	32 (43)	55 (45)	40 (42)	15 (23)	55 (34)
Age, years, mean (SD)	47.7 (12.4)	49.1 (12.9)	48.6 (12.7)	49.7 (12.1)	47.7 (13.9)	48.9 (12.9)
BMI, kg/m^2, mean (SD)	27.2 (5.8)	28.4 (5.8)	27.9 (5.8)	28.9 (5.6)	27.7 (4.5)	28.4 (5.2)
Time since diagnosis of severe CRSwNP, n (%)						
<1 year	1 (2)	0	1 (<1)	2 (2)	0	2 (1)
1 to <5 years	12 (25)	8 (11)	20 (16)	11 (11)	17 (27)	28 (18)
5 to <10 years	14 (29)	24 (32)	38 (31)	32 (33)	15 (23)	47 (29)
10 to <15 years	11 (23)	21 (28)	32 (26)	16 (17)	12 (19)	28 (18)
15 to <20 years	4 (8)	15 (20)	19 (16)	23 (24)	7 (11)	30 (19)
20 to <25 years	3 (6)	1 (1)	4 (3)	7 (7)	6 (9)	13 (8)
≥25 years	3 (6)	5 (7)	8 (7)	5 (5)	7 (11)	12 (8)
Time since diagnosis of severe CRSwNP, years, mean (SD)	10.4 (8.0)	11.8 (6.9)	11.3 (7.4)	12.0 (7.5)	11.9 (9.2)	12.0 (8.2)
Number of previous ESS for severe CRSwNP in the past 10 years, n (%)						
1	22 (46)	34 (46)	56 (46)	31 (32)	34 (53)	65 (41)
2	15 (31)	18 (24)	33 (27)	18 (19)	15 (23)	33 (21)
3	8 (17)	13 (18)	21 (17)	22 (23)	5 (8)	27 (17)
>3	3 (6)	9 (12)	12 (10)	25 (26)	10 (16)	35 (22)
Number of courses of OCS for severe CRSwNP in the previous 12 months, n (%)						
0	27 (56)	29 (39)	56 (46)	46 (48)	28 (44)	74 (46)
1	10 (21)	28 (38)	38 (31)	26 (27)	20 (31)	46 (29)
2	5 (10)	8 (11)	13 (11)	8 (8)	5 (8)	13 (8)
>2	6 (13)	9 (12)	15 (12)	16 (17)	11 (17)	27 (17)
Nasal polyp size score (0–8), mean (SD)	5.0 (1.3)	5.4 (1.0)	5.2 (1.1)	5.9 (1.3)	5.7 (1.2)	5.8 (1.3)
Nasal polyp size score (0–8), median (Q1, Q3)	5.0 (4.0, 6.0)	5.0 (4.0, 6.0)	5.0 (4.0, 6.0)	6.0 (5.0, 7.0)	6.0 (5.0, 6.0)	6.0 (5.0, 7.0)
Nasal obstruction (VAS 0–10), mean (SD)	9.1 (0.8)	8.9 (0.9)	8.98 (0.8)	9.1 (0.8)	9.0 (0.8)	9.05 (0.8)
Nasal obstruction (VAS 0–10), median (Q1, Q3)	9.1 (0.8)	8.9 (0.9)	8.98 (0.8)	9.1 (0.8)	9.0 (0.8)	9.05 (0.8)
Overall sinonasal symptoms / disease severity (VAS 0–10), mean (SD)	9.4 (8.7, 9.6)	9.1 (8.2, 9.6)	9.2 (8.3, 9.6)	9.1 (8.6, 9.8)	9.1 (8.3, 9.7)	9.1 (8.5, 9.8)
Overall sinonasal symptoms / disease severity (VAS 0–10), median (Q1, Q3)	9.2 (0.7)	9.1 (0.8)	9.09 (0.8)	9.1 (0.8)	9.0 (0.8)	9.08 (0.8)
SNOT-22 total score (0–110), mean (SD)	9.3 (8.9, 9.7)	9.2 (8.4, 9.7)	9.3 (8.5, 9.7)	9.3 (8.6, 9.8)	9.1 (8.3, 9.7)	9.2 (8.5, 9.8)
SNOT-22 total score (0–110), median (Q1, Q3)	73.5 (12.6)	69.7 (16.3)	71.2 (15.0)	63.7 (18.9)	63.5 (18.8)	63.6 (18.8)
Patients with N-ERD, n (%)	72.0 (64.0, 84.0)	69.0 (61.0, 81.0)	71.0 (63.0, 81.0)	62.0 (51.0, 77.0)	62.0 (51.0, 77.0)	62.0 (51.0, 77.0)
BEC, cells/µL, geometric mean (95% CI)	18 (38)	24 (32)	42 (34)	39 (41)	19 (30)	58 (36)
BEC category, n (%)						
≤300 cells/µL	15 (31)	19 (26)	34 (28)	26 (27)	16 (25)	42 (26)
>300 to 500 cells/µL	16 (33)	18 (24)	34 (28)	25 (26)	19 (30)	44 (28)
>500 to 700 cells/µL	6 (13)	12 (16)	18 (15)	17 (18)	11 (17)	28 (18)
>700 cells/µL	11 (23)	25 (34)	36 (30)	28 (29)	18 (28)	46 (29)

ACQ-5, Asthma Control Questionnaire-5 items; BEC, blood eosinophil count; BMI, body mass index; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; ESS, endoscopic sinus surgery; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; OCS, oral corticosteroid; SD, standard deviation; SNOT-22, Sino-Nasal Outcomes Test-22 items; VAS, visual analogue scale.

Supplementary Table 2. Baseline disease characteristics of patients with severe CRSwNP and asthma* who simultaneously achieved a MCID in SNOT-22 (≥28) and ACQ-5 (≥0.5) at Week 52 (responders) and those who did not (non-responders).

	Responders			Non-responders		
Characteristics	**Placebo (N=35)**	**Mepolizumab (N=62)**	**Total (N=97)**	**Placebo (N=109)**	**Mepolizumab (N=76)**	**Total (N=185)**
Female, n (%)	17 (49)	25 (40)	42 (43)	46 (42)	22 (29)	68 (37)
Age, years, mean (SD)	47.1 (12.6)	49.5 (13.3)	48.6 (13.0)	49.7 (12.1)	47.6 (13.4)	48.8 (12.6)
BMI, kg/m², mean (SD)	27.7 (6.3)	28.6 (6.1)	28.3 (6.2)	28.6 (5.5)	27.6 (4.4)	28.2 (5.1)
Time since diagnosis of severe CRSwNP, n (%)						
<1 year	1 (3)	0	1 (1)	2 (2)	0	2 (1)
1 to <5 years	7 (20)	6 (10)	13 (13)	16 (15)	19 (25)	35 (19)
5 to <10 years	11 (31)	18 (29)	29 (30)	35 (32)	21 (28)	56 (30)
10 to <15 years	7 (20)	20 (32)	27 (28)	20 (18)	13 (17)	33 (18)
15 to <20 years	4 (11)	14 (23)	18 (19)	23 (21)	8 (11)	31 (17)
20 to <25 years	2 (6)	0	2 (2)	8 (7)	7 (9)	15 (8)
≥25 years	3 (9)	4 (6)	7 (7)	5 (5)	8 (11)	13 (7)
Time since diagnosis of severe CRSwNP, years, mean (SD)	11.2 (8.8)	12.0 (6.8)	11.7 (7.6)	11.6 (7.3)	11.7 (8.9)	11.6 (8.0)
Number of previous ESS for severe CRSwNP in the past 10 years, n (%)						
1	15 (43)	29 (47)	44 (45)	38 (35)	39 (51)	77 (42)
2	10 (29)	16 (26)	26 (27)	23 (21)	17 (22)	40 (22)
3	7 (20)	8 (13)	15 (15)	23 (21)	10 (13)	33 (18)
>3	3 (9)	9 (15)	12 (12)	25 (23)	10 (13)	35 (19)
Number of courses of OCS for severe CRSwNP in the previous 12 months, n (%)						
0	19 (54)	25 (40)	44 (45)	54 (50)	32 (42)	86 (46)
1	8 (23)	26 (42)	34 (35)	28 (26)	22 (29)	50 (27)
2	3 (9)	7 (11)	10 (10)	10 (9)	6 (8)	16 (9)
>2	5 (14)	4 (6)	9 (9)	17 (16)	16 (21)	33 (18)
Nasal polyp size score (0–8), mean (SD)	5.0 (1.4)	5.4 (1.1)	5.3 (1.2)	5.8 (1.3)	5.6 (1.1)	5.7 (1.3)
Nasal polyp size score (0–8), median (Q1, Q3)	5.0 (4.0, 6.0)	5.0 (5.0, 6.0)	5.0 (5.0, 6.0)	6.0 (5.0, 7.0)	5.0 (5.0, 6.0)	6.0 (5.0, 6.0)
Nasal obstruction (VAS 0–10), mean (SD)	9.07 (0.8)	8.86 (0.9)	8.94 (0.9)	9.10 (0.8)	9.00 (0.8)	9.06 (0.8)
Nasal obstruction (VAS 0–10), median (Q1, Q3)	9.3 (8.6, 9.6)	9.1 (8.1, 9.6)	9.1 (8.2, 9.6)	9.2 (8.6, 9.8)	9.1 (8.3, 9.7)	9.2 (8.5, 9.8)
Overall sinonasal symptoms (VAS 0–10), mean (SD)	9.16 (0.8)	9.02 (0.8)	9.07 (0.8)	9.13 (0.8)	9.03 (0.8)	9.09 (0.8)
Overall sinonasal symptoms / disease severity (VAS 0–10), median (Q1, Q3)	9.3 (9.0, 9.7)	9.2 (8.2, 9.7)	9.2 (8.5, 9.7)	9.3 (8.6, 9.8)	9.2 (8.4, 9.7)	9.2 (8.5, 9.8)
SNOT-22 total score (0–110), mean (SD)	73.7 (13.4)	70.7 (16.2)	71.8 (15.2)	64.8 (18.4)	63.6 (18.4)	64.4 (18.3)
SNOT-22 total score (0–110), median (Q1, Q3)	71.0 (63.0, 85.0)	71.0 (61.0, 81.0)	71.0 (63.0, 83.0)	67.0 (53.0, 77.0)	63.0 (51.0, 77.0)	64.0 (52.0, 77.0)
Patients with N-ERD, n (%)	12 (34)	18 (29)	30 (31)	45 (41)	25 (33)	70 (38)
BEC, cells/μL, geometric mean (95% CI)	410 (310, 530)	500 (420, 600)	470 (400, 540)	430 (370, 500)	420 (350, 510)	430 (380, 480)
BEC category, n (%)						
≤300 cells/μL	11 (31)	14 (23)	25 (26)	30 (28)	21 (28)	51 (28)
>300 to 500 cells/μL	11 (31)	15 (24)	26 (27)	30 (28)	22 (29)	52 (28)
>500 to 700 cells/μL	5 (14)	11 (18)	16 (16)	18 (17)	12 (16)	30 (16)
>700 cells/μL	8 (23)	22 (35)	30 (31)	31 (28)	21 (28)	52 (28)

* Data missing for two patients in the mepolizumab group and five patients in the placebo group due to scores not being available.

ACQ-5, Asthma Control Questionnaire-5 items; BEC, blood eosinophil count; BMI, body mass index; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; ESS, endoscopic sinus surgery; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; OCS, oral corticosteroid; SD, standard deviation; SNOT-22, Sino-Nasal Outcomes Test-22 items; VAS, visual analogue scale.