Mepolizumab improves quality of life and reduces activity impairments in patients with CRSwNP*

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Dear Editor:

Severe chronic rhinosinusitis with nasal polyps (CRSwNP) is associated with a range of symptoms, such as nasal congestion and facial pain, that have a significant and detrimental impact on health-related quality of life (HRQoL) and patients' ability to work [1-5]. Substantial direct and indirect costs are also incurred from CRSwNP [3-5]. The Phase III SYNAPSE study assessed the efficacy and safety of mepolizumab, a humanised anti-interleukin-5 monoclonal antibody, in addition to standard of care in adults with severe CRSwNP [1]. In SYNAPSE, mepolizumab 100 mg administered subcutaneously (SC) reduced nasal polyp size, improved nasal obstruction and reduced the need for sinus surgery versus placebo [1]. This post hoc exploratory analysis of SYNAPSE evaluated the impact of mepolizumab compared with placebo on patients' HRQoL and work productivity and activity levels, outcomes that are of high importance to patients.

The study design and eligibility criteria of SYNAPSE have been published previously [1]. Briefly, SYNAPSE was a randomised, double-blind, placebo-controlled, parallel-group trial (GSK ID:205687; NCT03085797). Following a 4-week run-in period, adults with severe CRSwNP (endoscopic bilateral nasal polyp score ≥5, obstruction visual analogue scale [VAS] symptom score of >5 and overall VAS symptom score >7) who were eligible for repeat surgery were randomised 1:1 to treatment with mepolizumab 100 mg SC or placebo every 4 weeks for 52 weeks, in addition to standard of care (saline nasal irrigation, intranasal corticosteroids) and rescue medication (systemic corticosteroids [SCS], antibiotics) as required. The endpoints of focus in this analysis were change from baseline to Week 52 in: HRQoL, measured using the 36-item short-form (SF-36) survey; and work productivity and daily activity, measured by the Work Productivity and Activity Impairment (WPAI) questionnaire.

The SF-36, described in detail elsewhere [6], was completed at Weeks 0, 4 and then every 8 weeks with a 4-weekly recall period. The between-group mean differences in score were interpreted using minimally important differences (MID) [6]. The WPAI questionnaire measured absenteeism and presenteeism and was completed every 4 weeks from Weeks 0 to 52. Only the 304 employed patients (placebo=151, mepolizumab=153) reported on work impairment at baseline.

Of the 407 patients in the intention-to-treat SYNAPSE population, 403 (placebo=198, mepolizumab=205) had baseline HRQoL measurements. At baseline, patients showed impaired HRQoL: mean SF-36 scores of the whole population were <50, where 50 is the mean HRQoL score representative of the general US population [7] (Table 1). At Week 52, patients treated with mepolizumab showed greater improvements from baseline in SF-36 domain and summary scores versus placebo (Figure 1A, 1B). The adjusted mean differences between mepolizumab and placebo at Week 52 were statistically significant for all individual

Table 1. Baseline patient demographics, HRQoL, work productivity and activity scores

	Placebo (N=201)	Mepolizumab 100 mg SC (N=206)
Age* (years), mean (SD)	48.9 (12.5)	48.6 (13.6)
Female, n (%)	76 (37.8)	67 (32.5)
Duration of nasal polyps (years), mean (SD)	11.5 (8.3)	11.4 (8.5)
Number of previous surgeries for NP in the past 10 years, n (%)		
1	81 (40.3)	108 (52.4)
2–5	109 (54.2)	91 (44.2)
>5	11 (5.5)	7 (3.4)
Number of patients with ≥1 course of OCS for NP in previous 12 months, n (%)	91 (45.3)	106 (51.5)
Baseline total endoscopic score†, mean (SD)	5.6 (1.4)	5.4 (1.2)
Baseline nasal obstruction VAS† score, mean (SD)	9.0 (0.8)	8.9 (0.8)
Baseline overall VAS† score, mean (SD)	9.1 (0.7)	9.0 (0.8)
Baseline SNOT-22‡ total score, mean (SD)	64.4 (19.0)	63.7 (17.6)
Patients with asthma, n (%)	149 (74.1)	140 (68.0)
SF-36§ domain scores (norm based score^), mean (SD)		
Physical functioning	45.8 (9.2)	44.8 (9.4)
Role limitation due to physical health	44.4 (8.8)	42.9 (8.8)
Bodily pain	46.2 (10.2)	45.5 (9.6)
General health	41.4 (10.0)	40.5 (8.8)
Energy/fatigue (vitality)	46.0 (9.8)	44.7 (10.2)
Social functioning	44.9 (10.3)	44.6 (9.9)
Role limitation due to emotional health	45.1 (10.7)	44.4 (10.6)
Mental health (emotional well-being)	45.4 (10.6)	44.1 (10.2)
SF-36§ physical summary score^, mean (SD)	44.8 (7.8)	43.8 (8.1)
SF-36§ mental summary score^, mean (SD)	45.5 (10.8)	44.7 (10.6)
WPAI questionnaire**		
Patients in employment, n (%)	151 (75)	153 (74)
Work time missed due to health (%), mean (SD)	5.0 (12.9)	4.9 (12.9)
Impairment while working due to health (%), mean (SD)	50.1 (30.8)	48.1 (29.0)
Overall work impairment due to health (%), mean (SD)	50.8 (31.8)	49.5 (29.8)
Responses to regular daily activity impairment, n (%)	198 (99)	204 (99)
Regular daily activity impairment due to health (%), mean (SD)	53.2 (29.1)	53.4 (28.0)

* Age was derived at the date of the screening visit from reported year of birth and imputed day and month of 30 June; † Higher scores indicate greater disease severity; ‡ Higher scores indicate worse quality of life; § Lower scores indicate worse quality of life. ^ The physical summary score and mental summary score are scored using standardised domains based on the 2009 U.S. general population, with a range of 0 to 100[6]. **Higher scores indicate greater impairment. HRQoL, health-related quality of life; NP, nasal polyps; OCS, oral corticosteroids; SC, subcutaneous; SD, standard deviation; SF-36, 36-item short-form survey; SNOT, sino-nasal outcome test; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment.

domain and summary scores (Figure 1C). While the LS mean change in 7/8 domains and the physical summary score exceeded their respective MID (MID ranged from 2–4), the greatest improvement was seen for general health and the smallest improvement in role limitation due to emotional health. Interestingly, there was a large improvement in bodily pain score with mepolizumab versus placebo; significant bodily pain is an uncommon but important symptom for patients with CRSwNP [4, 8]. Due to lack of specificity of the bodily pain questions in SF-36, these data may reflect improvements in facial pain. Analysis of changes in the physical summary score over time showed that patients in both treatment groups experienced increases from baseline over 52 weeks, with the first response observed at Week 12; however, this had begun to reduce by Week 28 in the place-

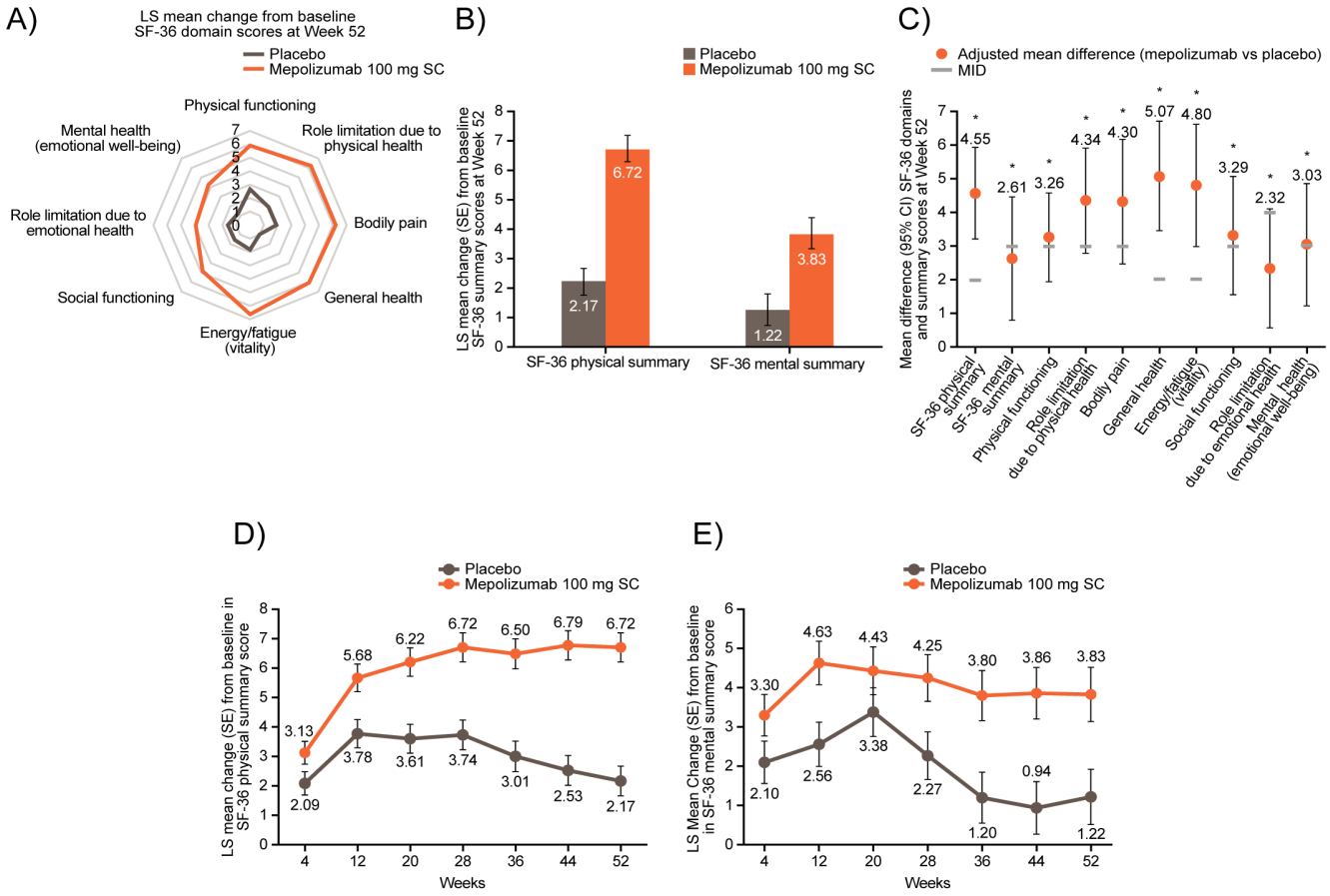

Figure 1. SF-36 scores. (A) LS mean change from baseline in SF-36 domains at Week 52; (B) LS mean change from baseline in SF-36 summary scores at Week 52; (C) adjusted mean difference (mepolizumab-placebo) at Week 52; (D) mean change from baseline in physical summary scores over time; (E) mean change from baseline in mental summary scores over time.

*p<0.05. Error bars for panels B), D) and E) represent SE and error bars for panel C) represent 95% CI. Analysis performed using mixed model repeated measures with covariates of treatment group, geographical region, baseline, log(e) baseline blood eosinophil count, visit plus interaction terms for visit by baseline and visit by treatment group. Estimates are based on weighting applied to each level of class variable determined from observed proportions. Patients with nasal surgery/sinuplasty prior to visit, patients who withdrew from study with no surgery/sinuplasty and subjects with missing visit data are assigned their worst observed score prior to nasal surgery/sinuplasty or study withdrawal or missing visit, respectively. 1 patient from the mepolizumab group and 3 patients from the placebo group with missing baseline score were excluded from the analysis.

CI, confidence interval; LS, least squares; MID, minimal important difference; SC, subcutaneous; SE, standard error; SF-36, 36-item short-form survey.

bo group, while the mepolizumab group generally maintained their improvements until Week 52 (Figure 1D). Improvements in the mental summary score were observed in both treatment groups; the largest numerical change from baseline was at Week 12 for mepolizumab and Week 20 for placebo. Mepolizumab-treated patients maintained their improvements over the 52 weeks, while improvements diminished in placebo-treated patients (Figure 1E). Overall, patients treated with mepolizumab reached SF-36 scores ≥50 in 3/8 individual domains (physical functioning, bodily pain, energy/fatigue) and the physical summary score at Week 52 compared with no domains for patients treated with placebo.

At baseline, patients in both treatment groups reported 50% impairment in work productivity (Table 1). At Week 52, mepolizumab demonstrated numerical improvements from baseline on all WPAI measures (Figure 2). A statistically significant improvement in regular daily activity impairment due to health was observed with mepolizumab versus placebo (p=0.002); however, no statistically significant differences were observed for work time missed, impairment while working and overall impairment, due to health (Figure 2). Regular daily activity impairment was assessed in the 401 patients who provided responses (placebo=197, mepolizumab=204).

One limitation of our analysis is that normalising SF-36 scoring to the 2009 US general population means these results may not be easily generalised to populations outside of the US.

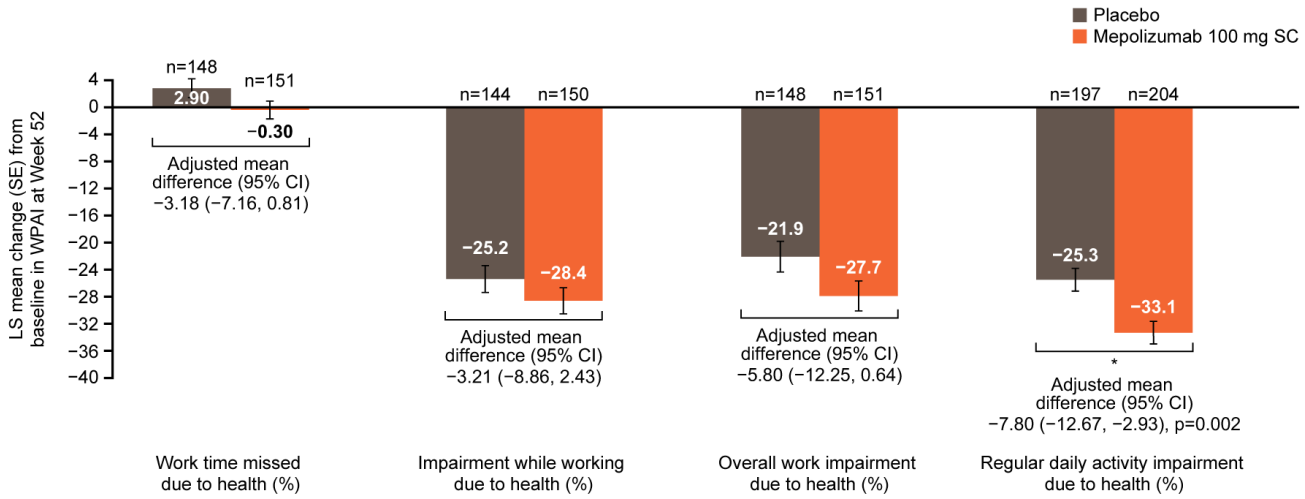

Figure 2. LS mean change from baseline and adjusted mean difference (mepolizumab – placebo) in WPAI scores at Week 52. *p<0.05. Analysis performed using mixed model repeated measures with covariates of treatment group, geographical region, baseline, log(e) baseline blood eosinophil count, visit plus interaction terms for visit by baseline and visit by treatment group. Estimates are based on weighting applied to each level of class variable determined from observed proportions.

LS, least squares; SC, subcutaneous; SE, standard error; WPAI, Work Productivity and Activity Impairment.

Furthermore, the WPAI questionnaire used here is the general health version; whilst widely used for assessing WPAI across a range of chronic conditions, this has not been specifically validated for use in patients with CRSwNP and may lack sensitivity to detect changes in these patients.

This analysis of the SYNAPSE study shows that patients with CRSwNP who were treated with mepolizumab had improved HRQoL and reduced activity impairment by Week 52 compared with placebo (standard of care treatment only). These data provide insight into the beneficial impact of mepolizumab on patient quality of life, activity levels and their ability to work, highlighting mepolizumab as a promising treatment for CRSwNP with meaningful impact on patient lives.

Abbreviations

CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; HRQoL, health-related quality of life; LS, least squares; NP, nasal polyps; MID, minimally important difference; SC, subcutaneous; SF-36, 36-item short-form survey; SCS, systemic corticosteroids; SE, standard error; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment.

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Authorship contribution

CB, PWH, VJL, RHC, SGS, ARS, RAC, SY, WJF and CH contributed to study conception or design, data analysis, and interpretation. BM contributed to data analysis and interpretation. All authors contributed to the analysis or interpretation of data, drafted the work, or revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Conflict of interest

Claus Bachert reports advisory board membership and speaker fees for Sanofi, Novartis, ALK, AstraZeneca, GSK and Mylan. Peter W. Hellings reports advisory board membership for Regeneron Pharmaceuticals, Inc., Sanofi, Viatris, Novartis and Stallergenes. Valerie J. Lund reports advisory board and lecture fees from Abbott, GSK, Novartis and Sanofi. Wytske J. Fokkens reports clinical trial funding from Sanofi, Mylan, ALK, Allergy Therapeutics, Novartis, Chordate and GSK and has received personal fees from Sanofi and GSK. Claire Hopkins has received advisory board fees from Sanofi, AstraZeneca, Olympus and GSK. Bhabita Mayer, Robert H. Chan, Steven G. Smith, Ana R. Sousa, Rafael Alfonso-Cristancho and Shibing Yang are employees of GSK and own stocks/shares.

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References

1. Bachert C, Han JK, Wagenmann M, et al. EUFOREA expert board meeting on uncontrolled severe chronic rhinosinusitis with nasal polyps (CRSwNP) and biologics: Definitions and management. J Allergy Clin Immunol. 2021;147(1):29-36.
2. 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(5):632-41.
3. Fokkens WJ, Lund VJ, Hopkins C, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020;58(Suppl S29):1-464.
4. Bachert C, Marple B, Schlosser RJ, et al. Adult chronic rhinosinusitis. Nat Rev Dis Primers. 2020;6(1):86.
5. Rudmik L. Economics of Chronic Rhinosinusitis. Curr Allergy Asthma Rep. 2017;17(4):20.
6. Maurish MEE. User's manual for the SF-36v2 Health Survey (3rd ed.). Lincoln, RI: QualityMetric Incorporated.; 2008.
7. Soler ZM, Colman S, Velez FF, Schlosser RJ. Exhalation delivery system with fluticasone improves quality of life and health status: pooled analysis of phase 3 trials NAVIGATE I and II. Int Forum Allergy Rhinol. 2020;10(7):848-55.
8. Eweiss AZ, Lund VJ, Barlow J, Rose G. Do patients with chronic rhinosinusitis with nasal polyps suffer with facial pain? Rhinology. 2013;51(3):231-5.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Supplementary methods

SF-36 analysis

Analysis was performed using mixed model repeated measures with covariates of treatment group, geographical region, baseline score, log(e) baseline blood eosinophil count, visit plus interaction terms for visit by baseline and visit by treatment group. Patients who underwent nasal surgery/sinuplasty, withdrew from the study or had missing visit data were assigned their worst observed score prior to nasal surgery/sinuplasty, study withdrawal or missing visit, respectively.

WPAI analysis

Analysis was performed using mixed model repeated measures with covariates of treatment group, geographic region, baseline score, log(e) baseline blood eosinophil count, visit plus interaction terms for visit by baseline and visit by treatment group.

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