Change in nasal polyp size as an indicator of treatment response: SYNAPSE trial analysis

Poster No. 336

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Introduction

CRSwNP is a chronic, inflammatory condition of the nose, paranasal sinuses, and upper airways,[1] causing nasal blockage, loss of smell, and facial pain, which negatively impact patients' HRQoL.[1,2]

The Phase III SYNAPSE study assessed the efficacy and safety of mepolizumab, a targeted, humanized, anti–IL-5 monoclonal antibody, plus standard of care, in patients with severe treatment-refractory CRSwNP.[3]

In SYNAPSE, mepolizumab 100 mg SC significantly reduced nasal polyp size (measured using total endoscopic NPS) and symptoms (measured using the VAS and SNOT-22 PROs) compared with placebo.[3]

This post hoc analysis investigated the relationship between NPS and (1) change in PNIF or (2) PROs and PRO responder rates, following treatment with mepolizumab or placebo.

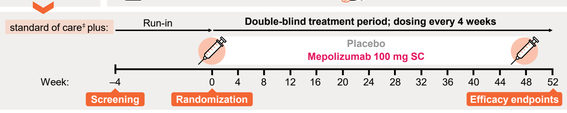
Methods

Study design
GSK ID: 205687/NCT03085797

Phase 3
- Randomized
- Double-blind
- Placebo-controlled
- Parallel group

Eligibility criteria

Inclusion criteria	Exclusion criteria
≥18 years of age	Current or former (<6 months) smokers
≥1 prior sinonasal surgery*	Pre-existing clinically significant conditions that are uncontrolled with standard treatment
Need for sinonasal surgery†	Biologic or immunosuppressant treatment
Bilateral NP diagnosis	Use of SCS <4 weeks prior to screening
Nasal obstruction VAS score >5	



Post hoc analysis

Endpoints

Change from baseline in:
- PNIF§ (Week 52)
- PROs:
  - Symptoms VAS‖ scores (Weeks 49–52)
    overall symptoms, nasal obstruction, loss of smell
  - SNOT-22** total score (Week 52)

Proportion of PRO responders:
- Overall symptoms VAS: ≥2.5-point improvement
- Nasal obstruction/loss of smell VAS: ≥3-point improvement
- SNOT-22: ≥8.9-point improvement

Subgroups and comparisons

NPS†† subgroups:
- ***No NPS improvement‡‡***
  Patients with <1-point improvement or worsening in NPS, from baseline to Week 52
- ***NPS improvement§§***
  Patients with ≥1-point improvement in NPS, from baseline to Week 52

Treatment comparison:
Mepolizumab 100 mg SC vs placebo

*Defined as any procedure involving instruments with resulting incision and removal of NP tissue from the nasal cavity, within the last 10 years; †defined as overall VAS symptom score >7 and total endoscopic NPS ≥5 (≥2 per nasal cavity); ‡daily intranasal mometasone furoate (200 or 400 µg/day) in addition to saline nasal irrigations and courses of SCS and/or antibiotics, as required; §measured using an N-CHECK flow meter; ‖patients used the VAS tool to quantify symptom severity on an electronic device representing a 0–10 cm scale, with 0 conferring total absence of symptom(s) and 10 conferring worst thinkable severity; **22 questions (scale: 0–5/question, 0–110 total; MCID: ≥8.9 points), reported every 4 weeks, with a 2-week recall period and higher scores indicating worse HRQoL; ††sum of the right and left nostril scores (scale: 0–4/nasal cavity, 0–8 total), with higher scores indicating worse status; ‡‡patients with sinonasal surgery prior to Week 52 and patients with no sinonasal surgery who withdrew from the study or had missing Week 52 visit data were assigned their worst score recorded prior to surgery, withdrawal, or missing visit, and were therefore included in the 'no NPS improvement' group; §§in the absence of sinonasal surgery prior to Week 52.

Results

Table 1. Patient baseline demographics and clinical characteristics

	Placebo (n=201)	Mepolizumab (n=206)
Age, years	48.9 (12.5)	48.6 (13.6)
Female, n (%)	76 (38)	67 (33)
Duration of nasal polyps, years	11.5 (8.3)	11.4 (8.5)
Comorbidities, n (%)		
Asthma	149 (74)	140 (68)
Allergic rhinitis	105 (52)	114 (55)
N-ERD	63 (31)	45 (22)
Hypertension	42 (21)	54 (26)
Hypercholesterolemia	31 (15)	20 (10)
NPS	5.6 (1.4)	5.4 (1.2)
NPS categories, n (%)		
<4	12 (6)	11 (5)
4–6	139 (69)	166 (81)
7–8	50 (25)	29 (14)
VAS scores		
Overall symptoms VAS	9.1 (0.7)	9.0 (0.8)
Nasal obstruction VAS	9.0 (0.8)	8.9 (0.8)
Loss of smell VAS	9.7 (0.6)	9.6 (0.8)
SNOT-22 total score	64.4 (19.0)*	63.7 (17.6)†

All values are mean (SD) unless otherwise specified.
*n=198; †n=205.

Figure 1. More patients receiving mepolizumab than placebo achieved ≥1-point improvements in NPS at Week 52

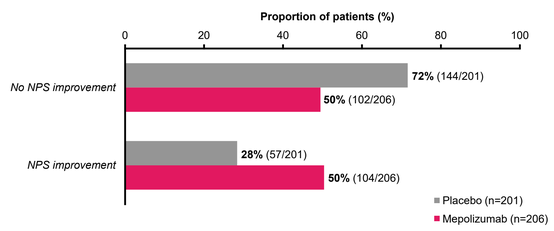
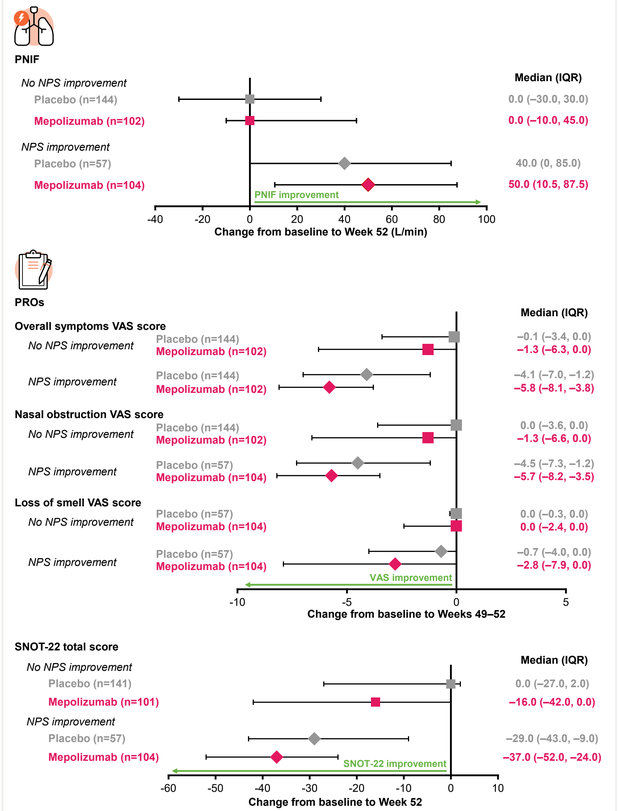


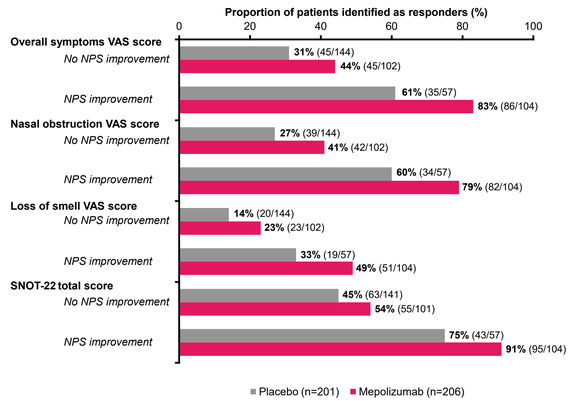
Figure 2. Patients with versus without ≥1-point improvements in NPS from baseline to Week 52 also had larger improvements in PNIF and PROs; consistently larger PRO improvements were seen with mepolizumab versus placebo



Conclusions

- A ≥1-point improvement in NPS from baseline to Week 52 was associated with an increase in PNIF in patients with CRSwNP, irrespective of treatment.
  - This suggests that PNIF could be a useful tool for monitoring nasal polyp size when endoscopy is not available.
- PRO improvements and proportions of PRO responders at study end were larger in patients with versus without ≥1-point NPS improvements from baseline to Week 52, irrespective of treatment.
  - Higher response rates were consistently seen with mepolizumab versus placebo, suggesting that mepolizumab has a clinical effect that is independent of NPS improvements.

Figure 3. Proportions of PRO responders were larger in patients with versus without ≥1-point NPS improvements from baseline to Week 52; consistently higher response rates were seen with mepolizumab versus placebo



References

1. Fokkens WJ et al. *Rhinology* 2020;58(Suppl. 29):1–481.
2. Mullol J et al. *J Allergy Clin Immunol Pract* 2022;10:1434–53.
3. Han JK et al. *Lancet Respir Med* 2021;9(1):1141–53.

Abbreviations

CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; HRQoL, health-related quality of life; IL-5, interleukin-5; IQR, interquartile range; MCID, minimal clinically important difference; N-ERD, non-steroidal anti-inflammatory drug-exacerbated respiratory disease; NP, nasal polyps; NPS, total endoscopic nasal polyp score; PNIF, peak nasal inspiratory flow; PRO, patient-reported outcome; SC, subcutaneous; SCS, systemic corticosteroid; SD, standard deviation; SNOT-22, sino-nasal outcome test; VAS, visual analog scale

Disclosures

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- **AUL** serves as a consultant for Lyra Therapeutics, Medtronic, Sanofi, and Stryker; has served on advisory boards for GSK and AstraZeneca (not associated with this study); and serves on the scientific advisory board for ENTvantage Dx, Maxwell Biosciences, and Third Wave Therapeutics; **JML** has been a consultant for AstraZeneca, GSK, Honeywell International, and Regeneron (not associated with this study); reports grants from Honeywell International, Sanofi/Regeneron, Genentech, and the NIH under awards 1R03TR004022-01 and HL-143541-02S2; **LK** reports grants and personal fees from Allergopharma, Novartis, Bionorica, GSK, and Lofarma, personal fees from MEDA and Boehringer Ingelheim, and grants from Biomay, HAL, LETI Pharma, Roxall, and Bencard, outside the submitted work; **RH** is a consultant/advisory board member with Medtronic, Novartis, Neilmed, Sanofi, GSK, and Viatris Pharmaceuticals. Research grant funding was received from GSK and Stallergenes. He has been on the speakers' bureau for Stallergenes, Sanofi, GSK, AstraZeneca, Viatris Pharmaceuticals, and Seqirus; **AF** is a contract resource for GSK; **PWH** has received research grants and/or consultancy or lecture fees from Sanofi, Regeneron, GSK, Novartis, and AstraZeneca; **JS**, **SGS**, and **RC** are employees of GSK and own stocks/shares.
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