Mepolizumab Improves Health-Related Quality of Life for Patients With Chronic Rhinosinusitis With Nasal Polyps: Data From the SYNAPSE Study

Poster No. 399

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Aims

- Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subtype of CRS, characterized by chronic inflammation of the paranasal sinuses with inflammatory, usually eosinophilic, outgrowths of sinonasal tissue.[1–4]
- Current standard of care includes intranasal corticosteroids, saline nasal douching, short courses of SCS, and sinus surgery.[4]
- The anti–IL-5 humanized monoclonal antibody mepolizumab is an add-on treatment for adults with CRSwNP. Treatment with mepolizumab (750 mg IV, 4-weekly) has been previously shown to reduce NP size, improve symptoms, and reduce need for sinus surgery compared with placebo.[5,6]
- The Phase III SYNAPSE trial assessed the efficacy and safety of 4-weekly mepolizumab 100 mg SC, added to standard of care, in adults with CRSwNP in need of revision surgery.[7]
- We conducted psychometric analyses using blinded data from the Phase III SYNAPSE trial to confirm the structure (eg, domains) and validity of the SNOT-22 for assessing HRQoL and propose a threshold for meaningful within-patient change in patients with CRSwNP in order to aid interpretation of scores in individuals.
- Using the information learned, we also report the efficacy of mepolizumab 100 mg SC for HRQoL in adults with CRSwNP.

Methods

Study design

GSK ID: 205687/NCT03085797 (SYNAPSE)

Phase III trial

Randomized, double blind, placebo-controlled

Patients were given placebo or mepolizumab 100 mg SC every 4 weeks for 52 weeks

Patients were also given standard of care: daily MF and saline nasal douching, occasional short courses of high dose OCS, and/or antibiotics when required

Eligibility criteria

- ≥18 years of age
- ≥1 prior* surgery†
- Need for surgery‡
- Bilateral NP diagnosis
- Obstruction VAS score >5
- Non- or former smoker (>6 month)
- No biologic or immunosuppressant treatment
- No SCS use <4 weeks prior to screening

Co-primary endpoints were:

Change from baseline in total endoscopic NP score at Week 52

Change from baseline in nasal obstruction VAS score during Weeks 49–52

Secondary endpoints included:

Change from baseline in SNOT-22§ Total score at Week 52

Blinded psychometric analyses (post hoc)

SNOT-22 structure and domains

Inter-item correlations for each pair of items on the SNOT-22 were examined using Week 20 data to provide evidence of domains (groupings) within the SNOT-22 and support use of a Total score

- Polychoric correlation coefficients of r>0.3 indicated moderate to strong correlations between items, with r>0.9 indicating possible redundancy

Confirmatory factor analysis (CFA) was performed using Week 20 data to test the structural validity of the hypothesized six-domain SNOT-22 model in CRSwNP

Within-patient meaningful change for SNOT-22

Changes in SNOT-22 Total score between baseline and Week 52 were examined among patients classified as stable, minimally improved, or moderately improved according to change in the overall VAS Symptom score

- Minimal improvement was defined as ≤-2 to >-4 change in overall VAS symptom score
- The mean change in SNOT-22 Total score within the minimally improved anchor group was used to define a threshold for meaningful within-patient change

Efficacy of mepolizumab versus placebo

Mean change in SNOT-22 score for mepolizumab versus placebo was determined for each domain

Efficacy of mepolizumab versus placebo was determined in patients using the threshold for meaningful within-patient change

*Within the last 10 years; †defined as any procedure involving instruments with resulting incision and removal of polyp tissue from the nasal cavity; ‡defined as overall VAS symptom score >7 and an endoscopic bilateral NP score ≥5 (with a minimum score of 2 per nasal cavity); §22 questions, scored 0–5, reported every 4 weeks and reflective of the preceding 2 weeks, with a higher score representing worse HRQoL.

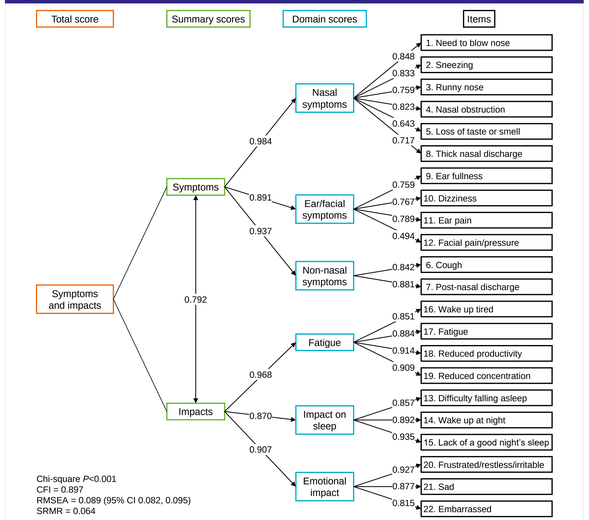
Results

- 206 patients were randomized to mepolizumab 100 mg SC and 201 to placebo.
- Mean (SD) baseline SNOT-22 scores were 63.7 (17.64) in the mepolizumab and 64.4 (19.04) in the placebo groups.

Inter-item correlations and CFA confirms use of a Total score and supports six-domain model in CRSwNP

- Inter-item correlations between each possible pairing of the 22 individual items of the SNOT-22 were moderate to strong (r>0.3), supporting acceptability of the SNOT-22 Total score. There was no item redundancy (ie, r≥0.9).
- The CFA of SNOT-22 data supported the six-domain model with second order symptoms and impact factors (**Figure 1**). All standardized loadings were ≥0.40; therefore, all SNOT-22 items were considered adequate indicators of their respective factors.[8] The validity of the Total score was also supported due to the high correlation between the second order symptoms and impact factors (r=0.792).

Figure 1. The six-domain model with standardized factor loadings

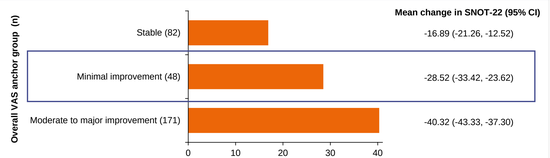


The CFA model, including the standardized factor loadings (numbers on arrows) from each hypothesized domain to the SNOT-22 items and Chi-squared, CFI, RMSEA, and SRMR fit statistics. Standardized factor loadings represent the correlation coefficients between factors.

The meaningful within-patient change threshold in SNOT-22 Total score is 28 points

- Based on responses from 301 patients and using the overall symptom VAS as an anchor, the mean (95% CI) change in SNOT-22 Total score (analyzed using observed data) for patients reporting minimal meaningful improvements in overall symptoms was -28.52 (-33.42, -23.62) points. This was used to define a 28-point meaningful improvement threshold for SNOT-22.

Figure 2. Mean change in SNOT-22 score by VAS anchor group

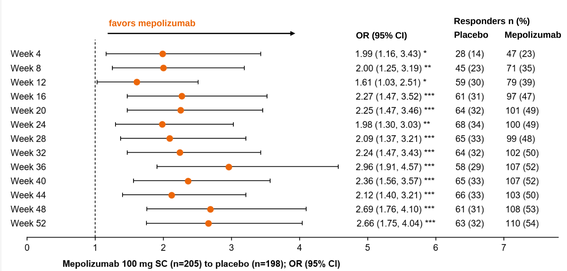


Overall VAS anchor groups were defined by change in overall VAS symptom score from baseline to Week 52: Moderate to major improvement: ≤-4 change VAS score; minimal improvement: ≤-2 to >-4 change VAS score; stable: >-2 to <2 change VAS score.

The odds of a meaningful improvement in HRQoL, as indicated by a ≥28-point improvement in SNOT-22 Total score, was greater with mepolizumab versus placebo at all time points measured

- A significantly higher percentage of patients reported a ≥28-point improvement from baseline SNOT-22 Total score in the mepolizumab versus placebo group from Week 4 to Week 52.

Figure 3. Percentage of patients reporting ≥28 point improvement in SNOT-22 Total score (OR mepolizumab vs placebo)



OR (mepolizumab vs placebo) of percentage of patients reporting ≥28-point improvement in SNOT-22 Total score from baseline (responders). OR >1 indicates greater efficacy of mepolizumab. *, **, *** denotes *P*≤0.05, 0.01, 0.001, respectively. Analysis performed using a logistic regression model with covariates of treatment group, geographic region, baseline score, and log(e) baseline blood eosinophil count.

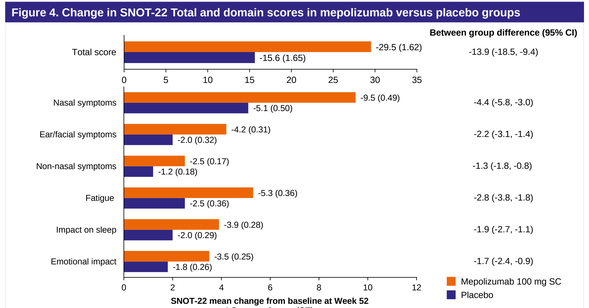
Conclusions

- SNOT-22 is a commonly used patient-reported measure of HRQoL. Psychometric analyses of SYNAPSE confirm the validity of the SNOT-22 Total score (as previously reported[9]) and support a six-domain structure for reporting SNOT-22 results.
- Psychometric analyses also support a 28-point threshold for within-patient meaningful change.
  - This 28-point threshold is substantially larger than estimates for between-group MCID in SNOT-22 score suggested by previous studies[9,10]; however, this larger value is consistent with the finding of qualitative patient research in patients with CRSwNP.[11]
- SYNAPSE data demonstrate significant and meaningful improvements in HRQoL with mepolizumab versus placebo in patients with CRSwNP when measured using the SNOT-22.
  - The likelihood of meaningful improvements in SNOT-22 score is higher with mepolizumab. The greatest change occurs between baseline and Week 4 with the separation between treatment groups sustained throughout the study period.
  - Improvements were seen with mepolizumab versus placebo across all six SNOT-22 domains in the SYNAPSE study.

Mepolizumab treatment resulted in greater improvement in SNOT-22 Total score and each domain score

- Analysis of mean change from baseline in SNOT-22 Total score at Week 52 showed a significant improvement between mepolizumab and placebo groups (*P*<0.001).
- Differences were also seen in each of the six domains.

Figure 4. Change in SNOT-22 Total and domain scores in mepolizumab versus placebo groups



LS mean change from baseline at Week 52 in mepolizumab (n=205) and placebo groups (n=198). Analysis performed using mixed model repeated measures with covariates of treatment group, geographic 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.

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Abbreviations

CFA, confirmatory factor analysis; CFI, comparative fit index; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; HRQoL, health-related quality of life; IL, interleukin; IV, intravenous; LS, least squares; MCID, minimal clinically important difference; MF, mometasone furoate; NP, nasal polyps; OCS, oral corticosteroids; OR, odds ratio; RMSEA, root mean square error of approximation; SC, subcutaneous; SCS, systemic corticosteroids; SD, standard deviation; SE, standard error; SNOT-22, sino-nasal outcome test-22; SRMR, standardized root mean square residual; VAS, visual analog scale

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