

Mepolizumab Induced Loss of Smell Improvement in Patients With Chronic Rhinosinusitis With Nasal Polyps From the SYNAPSE Study

Poster No. 481

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Introduction

In patients with severe chronic rhinosinusitis with nasal polyps (CRSwNP), loss of smell is one of the most bothersome and difficult-to-treat symptoms.¹

Although several factors can impact sense of smell for patients with CRSwNP, those with a history of previous sinus surgeries report higher levels of impaired sense of smell than those without² and can be more likely to experience poor olfactory outcomes following repeat sinus surgeries.³

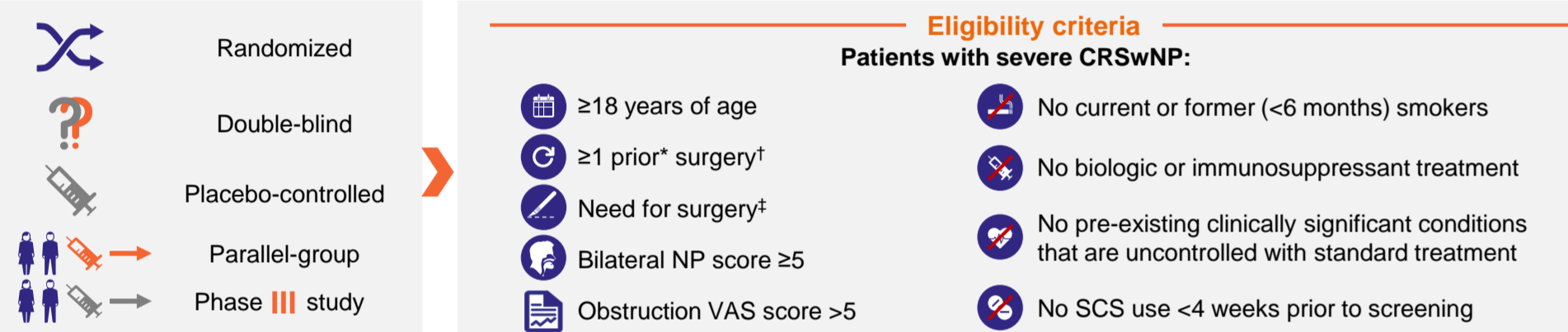
The phase III SYNAPSE study assessed the efficacy of mepolizumab, an anti-interleukin (IL)-5 monoclonal antibody, in patients with severe CRSwNP compared with placebo.⁴

- SYNAPSE demonstrated improvements in NP size and symptoms and a reduced risk of endoscopic sinus surgery with mepolizumab 100 mg SC versus placebo; improvements in HRQoL were also observed.⁴

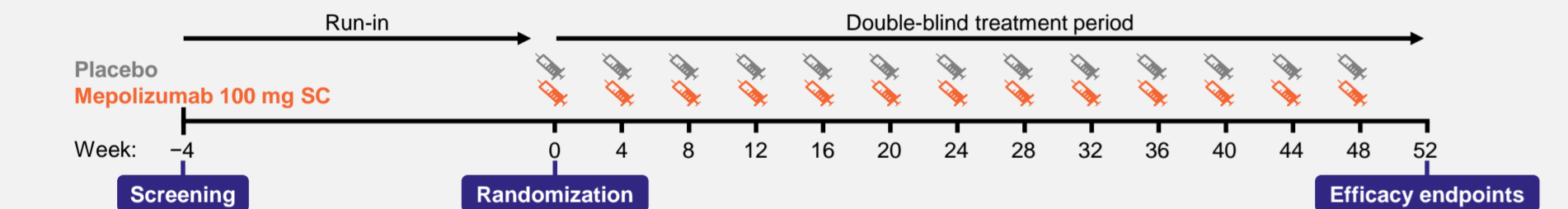
Post hoc analyses were conducted using data from patients with severe CRSwNP from SYNAPSE to further characterize the effect of mepolizumab on loss of smell.

Methods

Study design
GSK ID: 205687/NCT03085797



Plus standard of care: daily MF and saline nasal douching, occasional short courses of high-dose SCS and/or antibiotics when required



SYNAPSE primary and secondary endpoints

- Co-primary**
- Change from baseline in total endoscopic NP score at Week 52
 - Change from baseline in Nasal Obstruction VAS score during Weeks 49–52
- Key secondary**
- Time-to-first sinus surgery up to Week 52
- Other secondary**
- Change from baseline to Weeks 49–52 in:
 - Overall Symptoms VAS score
 - Loss of smell VAS score
 - Composite VAS score (combining scores for nasal obstruction, nasal discharge, throat mucus, and loss of smell)

Post hoc analyses

- Statistical analyses**
- Mean change from baseline in loss of smell VAS score at Weeks 49–52†
 - Proportion of patients with a ≥3-point improvement in loss of smell VAS score from baseline to Weeks 49–52†
- Descriptive analyses**
- Sense of smell specific disease characteristics of the SYNAPSE ITT patient population
 - Demographics and characteristics of patients with and without a ≥3-point improvement (meaningful within-patient change⁹) in loss of smell VAS score from baseline to Weeks 49–52

When using the VAS tool, patients quantify the severity of their symptoms on an electronic device which represents the 0–10 cm paper scale, with 0 points conferring total absence of symptom(s) and 10 points conferring the worst thinkable severity of symptom(s); VAS for loss of smell has been validated in patients with allergic rhinitis. *Within the last 10 years; †defined as any procedure involving instruments with resulting incision and removal of NP 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); §Analysis using mixed model repeated measures with covariates of treatment, geographic region, baseline log(e) baseline blood eosinophil count, and time period; interaction terms for time period by baseline and time period by treatment. Patients with sinus surgery prior to Weeks 49–52 were assigned the worst possible score. Missing data were imputed as though patients continued to receive their randomized treatment; there were 2000 imputations and estimates were combined using Rubin's rule; ¶Analysis using a logistic regression model with covariates of treatment group, geographic region, baseline score and log(e) baseline blood eosinophil count. Includes data reported up to Week 52.

References

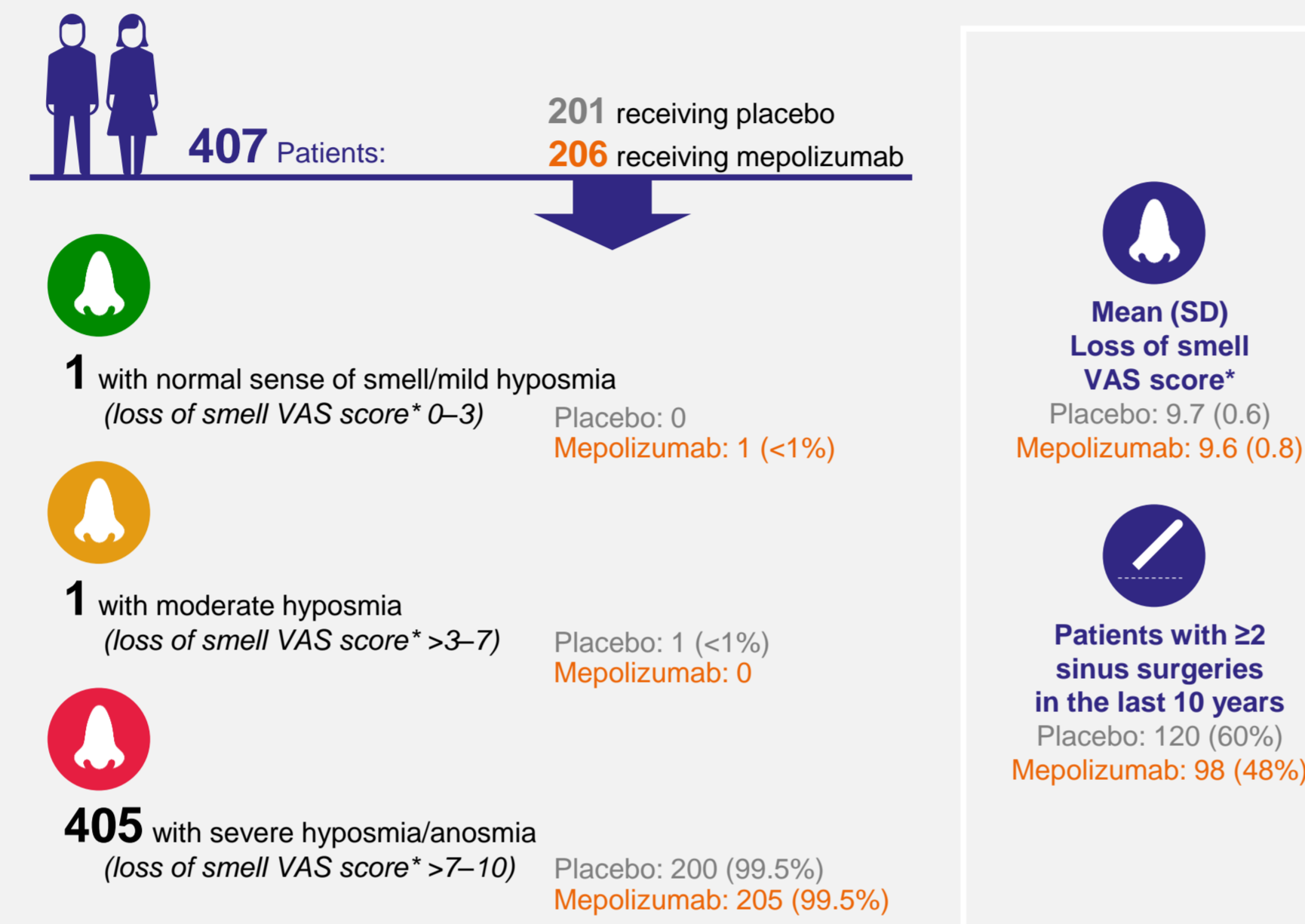
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- Han JK, et al. *Lancet Respir Med* 2021;9:1141–53.
- Tabberer M, et al. *J Allergy Clin Immunol* 2021;147(2): AB126–AB126.

Abbreviations

- BMI, body mass index; CI, confidence interval; CRSwNP, chronic rhinosinusitis with nasal polyps; HRQoL, health-related quality of life; IL, interleukin; ITT, intent-to-treat; LS, least squares; NP, nasal polyps; MF, mometasone furoate; OCS, oral corticosteroids; SC, subcutaneous; SCS, systemic corticosteroids; SD, standard deviation; VAS, visual analog scale.

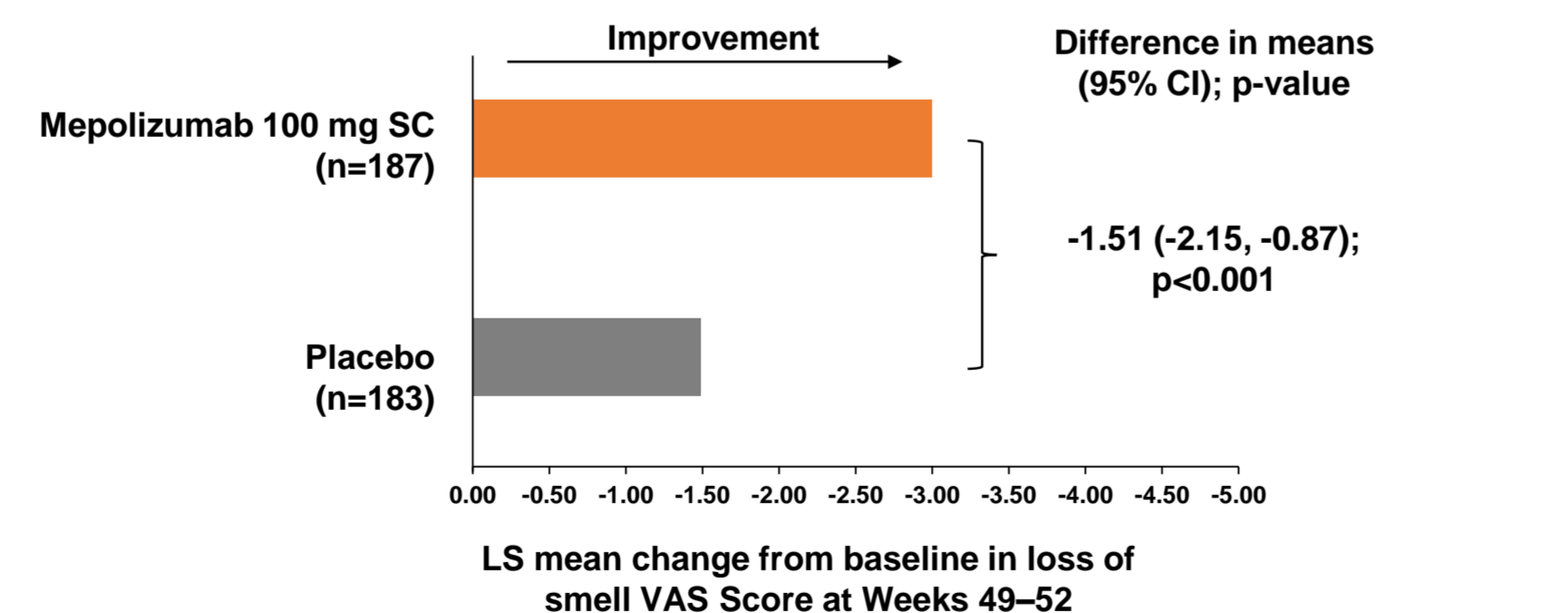
Results

Among the SYNAPSE ITT population, almost all patients had impaired sense of smell and 54% overall had a history of ≥2 sinus surgeries



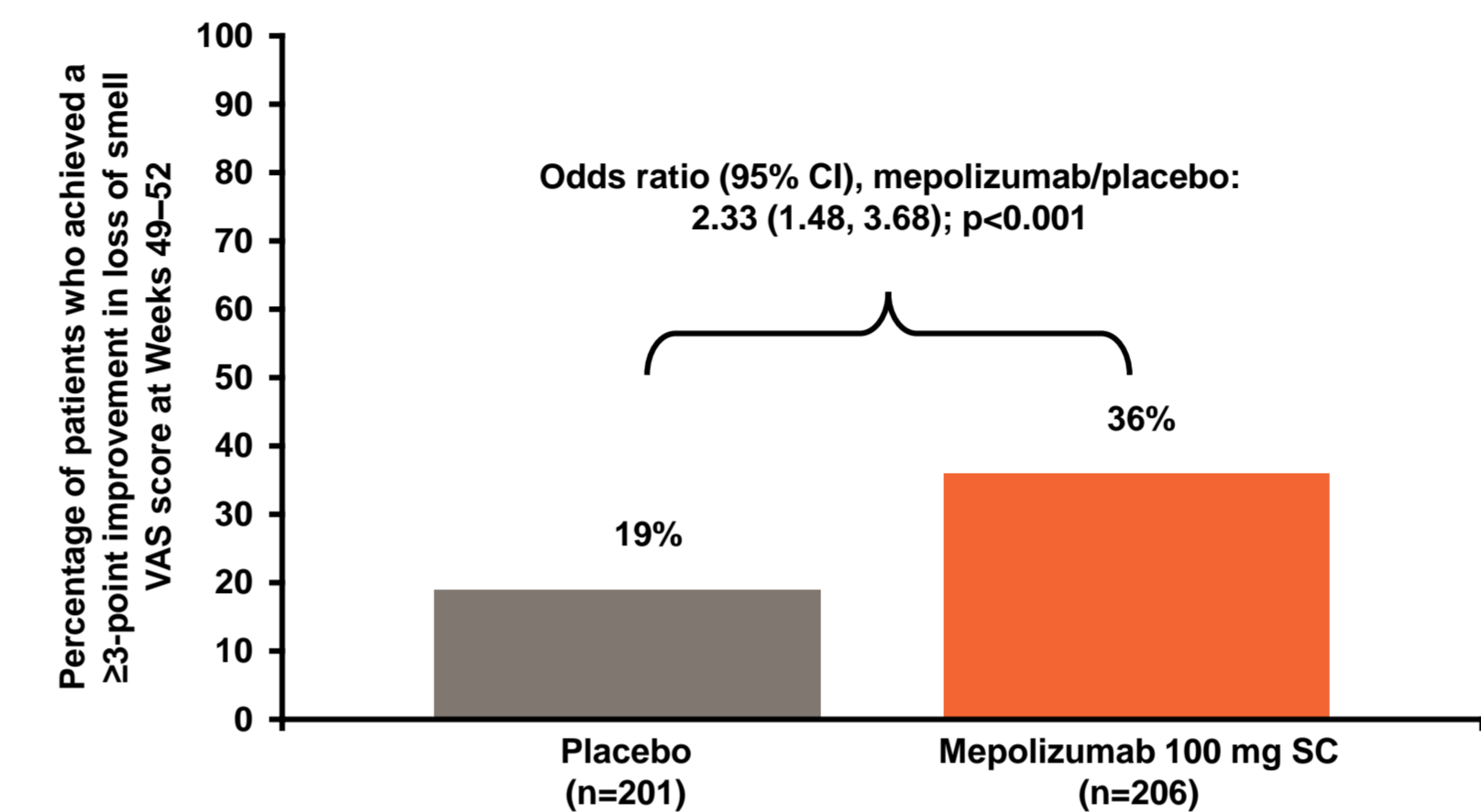
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Patients treated with mepolizumab had greater improvements in their sense of smell compared with those receiving placebo

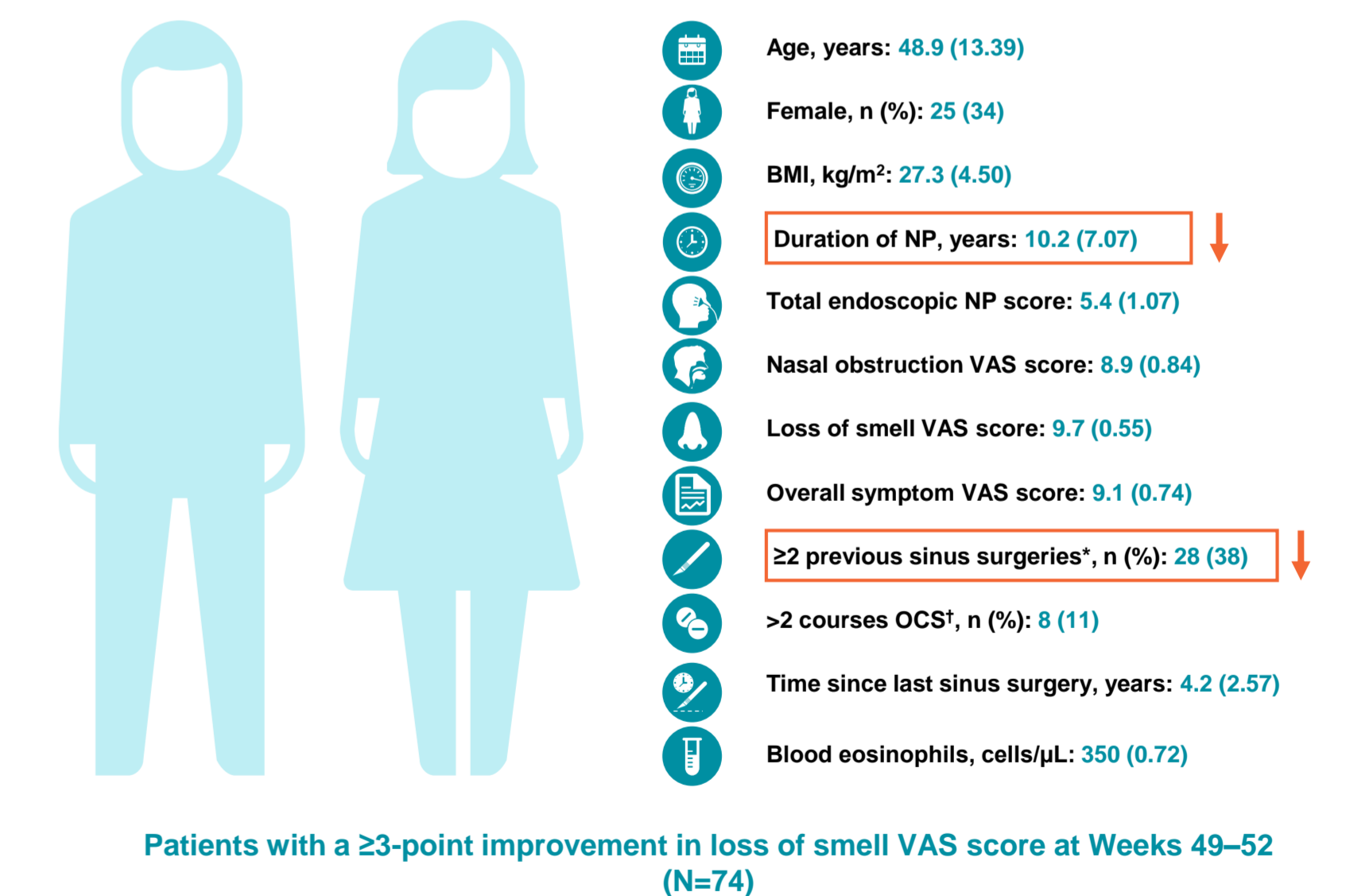
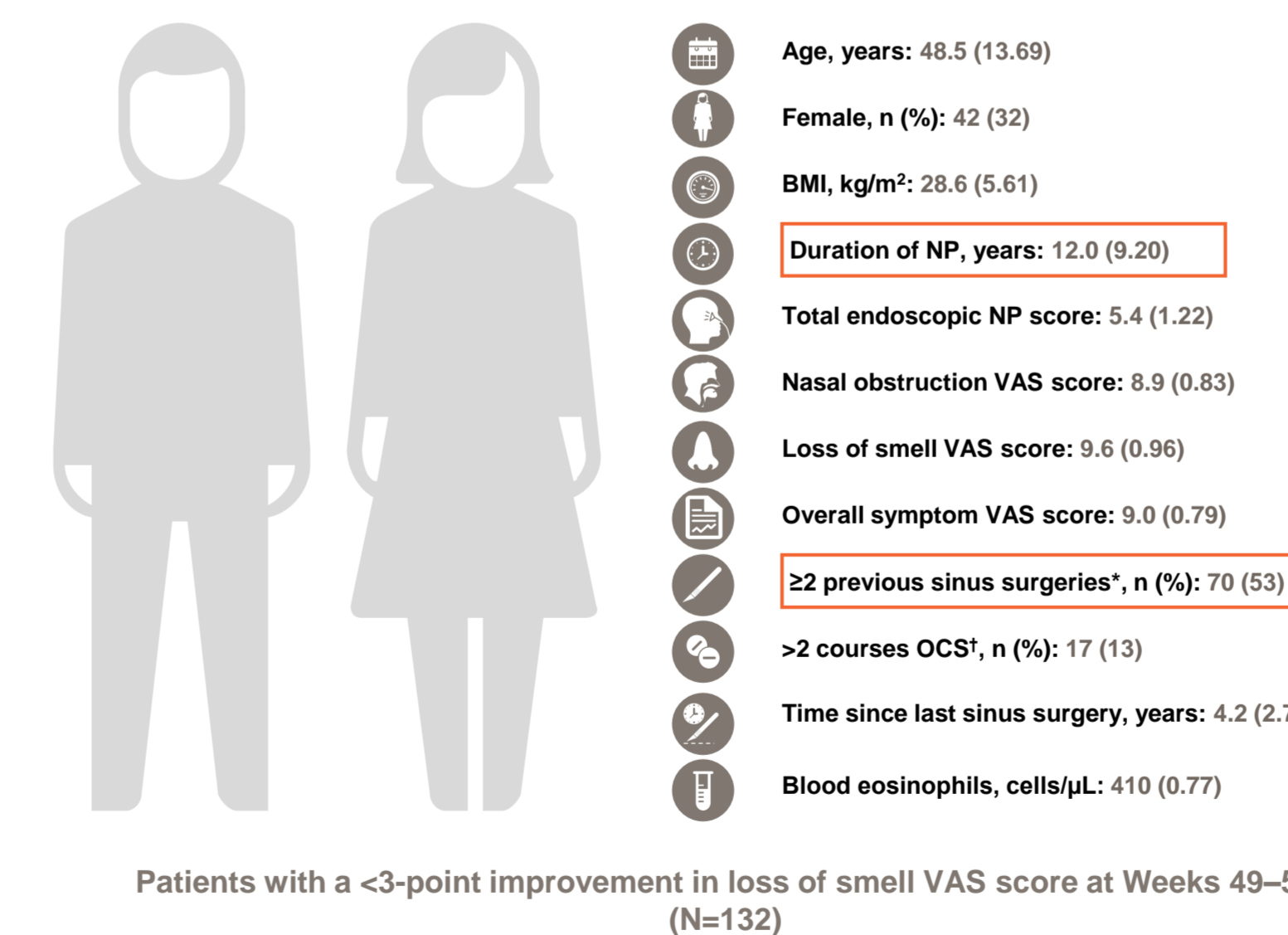


Analysis using mixed model repeated measures with covariates by treatment, geographic region, baseline log(e) baseline blood eosinophil count, and time period. Patients with NP surgery prior to time period were assigned worst possible score.

A greater proportion of patients achieved a ≥3-point improvement in loss of smell VAS symptom score with mepolizumab versus placebo



Mepolizumab-treated patients with larger sense of smell improvements had a shorter duration of disease and fewer previous surgeries versus those with smaller sense of smell improvements



Results are descriptive comparisons only; no statistical analyses were conducted. All values are mean (SD) unless otherwise specified; blood eosinophil counts are geometric mean (SD log). *In the last 10 years; †in the last 12 months.

Conclusions

- This post hoc analysis of data from the SYNAPSE study further supports that treatment with mepolizumab improves sense of smell versus placebo in patients with severe CRSwNP
- At baseline, loss of smell in these patients was very severe
- By study end, mepolizumab was associated with significantly greater improvements from baseline in loss of smell VAS score compared with placebo
- Mepolizumab-treated patients with the largest improvements in their sense of smell had fewer prior sinus surgeries and a shorter duration of NP, suggesting that early intervention with mepolizumab may lead to the greatest clinical benefit
 - These observations may be due to a shorter time for mechanical obstruction and inflammation of the respiratory and olfactory mucosa to occur
- Given the significant impact that loss of smell has among patients with severe CRSwNP, these data should be considered when making treatment decisions

References

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