Mepolizumab Therapy Improves Most Bothersome Symptoms in Patients With Hypereosinophilic Syndrome (HES)

Poster No. 446

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Aims

HES is characterized by persistent elevated blood and/or tissue eosinophil levels and resulting eosinophil-mediated organ damage.[1]

Presentation of HES is highly heterogenous, and patients experience symptoms affecting a variety of organ systems.[1]

Mepolizumab, a humanized monoclonal antibody against IL-5 has recently been approved for treatment of HES.[2] It has been shown to reduce blood eosinophil counts, occurrence of symptom flares, and the need for oral corticosteroids, which are commonly prescribed as a first-line treatment for HES.[3,4,5]

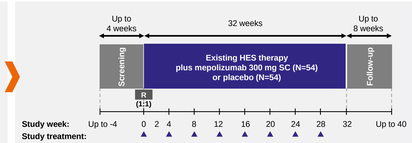
The aim of this analysis was to assess the effects of mepolizumab on the severity of HES-related symptom burden, based on data collected during the recent Phase III study of mepolizumab in patients with HES using the HES daily symptoms (HES-DS) questionnaire.

Methods

Study design

GSK ID: 200622; NCT02836496

Randomized · Double-blind · Multicenter · Placebo-controlled · Parallel-group · Phase III trial



Patient eligibility criteria

- ≥12 years of age
- Diagnosis of HES* ≥6 months previously
- Receiving stable HES therapy† ≥4 weeks before the baseline visit
- Uncontrolled HES ≥2 flares within the past 12 months and a baseline blood eosinophil count ≥1000 cells/μL at screening

Study period: 32 Weeks

Endpoint‡: Change from baseline in HES symptom severity based on HES daily symptom (HES-DS) score at Week 32

HES daily symptom (HES-DS) patient scoring and symptom subgroups

Using an eDiary, each of six HES-related symptoms were rated daily by patients using an 11-point scale (0 = not present, 10 = worst imaginable), recalling worst symptom experience over the previous 24 hours

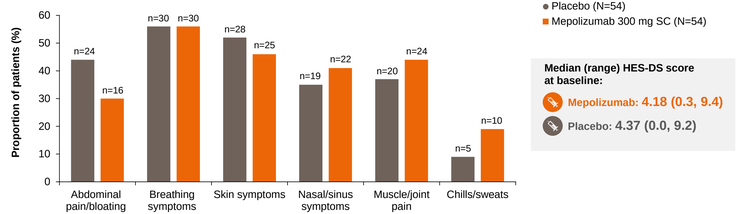
Abdominal pain/bloating · Breathing · Skin · Nasal/sinus · Muscle/joint pain · Chills/sweats

At baseline (randomization) patients reported up to three HES-related symptoms that were most bothersome§

*HES diagnosis was based on organ system involvement and/or dysfunction that could be directly related to a blood eosinophil count >1500 cells/μL on ≥2 occasions, and/or tissue eosinophilia, without a discernible secondary cause; †HES therapy could include (but was not limited to) OCS, immunosuppressive, and cytotoxic therapy; ‡the primary endpoint of the study was the proportion of patients who experienced a flare during the 32-week study period; here we present data on one of the exploratory endpoints, change from baseline in HES symptom severity; §1 patient reported four most bothersome symptoms at baseline.

Results

Symptoms reported as most bothersome at baseline were broadly similar in the mepolizumab and placebo groups, with comparable median HES-DS scores for most bothersome symptoms

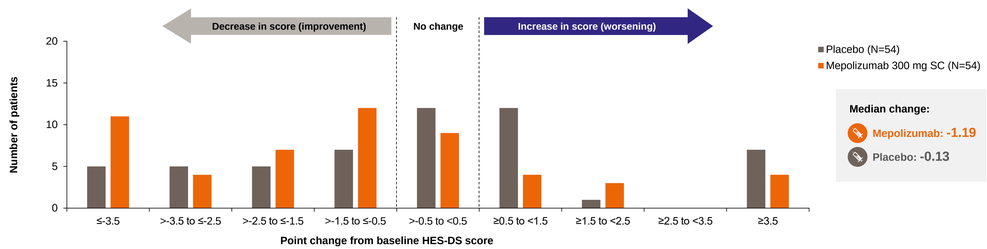


Median (range) HES-DS score at baseline:

- Mepolizumab: 4.18 (0.3, 9.4)
- Placebo: 4.37 (0.0, 9.2)

Up to three most bothersome symptoms were identified by patients at randomization (therefore patient numbers for each treatment arm add up to more than the number of enrolled patients in each arm). The most bothersome symptom score for each patient was the mean of these symptom scores over the seven days prior to each time point (scale 0 = not present to 10 = worst imaginable). The maximum possible score for each of the identified most bothersome symptoms and for the most bothersome symptom score was 10.

At Week 32, more patients receiving mepolizumab reported improvement in severity of most bothersome symptom score from baseline compared with patients receiving placebo

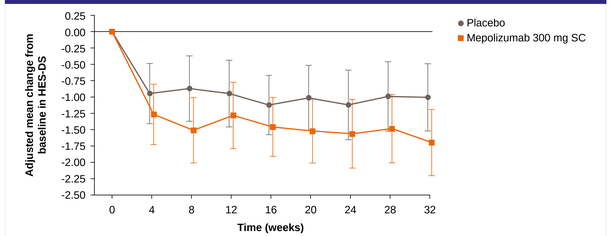


Median change:

- Mepolizumab: -1.19
- Placebo: -0.13

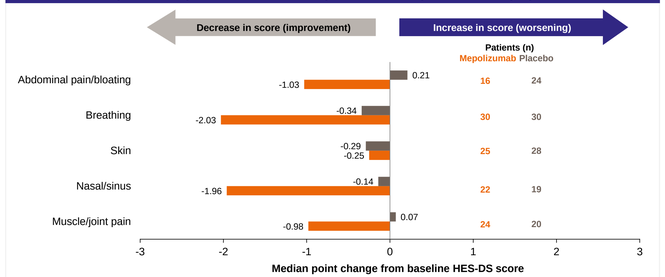
Wilcoxon Rank Sum test stratified by median baseline most bothersome HES symptom severity score, baseline OCS and region demonstrated a statistically significant reduction (improvement) in the most bothersome symptom score at Week 32 for patients treated with mepolizumab compared with placebo (P=0.001). The total number of patients who experienced an ≥0.5-point improvement in HES-DS symptom score was 22/54 for placebo and 34/54 for mepolizumab. Change from baseline as shown represents the average change in score for the most bothersome symptoms at baseline. Patients who had missing data were included in the analysis with the largest (ie, worst) change from baseline value observed for any patient; 7 placebo and 4 mepolizumab patients with missing change from baseline most bothersome HES-DS were included in the worst category (≥3.5).

Improvements were observed in most bothersome HES-DS score for patients treated with mepolizumab compared with patients treated with placebo after the first dose (Week 4) and maintained over time



Parametric analysis using mixed model repeated measures, with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. Data points represent adjusted least squares mean change from baseline; vertical bars represent 95% confidence intervals. Missing data was assumed missing at random. Change from baseline in most bothersome symptom score at the week of analysis was derived using mean symptom scores at that week and baseline for the up to three symptom groups identified by the participant as most bothersome at randomization.

Mepolizumab was associated with improvements in several of the symptoms reported as most bothersome compared with placebo at Week 32 in patients who reported these symptoms at baseline



Analysis performed post hoc. Patients who had missing data were included in the analysis with the largest (ie, worst) change from baseline value observed for any patient.

Conclusions

- Mepolizumab, when added to standard of care treatment for HES, was associated with improvements in the severity of those symptoms considered most bothersome by patients, compared with placebo.
- The greatest improvement for patients treated with mepolizumab compared with placebo was observed in breathing and nasal/sinus symptoms.
- These data provide further evidence of the clinical benefits of mepolizumab in the treatment of patients with HES.

References

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Abbreviations

HES, Hypereosinophilic syndrome; HES-DS, HES daily symptoms; IL, interleukin; OCS, oral corticosteroids; R, randomization; SC, subcutaneous.

Disclosures

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