Methods

Efficacy and Safety of Mepolizumab in Hypereosinophilic Syndrome: a Phase III, Randomized, Placebo-Controlled Trial

Originally accepted as an oral presentation [abstract A4212]. A video recording is available on the ATS virtual platform and the presentation slide deck are also available via http://tago.ca/ats03.


Background

Hypereosinophilic syndrome (HES) is a rare group of disorders, characterized by elevated eosinophil levels in the blood and/or tissues and eosinophil-mediated tissue damage and dysfunction. Mepolizumab is a humanized, anti-IL-5 monoclonal antibody approved for use in patients with other eosinophilic diseases, such as severe eosinophilic asthma (100 mg administered subcutaneously (SC) and eosinophil granulomatisis with polygala (300 mg SC)).

Methods

Study design

- GSK ID: 200322. NCT02506496
- Randomized, Double-blind, Multicenter, Placebo-controlled, Parallel-group
- Phase III

Patient eligibility criteria

- ≥12 years of age
- Diagnosis of FIP1L1-PDGFRA-negative HES
- Eosinophil count ≥1000 cells/μL at screening

Study endpoints

Primary endpoint

- The proportion of patients who experienced a flare during the full study period

Secondary endpoints

- Time to first flare (allowing assessment of the probability of first flare over time)
- Ratio to baseline blood eosinophil count
- Proportion of patients who experienced a flare during study Weeks 20–32

Other endpoints

- Frequency of AEs and SAEs
- Ratio to baseline blood eosinophil count
- Frequency of AEs and SAEs

Results

- 141 patients were screened for eligibility and 108 were randomized. Overall, 4 patients (2 per treatment group) withdrew from the study before Week 32. 2 additional patients (1 per treatment group) discontinued treatment.

For the duration of the trial, investigators, GSK staff, and patients were all blinded to the study treatment, absolute blood eosinophil counts, total white blood cell counts, and white blood cell differentials. Separate GSK staff (not involved in other aspects of the trial) monitored blood eosinophil counts and initiated treatment. The aim of this study was to investigate the clinical efficacy and safety of mepolizumab 300 mg SC versus placebo in patients with HES.

The occurrence of flares decreased with mepolizumab versus placebo across the full study period.

The occurrence of flares decreased with mepolizumab versus placebo during the study period.

The occurrence of flares also decreased with mepolizumab versus placebo during the full study period for patients receiving mepolizumab versus placebo; no new safety signals were identified with mepolizumab.

Mepolizumab is the first treatment shown to reduce disease flares in patients with FIP1L1-PDGFRA-negative HES and to demonstrate that the study represent an important advance for the management of this rare, debilitating disease.

Conclusions

- The randomized, placebo-controlled, Phase III study demonstrated that treatment with mepolizumab (300 mg SC) was associated with a 36% reduction in the occurrence of flares compared with standard of care plus placebo, in patients with uncontrolled HES.
- The risk of a flare and the annualized rate of flares were both 60% lower during the study period for patients receiving mepolizumab versus placebo; no new safety signals were identified with mepolizumab.
- Mepolizumab is the first treatment shown to reduce disease flares in patients with FIP1L1-PDGFRA-negative HES and the findings from this study represent an important advance for the management of this rare, debilitating disease.

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Frequencies of AEs were generally similar between patients receiving mepolizumab and placebo (data not shown).