Mepolizumab Treatment in Patients with Severe Eosinophilic Asthma

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ABSTRACT

BACKGROUND
Some patients with severe asthma have frequent exacerbations associated with persistent eosinophilic inflammation despite continuous treatment with high-dose inhaled glucocorticoids with or without oral glucocorticoids.

METHODS
In this randomized, double-blind, double-dummy study, we assigned 576 patients with recurrent asthma exacerbations and evidence of eosinophilic inflammation despite high doses of inhaled glucocorticoids to one of three study groups. Patients were assigned to receive mepolizumab, a humanized monoclonal antibody against interleukin-5, which was administered as either a 75-mg intravenous dose or a 100-mg subcutaneous dose, or placebo every 4 weeks for 32 weeks. The primary outcome was the rate of exacerbations. Other outcomes included the forced expiratory volume in 1 second (FEV₁) and scores on the St. George’s Respiratory Questionnaire (SGRQ) and the 5-item Asthma Control Questionnaire (ACQ-5). Safety was also assessed.

RESULTS
The rate of exacerbations was reduced by 47% (95% confidence interval [CI], 29 to 61) among patients receiving intravenous mepolizumab and by 53% (95% CI, 37 to 65) among those receiving subcutaneous mepolizumab, as compared with those receiving placebo (P<0.001 for both comparisons). Exacerbations necessitating an emergency department visit or hospitalization were reduced by 32% in the group receiving intravenous mepolizumab and by 61% in the group receiving subcutaneous mepolizumab. At week 32, the mean increase from baseline in FEV₁ was 100 ml greater in patients receiving intravenous mepolizumab than in those receiving placebo (P=0.02) and 98 ml greater in patients receiving subcutaneous mepolizumab than in those receiving placebo (P=0.03). The improvement from baseline in the SGRQ score was 6.4 points and 7.0 points greater in the intravenous and subcutaneous mepolizumab groups, respectively, than in the placebo group (minimal clinically important change, 4 points), and the improvement in the ACQ-5 score was 0.42 points and 0.44 points greater in the two mepolizumab groups, respectively, than in the placebo group (minimal clinically important change, 0.5 points) (P<0.001 for all comparisons). The safety profile of mepolizumab was similar to that of placebo.

CONCLUSIONS
Mepolizumab administered either intravenously or subcutaneously significantly reduced asthma exacerbations and was associated with improvements in markers of asthma control. (Funded by GlaxoSmithKline; MENSA ClinicalTrials.gov number, NCT01691521.)