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Dose-ranging study of mepolizumab in eosinophilic COPD

COPD - management, COPD - exacerbations, Treatments

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Background: Patients with eosinophilic COPD & frequent exacerbations may benefit from mepolizumab (MEP) treatment.

Objective: Assess efficacy & safety of 2 MEP doses vs placebo (PBO) in COPD with blood eosinophils ≥ 150 cells/ μ L [screening] or ≥ 300 cells/ μ L [prior yr], history of ≥ 2 moderate/ ≥ 1 severe exacerbations & ICS+ ≥ 2 bronchodilator maintenance therapies (ICS+MT).

Methods: Phase III, randomised, PBO-controlled, double-blind, parallel-group trial (METREO); patients received SC MEP 100mg, MEP 300mg or PBO plus ICS+MT, every 4 wks for 52 wks. Primary endpoint: rate/yr of moderate(systemic corticosteroids/antibiotics)/severe(hospitalisation or death) exacerbations. Secondary endpoints included: time to first moderate/severe exacerbation & rate/yr of exacerbations requiring ER visit and/or hospitalisation. Safety was assessed. Hochberg procedure applied to adjust for multiplicity of treatment comparisons.

Results: In the modified intent-to-treat population (n=674), rates/yr of moderate/severe exacerbations were 1.19, 1.27 & 1.49 for MEP 100mg, MEP 300mg & PBO, respectively. Rate ratios: MEP 100mg/PBO 0.80 (95%CI 0.65,0.98;p=0.034[unadjusted]; p=0.068[adjusted]); MEP 300mg/PBO 0.86 (95%CI 0.70,1.05;p=0.140[unadjusted]; p=0.140[adjusted]). Secondary endpoints were not significantly different vs PBO for either MEP dose after adjustment. Safety profiles were similar to PBO.

Conclusions: Clinically relevant, but not statistically significant, reductions in rate/yr of moderate/severe exacerbations were achieved for both MEP doses vs PBO, with no additional benefit from the higher dose. Both doses were well tolerated. This suggests that eosinophils are a potential target for assessing treatment response in COPD.

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