Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease (COPD): A Meta-Analysis of METREX and METREO Exacerbation Endpoints

M. Bafadhel[1], F. C. Sciurba[2], P. Paggiaro[3], I. D. Pavord[1], K. Chapman[4], S. W. Yancey[5], D. B. Rubin[5], B. Mayer[6], S. S. Harris[5], E. S. Bradford[5]; [1]Nuffield Department of Medicine and Oxford Respiratory NIHR BRC, University of Oxford, Oxford, United Kingdom, [2]Department of Medicine, University of Pittsburgh, Pittsburgh, PA, United States, [3]Department of Surgery, Medicine, Molecular Biology, and Critical care, Università di Pisa, Pisa, Italy, [4]Asthma & Airway Centre, UHN and University of Toronto, Toronto, ON, Canada, [5]Respiratory Therapeutic Area, GSK, Research Triangle Park, NC, United States, [6]Clinical Statistics, GSK, Stockley Park, United Kingdom.

Corresponding author's email: mona.bafadhel@ndm.ox.ac.uk

Rationale: A subset of patients with COPD have an eosinophilic phenotype associated with frequent COPD exacerbations. A pre-specified meta-analysis of this patient subset in METREX and METREO investigated if exacerbations are reduced by mepolizumab, an anti-interleukin-5 monoclonal antibody. Methods: METREX and METREO; Phase III, placebo-controlled, randomized, double-blind, multicenter trials; enrolled patients (aged ≥40 years) with COPD and a history of ≥2 moderate/≥1 severe exacerbations in the prior year despite inhaled corticosteroid (ICS)-based triple maintenance therapy. Patients received subcutaneous mepolizumab (100mg [METREX], 100 or 300mg [METREO]) every 4 weeks for 52 weeks as add-on therapy to inhaled triple therapy, consisting of ICS, a long-acting β2-agonist, and a long-acting muscarinic-receptor antagonist. Pre-specified meta-analyses were performed in patients from the modified intent-to-treat populations of METREX and METREO (with an eosinophilic phenotype: blood eosinophil count ≥150 cells/μL [screening] OR ≥300 cells/μL [prior year]). Two treatment comparisons: mepolizumab 100mg versus placebo and mepolizumab all-doses (100 and 300mg) versus placebo, were performed. Primary endpoint was annual rate of moderate (requiring systemic corticosteroids and/or antibiotics)/severe (leading to hospitalization/death) exacerbations. Secondary/other endpoints included time-to-first moderate/severe exacerbation, annual rate of exacerbations requiring emergency department (ED)/hospitalization, and annual rate of severe exacerbations. Results: 1136 patients were included in the meta-analysis (mepolizumab 100mg: N=456; mepolizumab 300 mg: N=225, placebo: N=455). 95% of patients were classified as GOLD group D. Mean annual exacerbation rate (prior year) was 2.6 events/year for both groups. Mepolizumab (100mg)-treated patients had an 18% significantly lower mean annual rate of moderate/severe exacerbations versus placebo (rate ratio: 0.82; 95% CI: 0.71, 0.95; p=0.006). Furthermore, mepolizumab 100mg versus placebo increased time to first moderate/severe exacerbation (hazard ratio: 0.80; 95% CI: 0.68-0.94; p=0.006). Mean annual rates of exacerbations requiring ED/hospitalization were reduced by 15% and severe exacerbations by 12% with mepolizumab 100mg versus placebo (rate ratios: 0.85; 95% CI: 0.61-1.18; p=0.328 and

0.88; 95% CI: 0.62-1.25; p=0.475). Similar results to mepolizumab 100mg were observed in the mepolizumab all-doses group. Conclusions: In patients with COPD and an eosinophilic phenotype, mepolizumab significantly improved the annual rate and time to first occurrence of moderate/severe exacerbations versus placebo, reductions in exacerbations requiring ED/hospitalization and severe exacerbations were apparent with mepolizumab 100mg relative to placebo. This suggests that mepolizumab treatment is beneficial for reducing exacerbations in patients with COPD and an eosinophilic phenotype, receiving inhaled triple therapy. Funding: GSK (207478, 117113/NCT02105961, and 117106/NCT02105948)

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