The novel bronchodilator navafenterol: a phase 2a, multicentre, randomised, double-blind, placebo-controlled crossover trial in COPD

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Navafenterol, a novel dual-pharmacology bronchodilator for COPD, improved lung function, reduced COPD symptoms and decreased objective cough counts, to a similar extent to umeclidinium/vilanterol https://bit.ly/3lV886y

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Abstract

Background Navafenterol (AZD8871) belongs to a new class of bronchodilator, the single-molecule muscarinic antagonist and β-agonist, developed for the treatment of COPD. This study aimed to evaluate the efficacy, pharmacokinetics and safety of navafenterol *versus* placebo and an active comparator treatment for moderate-to-severe COPD.

Methods This phase 2a, randomised, multicentre (Germany and UK), double-blind, double-dummy, three-way complete crossover study (ClinicalTrials.gov identifier: NCT03645434) compared 2 weeks' treatment of once-daily navafenterol 600 µg *via* inhalation with placebo and a fixed-dose combination bronchodilator (umeclidinium/vilanterol (UMEC/VI); 62.5 µg/25 µg) in participants with moderate-to-severe COPD. The primary outcome was change from baseline in trough forced expiratory volume in 1 s (FEV_1) on day 15. Secondary end-points included change from baseline in peak FEV_1; change from baseline in Breathlessness, Cough and Sputum Scale (BCSS); change from baseline in COPD Assessment Tool (CAT); adverse events; and pharmacokinetics.

Results 73 participants were randomised. After 14 days, trough FEV_1 was significantly improved with navafenterol compared with placebo (least-squares (LS) mean difference 0.202 L; p<0.0001). There was no significant difference in FEV_1 between navafenterol and UMEC/VI (LS mean difference −0.046 L; p=0.075). COPD symptoms (CAT and BCSS) showed significantly greater improvements with both active treatments *versus* placebo (all p<0.005). Novel objective monitoring (VitaloJAK) showed that cough was reduced with both active treatments compared with placebo. Safety profiles were similar across the treatment groups and no serious adverse events were reported in the navafenterol treatment period.

Conclusion Once-daily navafenterol was well tolerated, improved lung function and reduced COPD-related symptoms, similar to an established once-daily fixed-dose combination bronchodilator.