Results from FULFIL have shown statistically significant improvements in lung function and health-related quality of life, and a reduction in exacerbation rates with once-daily fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) 100 µg/62.5 µg/25 µg administered using a single ELLIPTA® inhaler compared with twice-daily budesonide/formoterol (BUD/FOR) 400 µg/12 µg using the Turbuhaler® in patients with symptomatic COPD at risk of exacerbations. The safety profile of FF/UMEC/VI reflected that of the components (Lipson, et al. Am J Respir Crit Care Med. 2017). Herein we present post-hoc subgroup analyses of exacerbation rates by prior COPD medication class, disease severity and exacerbation history during FULFIL. In the intent-to-treat (ITT: 24 weeks) population, the mean annual exacerbation rate, FF/UMEC/VI versus BUD/FOR ratios and annual exacerbation rates reductions were calculated for subgroups: by prior COPD medication class, inhaled corticosteroid (ICS) +long-acting beta agonists (LABA); BUD/FOR; ICS +LABA + long-acting muscarinic antagonists (LAMA); LAMA; tiotropium; LAMA +LABA; by disease severity, forced expiratory volume in 1 s (FEV₁) <50% predicted, no moderate/severe exacerbation; FEV₁ <50%/≥1 moderate/severe exacerbation; FEV₁ ≥50–<80%/≥2 moderate or ≥1 severe exacerbations; and by exacerbation history, 0/1 moderate exacerbations;≥2 moderate exacerbations;≥1 severe exacerbation. Up to Week 24 in the ITT population, FF/UMEC/VI versus BUD/FOR improved the mean annual exacerbation rate (range, 63%–24%) in all prior medication subgroups, except LAMA +LABA (annual exacerbation rate reduction, −44%) and improved mean annual exacerbation rates in all disease severity (range, 45%–27%) and exacerbation prior history (range, 57%–27%) subgroups (Table). Statistical significance of the FF/UMEC/VI:BUD/FOR ratio was observed for the subgroups: prior medication class ICS +LABA (0.37; 95% confidence interval [CI] 0.20–0.71; p=0.003) and ICS +LAMA + LABA (0.53; 95% CI 0.33–0.87; p=0.012); disease severity FEV₁ <50% and≥1 moderate/severe exacerbation (0.53; 0.34–0.89; p=0.013); exacerbation history 0/1 prior moderate exacerbation (0.62; 0.44 0.87; p=0.005) and ≥1 prior severe exacerbation (0.43; 0.22 0.86; p=0.017) (Table). Improvements in mean annual exacerbation rates with once-daily FF/UMEC/VI compared with twice-daily BUD/FOR were observed in all patients regardless of disease severity or exacerbation history and all prior COPD medication class subgroups except for LAMA +LABA. Funding GSK (NCT02345161; CTT116853)

Please refer to page A260 for declarations of interest in relation to abstract P272.
Several fixed-dose combination inhaled corticosteroid (FDC ICS/LABA) inhalers are licensed for chronic obstructive pulmonary disease (COPD) in the UK. This study compares effectiveness of Fostair 100/6 (BDP/FOR) metered dose inhalers (MDI) against other licensed FDC ICS/LABAs, namely; Seretide Accuhaler 500 (FP/SAL) (OR 0.89, 95% CI: 0.67–1.19) or BUD/FOR (OR 0.79, 95% CI: 0.58–1.08). Cost was significantly lower for BDP/FOR versus FP/SAL (adjusted mean £730.0 versus £850.1 respectively, p<0.001) and lower for BDP/FOR versus BUD/FOR (adjusted mean £732.4 versus £757.2 respectively, p=0.054). Treatment with BDP/FOR is non-inferior in terms of exacerbation risk and is additionally associated with a lower point estimate of exacerbation risk, a lower cost compared to FP/SAL and BUD/FOR, and a lower ICS dose compared to FP/SAL.

### P275 COMPARING CLINICALLY RELEVANT IMPROVEMENT WITH UMECLIDINIUM/VILANETEROL AND TIOPTROPUM/OLODATEROL IN SYMPTOMATIC COPD: A RANDOMISED NON-INFERIORITY CROSSOVER TRIAL

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Introduction and Objectives Here we report the Results of the first direct comparison of the once-daily fixed-dose long-acting muscarinic antagonist/long-acting β2-agonist (LAMA/LABA) combinations umclidinium/vilanterol (UMEC/VI) 62.5/25 mcg and tiotropium/olodaterol (TIO/OLO) 5/5 mcg in patients with chronic obstructive pulmonary disease (COPD).

Methods This randomised, 2-period crossover study (204990, NCT02799798) included inhaled corticosteroid-free patients with COPD, a modified Medical Research Council dyspnoea score ≥2, forced expiratory volume in 1 s (FEV1) forced vital capacity ratio <0.70 and post-salbutamol FEV1 >70%. Patients were randomised to UMEC/VI (62.5/25 mcg once daily) via an ELLIPTA dry powder inhaler followed by TIO/OLO 5/5 mcg (2 puffs once daily) via a RESPIMAT inhaler (each for 8 weeks with an interim 3 week washout period), or vice versa. The primary endpoint was change from baseline (CFB) in trough FEV1 at Week 8 with a non-inferiority (NI) margin of −50 mL in the per protocol (PP) population. Additional outcomes included inspiratory capacity (IC), rescue medication use and ease of inhaler use (assessed using a six-point questionnaire). Adverse events (AEs) were also assessed.

Results 236 patients (mean age 64.4 years, 60% male) were included in the intent-to-treat (ITT) population and 227 in the PP population. The primary endpoint of CFB in trough FEV1 at Week 8 confirmed NI of UMEC/VI vs TIO/OLO (175 mL vs 122 mL; least squares mean difference 53 mL [95% confidence interval: 26, 80]; p<0.001; PP population) and demonstrated superiority in the ITT population (Table). Patients receiving UMEC/VI were significantly more likely to achieve clinically meaningful improvements (≥100 mL) in trough FEV1 at Weeks 4 and 8 vs TIO/OLO, and showed significant improvements at Weeks 4 and 8 in IC and rescue medication use (Table). The