per year) versus 25 pneumonias (rate: 0.039 events per patient per year) with fixed triple and 353 exacerbations (0.565) versus 18 pneumonias (0.029) with Fostair (figure 1A). In TRINITY study, the number of events was 485 exacerbations (0.472) versus 30 pneumonias (0.029) with fixed triple and 569 exacerbations (0.583) versus 20 pneumonias (0.020) with tiotropium (figure 1B). Overall, treatment with fixed triple therapy reduced exacerbations by 65 events compared to Fostair (adjusted rate ratio: 0.773, p=0.005) and by 84 events compared to tiotropium (0.801, p=0.003). No fatal pneumonias occurred in TRILOGY while 5 pneumonias led to death in TRINITY (1 with fixed triple versus 4 with tiotropium). All pneumonias were classified as non-related to treatment.

Conclusions This analysis confirms that, in two independent populations of COPD patients treated with an ICS containing extrafine fixed triple combination, the number of incident pneumonia remains very small compared to that of moderate/severe exacerbations. The benefit observed in reducing the absolute number of exacerbations outweighs the increase observed in absolute number of pneumonias, thus confirming the positive risk benefit balance of extrafine fixed triple in severe/very severe COPD patients.

Please refer to page A260 for declarations of interest in relation to abstract P273.

P274 COMPARISON OF THE INITIATION OF COPD TREATMENT WITH LICENSED FDC ICS/LABA TREATMENTS IN TERMS OF DISEASE CONTROL AND COST EFFECTIVENESS

[1]S Wan Yau Ming, [2]J Haughney, [3]D Ryan, [4]I Small, [5]F Lavorini, [6]K Gruffydd-Jones, [7]A Papi, [8]D Singh, [8]D Halpin, [9]J Hurst, [10]S Patel, [10]M Ochel, [1]D Price. *[1]Observational and Pragmatic Research Institute, Singapore; [2]Academic Primary Care, University of Aberdeen, Aberdeen, UK; [3]Optimum Patient Care, UK; [4]Peterhead Health Centre, Aberdeen, UK; [5]Department of Critical Care, University of Florence, Florence, Italy; [6]University of Bath, Bath, UK; [7]University of Ferrara, Ferrara, Italy; [8]Royal Devon and Exeter University Hospital, UK; [9]University College London, London, UK; [10]Chiesi Ltd, Singapore*

10.1136/thoraxjnl-2017-210983.416

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) dry powder inhaler (DPI) and Symbicort Turbohaler 200/6 and 400/24 DPI (BUD/FOR) in a patient group with recent exacerbations and poor lung function. A historical cohort study using data extracted from the Optimum Patient Care Research Database. Patients with diagnostic read codes for COPD, smoking history, age ≥35 years, postdose FEV_1 percent predicted <55%,≥1 previous long acting bronchodilator ever, and ≥1 previous exacerbation in the 18 months prior initiation of FDC ICS/LABA therapy. The observation period consisted of one year after the initiation of FDC ICS/LABA for follow up and one year prior for patient characterisation. Patients were excluded if they switched or halted ICS/LABA treatment during the 1 year follow up period. The primary outcome was the proportion of patients with ≥1 exacerbation. The non-inferiority margin was defined as 20%. Patients were directly matched 1:1 on categorised age, smoking status, FEV_1 percent predicted and exacerbations. Mean total costs consisting of medication/resource costs were compared between treatment arms after adjusting for confounders. Out of the patients prescribed BDP/FOR (n=537) and 537 FP/SAL (n=537), the median age was 70 and 69 respectively and 41.7% were current smokers. In the BDP/FOR (n=540) and BUD/FOR (n=540) comparison, the median age was 70 and 69 respectively, and 42% were current smokers. The risk of ≥1 exacerbation in BDP/FOR group was non-inferior during the year following the initiation of ICS/LABA compared to 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/VILANTEROL AND TIOTROPIUM/OLODATEROL IN SYMPTOMATIC COPD: A RANDOMISED NON-INFERIORITY CROSSOVER TRIAL

[1]C Compton, [2]G Feldman, [3]AR Sousa, [4]D Lipson, [5]I Naya, [6]L Tombs, [1]S Patel, [7]B Alcázar Navarrete. *[1]Global Respiratory Franchise, GSK, Brentford, UK; [2]South Carolina Pharmaceutical Research, Spartanburg, US; [3]Discovery Medicine, GSK, Uxbridge, UK; [4]Respiratory Research and Development, GSK, King of Prussia, US; [5]Respiratory Medicine, GSK, Brentford, UK; [6]GSK, Uxbridge, UK; [7]Neumología, Hospital de Alta Resolución de Loja, Granada, Spain*

10.1136/thoraxjnl-2017-210983.417

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 β_2-agonist (LAMA/LABA) combinations umeclidinium/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, NCT02799784) included inhaled corticosteroid-free patients with COPD, a modified Medical Research Council dyspnoea score ≥2, forced expiratory volume in 1 s (FEV_1)/forced vital capacity ratio of <0.70 and post-salbutamol $FEV_1$50%–70% predicted. 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 FEV_1 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 FEV_1 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 FEV_1 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

ELLIPTA inhaler was rated higher than RESPIMAT in all ease-of-use questionnaire items (p≤0.001). The incidence of on-treatment AEs was similar in both groups (UMEC/VI, n=59 [25%]; TIO/OLO, n=71 [31%]).

Conclusions In this first, direct, once-daily LAMA/LABA comparison, a greater likelihood of improvements in lung function was demonstrated with UMEC/VI vs TIO/OLO. The ELLIPTA inhaler was preferred to RESPIMAT. Both LAMA/LABAs were well tolerated.

Funding GSK (204990 [NCT02799784])

Please refer to page A261 for declarations of interest in relation to abstract P275.

Abstract P275 Table 1 Summary of changes from baseline in lung function endpoints and rescue medication use, and trough FEV_1 responder analysis (ITT population)

	N	UMEC/VI	N	TIO/OLO	Difference/OR (95% CI) UMEC/VI vs TIO/OLO
Trough FEV_1, mL					
Week 4	231	189 (13)	224	141 (13)	+48 (25, 71)*
Week 8	225	180 (13)	224	128 (13)	+52 (28, 77)*
Trough FEV_1 responders,† n (%)					
Week 4	234	162 (69)	227	116 (51)	**OR:** 2.09 (1.39, 3.14)*
Week 8	234	154 (66)	229	109 (48)	**OR:** 2.05 (1.34, 3.14)*
IC, mL					
Week 4	223	164 (17)	215	112 (18)	+52 (16, 88)**
Week 8	212	169 (17)	212	122 (17)	+47 (14, 81)**
Rescue medication use (Weeks 1–8), puffs/day	222	−0.94 (0.08)	217	−0.68 (0.08)	−0.25 (-0.37,–0.14)*

All data are presented as LS mean (SE) change from baseline, unless otherwise stated; *p<0.001; **p<0.01; †Defined as a change from baseline in trough FEV_1 of ≥100 mL
CI, confidence interval; FEV_1, forced expiratory volume in 1 s; IC, inspiratory capacity; ITT, intent-to-treat; LS, least squares; OR, odds ratio; SE, standard error; TIO/OLO, tiotropium/olodaterol 5/5 mcg; UMEC/VI, umeclidinium/vilanterol 62.5/25 mcg

P276 CARDIOVASCULAR SAFETY OF EXTRAFINE SINGLE INHALER TRIPLE COMBINATION OF BECLOMETASONE DIPROPIONATE, FORMOTEROL FUMARATE, AND GLYCOPYRRONIUM BROMIDE IN COPD: RESULTS OF SAFETY ANALYSIS FROM THE TRILOGY AND TRINITY STUDIES

[1]M Scuri, [2]D Singh, [3]A Papi, [4]M Corradi, [1]I Montagna, [1]C Francisco, [1]G Cohuet, [1]S Vezzoli, [1]A Muraro, [1]S Petruzzelli, [2]J Vestbo. *[1]Chiesi Farmaceutici S.p.A, Parma, Italy; [2]University of Manchester, Manchester, UK; [3]University of Ferrara, Ferrara, Italy; [4]University of Parma, Parma, Italy*

10.1136/thoraxjnl-2017-210983.418

Rationale COPD often co-exists with other chronic diseases that can contribute to patients' health status and prognosis. In particular, patients with COPD are at greater risk of cardiovascular disease compared with age and sex-matched controls.

Methods Two 52 week multi-centre, randomised, double-blind, active-controlled studies recruited patients with symptomatic COPD, severe to very severe airflow limitation, and an exacerbation history. In TRILOGY, patients were randomised (1:1) to an extrafine fixed triple combination of beclometasone dipropionate, formoterol fumarate, and glycopyrronium bromide (BDP/FF/GB; 100/6/12.5 mcg, two actuations twice daily [BID] via pressurised metered dose inhaler [pMDI]; 'fixed triple') or an extrafine fixed combination of BDP/FF (100/6 mcg, two actuations BID via pMDI; Fostair) (Singh et al. Lancet 2016; 388: 963–73). In TRINITY patients were randomised 2:2:1 to BDP/FF/GB, tiotropium (18 mcg once daily via single-dose dry powder inhaler [SDDPI]), or BDP/FF+tiotropium: free triple (Vestbo et al. Lancet 2017; 389: 1919–29). In this analysis, we evaluated the occurrence of Major Adverse Cardiovascular Events (MACEs). MACEs included acute myocardial infarction, stroke, cardiovascular death, arrhythmias, and heart failure.

Results MACE incidence and rate in the two BDP/FF/GB groups was similar to the BDP/FF and tiotropium groups (Table 1). The majority of reported MACEs were severe in intensity, with a slightly higher percentage of fatal events in the Tiotropium only group. Importantly, in patients with relevant concomitant cardiovascular diseases, the trend was similar to that seen in the overall populations. None of the other subgroup analyses (by age, spacer use and gender) highlighted relevant differences in the safety profiles compared with the overall population.

Conclusions These Results provide further reassurance that the additional clinical benefits of this extrafine fixed triple compared to standard treatment are not associated with a greater impact on the cardiovascular safety in severe to very severe COPD patients, further supporting its positive benefit/risk ratio. Importantly, the presence of concomitant cardiac comorbidities did not influence the rate of cardiovascular events.

Please refer to page A261 for declarations of interest in relation to abstract P276.

Abstract P276 Table 1 Patients (%) with MACE, and MACE rate per 1000 patient years in TRILOGY and TRINITY

	TRILOGY		TRINITY		
	BDP/FF/GB (Fixed Triple) (n=687)	BDP/FF (Fostair®) (n=680)	BDP/FF/GB (Fixed Triple) (n=1077)	Tiotropium (n=1076)	BDP/FF +Tiotropium (Free Triple) n=537
Treatment-emergent MACEs, n(%)	15 (2.2%)	15 (2.2%)	20 (1.9%)	23 (2.1%)	7 (1.3%)
Acute Myocardial infarction	1 (0.1%)	6 (0.9%)	2 (0.2%)	4 (0.4%)	0
Arrhythmias	3 (0.4%)	2 (0.3%)	1 (0.1%)	1 (0.1%)	1 (0.2%)
Cardiovascular death	3 (0.4%)	3 (0.4%)	8 (0.7%)	6 (0.6%)	2 (0.4%)
Heart failure	6 (0.9%)	3 (0.4%)	0	8 (0.7%)	2 (0.4%)
Stroke	2 (0.3%)	2 (0.3%)	9 (0.8%)	3 (0.3%)	2 (0.4%)
Unknown cause of death	0	0	0	1 (0.1%)	0
Any fatal MACE	4 (0.6%)	5 (0.7%)	10 (0.9%)	12 (1.1%)	2 (0.4%)
MACE rate per 1000 patient years	24.9	25.6	19.5	23.5	13.6

P277 BISOPROLOL BLUNTS DOMICILIARY FEV1 IN COPD PATIENTS TAKING CONCOMITANT DUAL OR TRIPLE INHALER THERAPY

S Jabbal, B Lipworth. *University of Dundee, Dundee, UK*

10.1136/thoraxjnl-2017-210983.419