P272 IMPROVEMENTS IN EXACERBATION RATES WITH SINGLE INHALER TRIPLE THERAPY VERSUS DUAL ICS/LABA THERAPY IN PATIENTS WITH ADVANCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): SUBGROUP ANALYSES OF THE PHASE III FULFIL STUDY

[1]E Hilton, [1]N Brealey, [1]R Birk, [1]C-Q Zhu, [2]GJ Criner, [3]MT Dransfield, [4]D Halpin, [5]DA Lomas, [6]DA Lipson. *[1]GSK, Uxbridge, UK; [2]Lewis Katz School of Medicine at Temple University, Philadelphia, US; [3]Division of Pulmonary, Allergy, and Critical Care Medicine, Lung Health Centre, University of Alabama at Birmingham, Birmingham, US; [4]Department of Respiratory Medicine, Royal Devon and Exeter Hospital, Exeter, UK; [5]UCL Respiratory, University College London, London, UK; [6]GSK and Perelman School of Medicine, University of Pennsylvania, King of Prussia and Philadelphia, US*

10.1136/thoraxjnl-2017-210983.414

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 (FEV_1) <50% predicted, no moderate/severe exacerbation; FEV_1 <50%,≥1 moderate/severe exacerbation; FEV_1 ≥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 FEV_1 <50% and≥1 moderate/severe exacerbation (0.55; 0.34–0.89; p=0.015); 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.

Abstract P272 Table 1 Mean annual exacerbation rates by subgroup (ITT population; up to Week 24)

Subgroup	FF/UMEC/VI 100/62.5/25 µg (n=911)		BUD/FOR 400/12 µg (n=899)		Reduction in annual exacerbation rate	
	n	rate	n	rate	%	(95% CI)
Prior medication						
ICS+LABA	266	0.10	258	0.27	63*	(29–80)
BUD+FOR	87	0.05	83	0.10	54	(−74–88)
ICS+LABA+LAMA	256	0.28	254	0.53	47*	(13–67)
LAMA alone	79	0.12	79	0.23	49	(−42–81)
TIO alone	65	0.15	67	0.20	24	(−125–74)
LAMA+LABA	100	0.38	83	0.26	−44	(−194–29)
Disease severity						
FEV_1<50%, no moderate/severe exacerbations	311	0.22	315	0.33	33	(−4–57)
FEV_1<50%,≥1 moderate/severe exacerbation	299	0.22	290	0.41	45*	(11–66)
FEV_1≥50–≤80%,≥2 moderate/≥1 severe exacerbations	296	0.22	289	0.30	27	(−21–56)
Exacerbation history						
0/1 moderate	599	0.23	609	0.37	38*	(13–56)
≥2 moderate	308	0.01	283	0.02	27	(−20–55)
≥1 severe	185	0.12	200	0.29	57*	(14–78)

*Statistically significant difference for FF/UMEC/VI:BUD/FOR ratio; CI, confidence interval; ICS, inhaled corticosteroid; ITT, intent-to-treat; LABA, long-acting beta agonists; LAMA, long-acting muscarinic antagonists; TIO, tiotropium.

P273 ASSOCIATION OF INCIDENT PNEUMONIA AND EXACERBATIONS WITH EXTRAFINE TRIPLE THERAPY IN ONE SINGLE INHALER IN COPD PATIENTS: A POST-HOC ANALYSIS FROM TRILOGY AND TRINITY STUDIES

[1]M Scuri, [2]J Vestbo, [3]A Papi, [4]M Corradi, [1]M Spinola, [1]I Montagna, [1]C Francisco, [1]G Cohuet, [1]S Vezzoli, [1]A Muraro, [1]S Petruzzelli, [2]D Singh. *[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-2017-210983.415

Rationale Efficacy and safety of extrafine fixed triple combination of beclometasone dipropionate, formoterol fumarate, and glycopyrronium bromide (BDP/FF/GB; 100/6/12.5 mcg, two actuations BID via pMDI; 'fixed triple') has been recently demonstrated in two phase III trials. Fixed triple has shown superiority in improving lung function and reducing moderate/severe exacerbations versus BDP/FF (Fostair 100/6 mcg, two actuations BID via pMD; TRILOGY – Singh et al. Lancet 2016; 388: 963–73) and versus tiotropium (18 mcg one inhalation OD via DPI; TRINITY – Vestbo et al. Lancet 2017; 389: 1919–29). Increase in pneumonia risk associated with ICS containing medications is a known class effect. The risk/benefit balance of extrafine fixed triple was evaluated by comparing variations in pneumonia and exacerbation events.

Methods Information on moderate/severe exacerbations and confirmed pneumonia was extracted from TRINITY and TRILOGY. A frequency plot was generated considering days in the study versus cumulative number of events.

Results In TRILOGY study, the number of recorded events was 288 exacerbations (rate: 0.448 exacerbations per patient