ELLIPTA inhaler was rated higher than RESPIMAT in all ease-of-use questionnaire items ($p \leq 0.001$). 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.

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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 FEV₁ responder analysis (ITT population)

	N	UMEC/VI	N	TIO/OLO	Difference/OR (95% CI) UMEC/VI vs TIO/OLO
Trough FEV₁, mL					
Week 4	231	189 (13)	224	141 (13)	+48 (25, 71)*
Week 8	225	180 (13)	224	128 (13)	+52 (28, 77)*
Trough FEV₁ 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 FEV₁ of ≥ 100 mL; CI, confidence interval; FEV₁, 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 EXTRA-FINE SINGLE INHALER TRIPLE COMBINATION OF BECLOMETASONE DIPROPIONATE, FORMOTEROL FUMARATE, AND GLYCOPYRRONIUM BROMIDE IN COPD: RESULTS OF SAFETY ANALYSIS FROM THE TRILOGY AND TRINITY STUDIES

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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

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We investigated if serial domiciliary measures of spirometry were sensitive at detecting subtle effects of beta-2 blockade associated with bisoprolol. This was a sub-study of NCT01656005 where domiciliary diary data were available on n=17 patients with GOLD B/C COPD comprising domiciliary FEV₁(am/pm), heart rate, oxygen saturation, salbutamol use, and global symptom score. Patients received a two week run in (baseline) on inhaled corticosteroid (ICS) and long acting beta-2 agonist (LABA): beclomethasone/formoterol 100/6 µg, 2 puffs BID. Thereafter they were placed on triple therapy with the addition of a long acting muscarinic receptor antagonist (LAMA) as Tiotropium 18 µg OD, with concomitant weekly dose titration of bisoprolol as: 1.25 mg-2.5 mg-5 mg. After a further week of bisoprolol 5 mg, they were stepped back down to dual therapy (ICS/LABA) and continued this for one week. Mean age was 64 years, mean FEV₁52% predicted, mean FEV₁/FVC ratio of 0.46, mean 50 pack year smoking history, and 7% mean FEV₁ reversibility to salbutamol 400 µg. Compared to a baseline am FEV₁ of 1.38 L (95% CI 1.14–1.61 L), both ICS/LABA/LAMA and ICS/LABA in conjunction with bisoprolol showed statistically significant mean falls in amounting to 100 ml 1.28 L (95% CI 1.03–1.53 L) and 120 ml respectively 1.26 L (95% CI 1.01–1.51 L); equaling and exceeding the MCID of 100 ml respectively. Bisoprolol produced a significant heart reduction of 11 beats/min from a baseline of 80 bpm (95% CI 74–85 bpm) to 69 bpm (95% CI 64–73 bpm) and 69 bpm (95% CI 65–73 bpm) for ICS/LABA/LAMA and ICS/LABA respectively. There was no change in salbutamol use, symptom score or oxygen saturation, pre and post bisoprolol, irrespective of triple or dual therapy. In the context of dual or triple therapy, bisoprolol was associated with subtle but significant falls in domiciliary FEV₁, which were disconnected from symptoms, reliever use and oxygen saturation.

P278 ASSESSING DIFFERENT VALVED HOLDING CHAMBERS (VHC) WITH FACEMASK FOR DELIVERED MASS TO CARINA WITH INHALED CORTICOSTEROID BY PRESSURISED METERED-DOSE INHALER (PMDI)

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Introduction and Objectives Laboratory evaluation of VHC-facemask add-ons is ideally undertaken simulating conditions of use. We report a study in which such devices for small child use were evaluated using an anatomical face-model and upper airway commensurate with that of a 4 year old child.

Methods A number of VHCs with facemask (n=3 devices/group) were evaluated using an anatomical face-model and upper airway commensurate with that of a 4 year old child. Each VHC was prepared to manufacturer instructions, then evaluated by breathing simulator (ASL5000), mimicking a short coordination delay of 2 s followed by tidal breathing (tidal volume (Vt)=155 mL, I:E ratio=1:2, rate=25 cycles). The facemask was attached to ADAM-III small child model. The airway was coupled directly to the breathing simulator via a filter below its exit to capture drug particles that would penetrate as far as the carina in a real patient. 5-actuations of fluticasone propionate (50 µg, FP) were delivered at 30 s intervals. FP recovered from various locations in the aerosol pathway was subsequently assayed by HPLC-UV spectrophotometry.

Results Distribution of recovered FP from each type of VHC is summarised in Table 1.

Conclusions Significantly more FP was delivered to the model 'carina' from the AC Plus VHC with child mask (p<0.001), the increased mass counterbalanced by decreased retention of medication within the VHC. It is important that clinicians are aware that large differences in delivery efficiency may exist when a facemask is present.

P279 PRIMING OF A NON-CONDUCTING VALVED HOLDING CHAMBER (VHC) MAY RESULT IN INCONSISTENT MEDICATION DELIVERY

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Introduction and Objectives Priming VHCs with several actuations of medication before use may be an established practice to prepare the spacer before use. However this practice can have a significant influence on subsequent medication delivery. The present study set out to test the hypothesis that priming is not effective, or better than the use of anti-static materials.

Methods The following VHCs, each with mouthpiece as patient interface (n=5 devices/group) were evaluated: AeroChamber Plus Flow-Vu Antistatic VHC (AC +FV AVHC); AeroChamber Plus; Volumatic™; Able Spacer 2™; Anti-Static Compact Space Chamber plus™. Each VHC was connected via a filter holder to a vacuum source operated at 28.3 L/min, evaluated with a pMDI (Flovent 125 µg, FP) and the Emitted Mass of FP (EM_{FP}) determined by HPLC-UV assay. The following sequence of testing was conducted: 1) Test VHC immediately after removal from packaging (no pre-treatment) and evaluate EM_{FP} following one actuation. 2) Supply two more actuations into the same VHC and evaluate EM_{FP}

Abstract P278 Table 1 FP (mean µg±SD) recovered from VHCs indicated for small child use, simulating a 2 s coordination delay followed by tidal breathing

Retention Location	AeroChamber Plus Flow-Vu	Pocket-Chamber	Vortex	Compact SpaceChamber Anti-Static	A2A Spacer	Volumatic	Able* Spacer2	Optichamber Diamond*
VHC	17.5±1.6	36.6±0.2	39.7 ±6.7	36.1±3.6	28.3±2.8	33.6±1.9	13.2±1.6	22.7±2.7
Facemask	1.4±0.2	1.9±0.8	1.2±0.2	0.0±0.0	0.2±0.1	0.1±0.1	0.0±0.0	3.4±0.8
Airway	1.1±0.2	0.4±0.2	0.6±0.3	0.1±0.1	0.4±0.1	0.0±0.0	0.2±0.0	0.7±0.1
Filter at 'Carina'	10.1±1.0	4.0±1.7	2.7±1.5	2.1±0.8	4.1±0.9	1.5±0.8	5.1±0.9	5.1±0.9

Abstract P279 Figure 1

(representing 3 actuations of priming).3) Deliver 17 more actuations into the same VHC and evaluate EM_{FP} (representing priming of 20 actuations). 4) Clean VHC, then repeat part (1) (representing pre-conditioning by washing as an alternative to priming).

Results The behaviour of EM_{FP} (mean ±SD) with VHC type is summarised in figure 1.

Conclusions Clinicians should be aware that priming of VHCs Results in inconsistent medication delivery, and is wasteful of medication.

P280

HOW DO WE CHOOSE INHALERS? PATIENT AND PHYSICIAN PERSPECTIVES ON ENVIRONMENTAL, FINANCIAL AND EASE-OF-USE FACTORS

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Introduction Inhaled therapy is widely used as mainstay treatment in chronic respiratory conditions, however the environmental impact of inhalers is rarely considered when

prescribing inhalers. A recent BTS position statement “encourages all prescribers and patients to consider switching pMDIs to non-propellant devices whenever they are likely to be equally effective.”(1) Little is known about Patients’ or Physicians’ perspectives on making such a switch.

Methods A survey was carried out to assess the importance of three factors to consider, if changing to a different but equally effective inhaler – cost, carbon footprint and ease-of-use. Information about the typical costs and carbon footprints of inhalers was provided. 50 patients already using regular inhalers were randomly recruited via Respiratory Clinics at a district general hospital and Pulmonary Rehabilitation sessions. Responses were rated on a 5-point scale from not important to very important. The same survey was also completed by 50 medical professionals who regularly prescribe inhalers.

Results 80% of patients surveyed rated the ease-of-use as important or very important consideration when changing inhalers. The ‘cost’ and ‘carbon footprint’ of the inhaler were equally important to patients (3.4 out of 5); only 14% of patients indicated that carbon footprint was of no importance to them.

Abstract P280 Table 1 Comparison of the importance given by patients and physicians to consideration of cost, carbon footprint and ease-of-use when changing inhalers

Importance Ranking	Score	Inhaler Cost		Carbon Footprint		Ease-of-use	
		Patient	Physician	Patient	Physician	Patient	Physician
Not important	1	12%	14%	14%	14%	8%	0%
Slightly important	2	8%	8%	8%	18%	0%	2%
Moderately important	3	32%	16%	34%	22%	12%	2%
Important	4	22%	44%	16%	30%	16%	12%
Very important	5	26%	18%	28%	16%	64%	84%
Important & Very Important	4 & 5	48%	62%	44%	46%	80%	96%
Average (mean score out of 5)		3.4	3.4	3.4	3.2	4.3	4.9

Physicians rated ease-of-use even higher than patients, with 96% deeming this as an important or very important factor. Physicians rated carbon footprint slightly less importantly (3.2) than cost (3.4) and also lower than patients rated carbon footprint. 14% of physicians thought that carbon footprint was of no importance.

Conclusions Patients and Physicians agree that ease-of-use is the most important factor when choosing a new inhaler. This

appears to contradict the fact that overall patients make fewer errors using DPIs(2), while the majority of inhalers prescribed in the UK are pMDIs(3). The data suggests that patients rate carbon footprint more importantly than physicians. The carbon footprint of inhalers is an important factor for the majority of patients, which should encourage physicians to discuss this consideration with patients prior to commencing or changing inhalers.