S59 USING VENOUS BLOOD GAS ANALYSIS IN THE MANAGEMENT OF COPD EXACERBATIONS; A PROSPECTIVE COHORT STUDY

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Introduction COPD exacerbations are a common cause of emergency hospital admission in the UK, with an estimated 94,000 per year. Identifying hypercapnic respiratory failure is crucial. Guidelines recommend obtaining arterial blood samples but these are more difficult to obtain than venous samples. Furthermore, administration of local anaesthetic prior to arterial sampling is seldom used. We assessed whether blood gas values derived from venous samples could replace arterial at initial assessment.

Methods Patients treated for a COPD exacerbation had paired arterial and venous samples taken. Bland Altman analyses were performed to assess agreement between arterial and venous pH, PCO_2 and HCO_3^-, and between SpO_2 and SaO_2. The number of attempts and pain scores for each sample were measured.

Results 234 patients had paired arterial and venous samples. There was good agreement between arterial and venous measures of pH and HCO_3^- (mean difference 0.03 and -0.04, limits of agreement -0.54 to 0.11, and -2.90 to 2.82), and between SaO_2 and SpO_2 (in patients with a SpO_2 of greater than 80%).

We calculated the sensitivity and specificity of a VBG pH and HCO_3^- to correctly identify an arterial pH of $\geq$7.35, and an arterial HCO_3^- of $\geq$21, as well as a SpO_2 to identify a SaO_2 of $\geq$ 92%. A venous pH of 7.34, a venous HCO_3^- of 21.45 and a SpO_2 of 91.5 would have correctly classified 87% (95% CI 82% to 91%), 97% (95% CI 93% to 98%), and 71% (95% CI 65% to 77%), of patients respectively. 96% of patients with an ABG pH of $\geq$7.35 also had a VBG pH of $\geq$7.35.

Arterial sampling took more attempts and was more painful than venous (mean pain score 4 (IQR 2–5) and 1 (IQR 0–2), p < 0.001).

Abstract S59 Table 1 Agreement between arterial and venous pCO_2, pH and HCO_3^-

	ABG (Mean) (SD)	VBG (Mean) (SD)	Mean Difference (ABG- VBG) (95% CI)	95% Limits of agreement	N
pH	7.40 (0.09)	7.37 (0.08)	0.03 (0.02 to 0.04)	-0.54 to 0.11	234
HCO_3^-(mEq/L)	29.7 (6.3)	29.7 (6.4)	-0.04 (-0.22 to 0.15)	-2.90 to 2.82	232
pCO_2 (kPa)	6.89 (2.40)	7.63 (2.41)	1.93 (1.58 to 2.28)	-3.38 to 7.24	225

Abstract S59 Table 2 Agreement between SaO_2 and SpO_2

	SaO_2 (Mean) (SD)	SpO_2 (Mean) (SD)	Mean Difference (SaO_2- SpO_2) (95% CI)	95% Limits of agreement	N
Oxygen percentage saturation*	91.2 (6.0)	91.0 (4.0)	-0.17 (CI -0.89 to 0.56)	-11.12 to 10.78	224

*in patients with SpO_2 >80%.

Conclusion Arterial sampling is more difficult and painful than venous sampling. There is good agreement between pH and HCO_3^- values derived from venous and arterial blood, and between pulse oximetry and arterial blood gas oxygen saturations. This could allow the initial assessment of COPD exacerbations to be based on venous blood gas analysis and pulse oximetry, simplifying the care pathway and improving the patient experience.

S60 EFFICACY AND SAFETY OF ACLIDINIUM/FORMOTEROL FIXED-DOSE COMBINATION IN PATIENTS WITH COPD, STRATIFIED BY ICS USE

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Introduction and objectives This was a secondary analysis, stratified by concomitant inhaled corticosteroid (ICS) use, based on pooled data from ACLIFORM (NCT01462942) and AUGMENT (NCT01437397), two Phase III, 24-week, randomised, double-blind studies of twice-daily aclidinium/formoterol (AB/FF) fixed-dose combination in patients with moderate to severe airflow obstruction.

Methods Patients received twice-daily AB/FF 400/12 µg, AB/FF 400/6 µg, AB 400 µg, FF 12 µg or placebo (PBO). Any baseline ICS use was continued throughout. Assessments: change from baseline in 1-hour morning post-dose and morning pre-dose (trough) forced expiratory volume in 1 s (FEV_1) at Week 24 and Transition Dyspnoea Index (TDI) score (pre-planned), rate of exacerbations and adverse events (AEs).

Results Analyses included 3398 patients (mean age 63.5 years; 60.5% male; baseline ICS use range 38.7–40.0%). In patients using ICS, AB/FF 400/12 µg improved post-dose FEV_1, trough FEV_1 (Table 1), and TDI vs PBO by 297 mL, 145 mL and 1.59 units, respectively (all p < 0.001). In addition, in patients receiving concomitant ICS, AB/FF 400/12 µg improved post-dose FEV_1 and trough FEV_1 (Table 1) by 109 mL and 71 mL, respectively, vs FF alone (both p < 0.001) and by 151 mL and 54 mL, respectively, vs AB alone (p < 0.001 and p < 0.05, respectively). In patients not using ICS, there were improvements with AB/FF 400/12 µg in post-dose FEV_1, trough FEV_1 (Table 1) and TDI of 290 mL, 135 mL and 1.36 units vs PBO, respectively (all p < 0.001). The exacerbation rate was higher in patients using ICS

(0.67) vs those who did not (0.36) and AB/FF 400/12 μg significantly reduced the rate of exacerbations vs PBO ($p < 0.05$; Table 1). The overall AE frequency was similar throughout (range with ICS, 54.8–60.7%; without, 56.0–60.3%). The most common AEs across patient groups were COPD exacerbation, nasopharyngitis and headache, irrespective of ICS use.

Conclusion In this analysis, aclidinium/formoterol 400/12 μg twice daily improved bronchodilation and dyspnoea in patients independent of ICS use and reduced exacerbations in patients using ICS. Combining AB and FF along with an ICS increased bronchodilation vs either monotherapy. AE frequencies were similar between the patient groups, regardless of ICS use.

Abstract S60 Table 1 Change from baseline in morning pre-dose (trough) FEV_1 at Week 24 and rate of exacerbations by concomitant ICS use

	AB/FF 400/12 μg BID	AB/FF 400/6 μg BID	AB 400 μg BID	FF 12 μg BID	Placebo BID
LS mean change from baseline in morning pre-dose (trough) FEV_1 at Week 24 by ICS use, mL[a]					
ICS use	98***	47***	44***	27**	-47
No ICS use	85***	71***	71***	18***	-50
Rate of exacerbations per patient/year by ICS use[b]					
ICS use	0.40*	0.53	0.59	0.45	0.67
No ICS use	0.31	0.27	0.29	0.44	0.36

[a]Analyses based on the mixed model for repeated measures: treatment effects and treatment comparisons.
[b]Analysis based on the log-linear model.
*$p < 0.05$ vs placebo; **$p < 0.01$ vs placebo; ***$p < 0.0001$ vs placebo.
AB, aclidinium bromide; BID, twice daily; FEV_1, forced expiratory volume in 1 s; FF, formoterol fumarate; ICS, inhaled corticosteroid; LS, least squares.

S61 ANALYSIS OF THE EFFICACY AND SAFETY OF THE COMBINATION OF TIOTROPIUM + OLODATEROL IN PATIENTS WITH COPD BY PREVIOUS USAGE OF INHALED CORTICOSTEROIDS

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Rationale Tiotropium (T), a long-acting muscarinic antagonist, and olodaterol (O), a long-acting β_2-agonist (both administered once daily), have been studied as a once-daily combination. Two Phase III studies have demonstrated that T+O significantly improved lung function and symptoms over T and O monotherapy treatments in patients with moderate to very severe chronic obstructive pulmonary disease (COPD).[1] During these studies, patients were allowed to continue existing treatment with inhaled corticosteroids (ICS); this analysis was conducted to determine the effects of study treatment in patients receiving or not receiving ICS as reported at baseline.

Methods A total of 5162 patients were randomised to treatment with O 5 μg, T 2.5 μg, T 5 μg, T+O 2.5/5 μg or T+O 5/5 μg (Respimat® inhaler) in two 52-week, double-blind, parallel-group studies (NCT01431274 and NCT01431287). Primary efficacy end points were trough forced expiratory volume in 1 s (FEV_1) response (ie, change from baseline), FEV_1 area under the curve from 0–3 h (AUC_{0-3}) response and St George's Respiratory Questionnaire (SGRQ) total score after 24 weeks. Pooled data are presented for the patient subgroups either using or not using ICS at baseline.

Results In the overall population, all treatments resulted in clinically relevant improvements in lung function, with significant increases with both T+O doses over the individual components ($p < 0.01$).[1] These effects on lung function were observed irrespective of whether or not patients had reported concomitant use of ICS at baseline (see Table 1). In the 'ICS usage' and 'no ICS usage' subgroups, there were no statistically significant differences between the combinations and monotherapy treatments in changes in SGRQ total scores from baseline to Week 24, although SGRQ total scores were improved during this period with T+O.

Abstract S61 Table 1 Lung function responses at 24 weeks according to baseline ICS usage[a]

	Trough FEV_1, L		FEV_1 AUC_{0-3}, L	
	n	Adjusted mean (SE) change	n	Adjusted mean (SE) change
ICS usage				
O 5	497	0.046 (0.009)	503	0.129 (0.009)
T 2.5	471	0.084 (0.009)	476	0.142 (0.009)
T 5	464	0.088 (0.009)	465	0.147 (0.009)
T+O 2.5/5	489	0.114 (0.009)$^{\dagger\#*}$	492	0.246 (0.009)$^{\dagger;\#\#**}$
T+O 5/5	503	0.133 (0.009)$^{\dagger;\#\#**}$	505	0.260 (0.008)$^{\dagger\#\#**}$
No ICS usage				
O 5	510	0.067 (0.009)	514	0.139 (0.009)
T 2.5	533	0.062 (0.009)	537	0.132 (0.008)
T 5	536	0.073 (0.009)	543	0.155 (0.008)
T+O 2.5/5	511	0.122 (0.009)$^{\dagger\#\#**}$	517	0.252 (0.008)$^{\dagger\#\#**}$
T+O 5/5	500	0.149 (0.009)$^{\dagger\#\#**}$	503	0.263 (0.009)$^{\dagger\#\#**}$

$^{\dagger}p < 0.0001$ vs O 5; $^{\#\#}p < 0.0001$ vs T 2.5; **$p < 0.001$ vs T 5.
[a]Patients were not recorded as receiving LAMA or LABA at baseline in this study.
SE, standard error.

Conclusions In patients with COPD, T+O 5/5 μg significantly improved lung function over T 5 μg and O 5 μg monotherapy, irrespective of whether patients had reported ICS use at baseline.

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Mechanisms of lung injury and fibrosis remodelling on the fly

S62 USING DROSOPHILA MELANOGASTER TO STUDY PATHOGENIC MUTANTS OF SURFACTANT PROTEIN C

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Introduction and objectives Surfactant protein C (SFTPC) is secreted by type II pneumocytes to reduce alveolar lining fluid surface tension and thus prevent alveolar collapse at low lung volumes. The immature form of SFTPC must undergo proteolytic