Conclusion Aclidinium 200 μg and 400 μg twice daily provided clinically meaningful improvements in bronchodilation, health status, symptoms, breathlessness and exacerbation rate. Aclidinium was well tolerated with a similar safety profile for both doses; the incidence of AEs was similar to placebo.

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P256 ACLIDINIUM BROMIDE: A PHASE IIB, DOSE-FINDING STUDY

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Introduction and Objectives Aclidinium bromide, a second-generation, long-acting muscarinic antagonist with low systemic activity, is in clinical development for the twice daily maintenance treatment of chronic obstructive pulmonary disease (COPD). This Phase IIb study investigated the dose-response bronchodilation of aclidinium twice daily vs placebo and an active control (formoterol 12 μg twice daily) in patients with moderate to severe COPD.

Methods In this double-blind, double-dummy, cross-over study, 79 patients received 7-day treatments of aclidinium 100 μg, 200 μg and 400 μg, formoterol 12 μg and placebo twice daily over five treatment periods separated by a 7-day washout. The primary endpoint was change from baseline in normalised forced expiratory volume in 1 second (FEV_1) area under the curve $(AUC)_{0-12}$ at Day 7. Other efficacy assessments included change from baseline at Day 7 in normalised FEV_1 AUC_{0-24} and morning pre-dose (trough) and peak FEV_1. Adverse events (AEs) were reported throughout the study.

Results Aclidinium provided dose-dependent bronchodilation compared with placebo as assessed by change from baseline in normalised FEV_1 AUC_{0-12} and FEV_1 AUC_{0-24} at Day 7 (Abstract P256 table 1). The bronchodilation provided by aclidinium 400 μg during the first 12 h was comparable to the active control, formoterol 12 μg. Aclidinium improved morning pre-dose trough FEV_1 and peak FEV_1 after 7 days compared with placebo; the 400 μg dose was most comparable to formoterol 12 μg. Aclidinium was well tolerated; the safety profile of all doses was comparable to that of placebo.

Abstract P256 Table 1 Adjusted mean (SE) change from baseline (L) on Day 7

	Aclidinium 100 μg	Aclidinium 200 μg	Aclidinium 400 μg	Formoterol 12 μg	Placebo
Normalised FEV_1 AUC_{0-12h}	0.128* (0.022)	0.151* (0.022)	0.183* (0.022)	0.185* (0.022)	−0.026 (0.022)
Normalised FEV_1 AUC_{0-24h}	0.089* (0.021)	0.100* (0.021)	0.133* (0.021)	0.163* (0.020)	−0.062 (0.021)
Morning pre-dose FEV_1	0.081* (0.023)	0.089* (0.023)	0.130* (0.023)	0.123* (0.023)	−0.025 (0.023)
Morning peak FEV_1	0.287* (0.023)	0.299* (0.023)	0.340* (0.023)	0.344* (0.023)	0.098 (0.023)

*p<0.0001 vs placebo.

Conclusion A dose-dependent bronchodilation was observed with aclidinium twice daily. The bronchodilation provided by the highest dose of aclidinium (400 μg) twice daily was comparable to formoterol 12 μg twice daily. The safety profile of aclidinium was similar to placebo, with no dose-dependent AEs observed.

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P257 EFFECTS OF EXTRA-FINE INHALED AND ORAL CORTICOSTEROIDS ON ALVEOLAR NITRIC OXIDE IN COPD

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Introduction and Objectives Alveolar nitric oxide or (CA_{NO}), has been used as a surrogate marker of distal airway inflammation, which isimportant in COPD. Coarse particle inhaled corticosteroids (ICS) have been shown not to suppress CA_{NO}. We evaluated whether extra-fine particlesize inhaled corticosteroids (HFA-BDP) or systemic oral corticosteroids could suppress CA_{NO} in COPD.

Methods COPD patients with a smoking pack history >15 years, FEV_1/FVC ratio <0.7, FEV_1<80% predicted with small airways inflammation characterised by CANO >2 ppb underwent a double-blind randomised controlled crossover trial with an open label systemic steroid comparator. Following a 2 wk steroid washout period, patients were randomised to 3 weeks, 100 mcg HFA-BDP twice daily and then 3 weeks 400 mcg HFA-BDP twice daily or matched placebos with subsequent crossover. All patients then received 1 week open-label, 25 mg/day prednisolone. Spirometry, bodyplethysmography, impulse oscillometry, plasma cortisol and exhaled nitric oxide were recorded. CA_{NO} was corrected for axial diffusion.

Results 16 patients completed per protocol. Compared to respective placebo there were no significant differences seen with either dose of HFA-BDP. Oral prednisolone caused a significant reduction in FE_{NO} and $J'aw_{NO}$ but not CA_{NO}. Plasma cortisol was significantly suppressed by oral prednisolone compared to all other treatments. There was no suppression seen with HFA-BDP at either dose verses placebo.

Conclusions While CA_{NO} remains a biomarker of interest in COPD, it is not suppressed by systemic or extra-fine particle ICS. Hence CA_{NO} is unlikely to be a useful marker for monitoring response of small airway disease to therapies in COPD.

P258 ROLE OF 7-DAY AND 14-DAY COURSES OF ORAL PREDNISOLONE TREATMENT IN ACUTE EXACERBATION OF COPD

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Purpose The purpose of this study was to compare the efficacy of 7-day and 14-day courses of oral prednisolone treatment in patients with acute exacerbation of COPD with FEV_1<50% predicted.

Methods It was a prospective randomised, single blind study in a tertiary care centre, the study patients were included and randomised into two groups: 7-day group received oral prednisolone 30 mg/day for 7 days, and 14-day group was administered the same dosage of oral prednisolone for 14 days. There was no significant difference between the groups for age, smoking pack years, symptoms of COPD in years, no. of previous exacerbations, blood eosinophilia, baseline FEV_1, and FVC levels. One patient from 7-day group developed pneumothorax and one from 14-day group died of acute Myocardial Infarction.

Results Both groups showed significant improvements of FEV_1 and FVC on D-1, D-3, D-5, D-7, D-10 and Day-14 from the baseline (7-day group, p=0.0001, 0.0001, 0.008, 0.009, 0.008, 0.011and 14-day group, p=0.000, 0.000, 0.000, 0.000, 0.000, 0.000) and the improvement of FVC is also significant in both the groups, but there was no significant difference of improvement between the two groups on day-7 and day-14 (p=0.100, 0.079). There was also significant improvement of symptom score from baseline on day-7 and day-14, but no significant difference of improvement between two groups.