

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

Funding This study was supported by Almirall S.A., Barcelona, Spain, and Forest Laboratories, Inc., New York, USA.

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

doi:10.1136/thoraxjnl-2011-201054c.256

¹D Singh, ²H Magnussen, ²A Kirsten, ³S Mindt-Pruefert, ⁴C Caracta, ⁵D Jarreta, ⁵E Garcia Gil. ¹Medicines Evaluation Unit, University of Manchester, Manchester, UK; ²Pulmonary Research Institute, Hospital Grosshansdorf, Grosshansdorf, Germany; ³Klinische Forschung Hamburg GmbH, Hamburg, Germany; ⁴Forest Research Institute, New Jersey, USA; ⁵Almirall S.A., Barcelona, Spain

Introduction and Objectives Acclidinium 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 acclidinium 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 acclidinium 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 (FEV₁) area under the curve (AUC)₀₋₁₂ at Day 7. Other efficacy assessments included change from baseline at Day 7 in normalised FEV₁ AUC₀₋₂₄ and morning pre-dose (trough) and peak FEV₁. Adverse events (AEs) were reported throughout the study.

Results Acclidinium provided dose-dependent bronchodilation compared with placebo as assessed by change from baseline in normalised FEV₁ AUC₀₋₁₂ and FEV₁ AUC₀₋₂₄ at Day 7 (Abstract P256 table 1). The bronchodilation provided by acclidinium 400 µg during the first 12 h was comparable to the active control, formoterol 12 µg. Acclidinium improved morning pre-dose trough FEV₁ and peak FEV₁ after 7 days compared with placebo; the 400 µg dose was most comparable to formoterol 12 µg. Acclidinium 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

	Acclidinium 100 µg	Acclidinium 200 µg	Acclidinium 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 acclidinium twice daily. The bronchodilation provided by the highest dose of acclidinium (400 µg) twice daily was comparable to formoterol 12 µg twice daily. The safety profile of acclidinium was similar to placebo, with no dose-dependent AEs observed.

Funding This study was supported by Almirall S.A., Barcelona, Spain, and Forest Laboratories, Inc., New York, USA.

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

doi:10.1136/thoraxjnl-2011-201054c.257

P M Short, P A Williamson, B J Lipworth. *Asthma and Allergy Research Group, Ninewells Hospital and Medical School, University of Dundee, Dundee, UK*

Introduction and Objectives Alveolar nitric oxide or (CA_{NO}), has been used as a surrogate marker of distal airway inflammation, which is important 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, FEV₁/FVC ratio <0.7, FEV₁<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**

doi:10.1136/thoraxjnl-2011-201054c.258

S M Abdullah Al Mamun, S Rahman. *Sher E Bangla Medical college, Barisal, Bangladesh*

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 FEV₁<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 FEV₁, 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 FEV₁ 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.