European Respiratory Society
Annual Congress 2012

Abstract Number: 1618

Publication Number: P2088

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Asthma - management **Keyword 2:** Nitric oxide **Keyword 3:** Inflammation

Title: Effects of inhaled corticosteroids on asthmatic inflammation: The FeNOtype trial

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Body: BACKGROUND: Personalised treatment for inflammatory asthma phenotypes confers superior benefits. The elevated exhaled nitric oxide (FeNO) inflammatory phenotype requires evaluation of dose-response to inhaled corticosteroids (ICS). METHODS: Randomised, crossover trial in mild-to-moderate asthmatics receiving ICS with elevated FeNO>40ppb after ICS washout. Patients received 2 weeks of: fluticasone propionate 50ug twice-daily (FP100) or 250ug twice-daily (FP500). Primary outcome: response in diurnal domiciliary FeNO levels. Secondary outcomes included: mannitol challenge; serum eosinophilic cationic protein (ECP); blood eosinophil count; and asthma control questionnaire (ACQ). RESULTS: 21 patients completed. We found significant dose-related reductions of diurnal FeNO compared to baseline: am FeNO: baseline=71ppb; FP100=34ppb, $p<0.001$; FP500=27ppb, $p<0.001$; and significant dose separation for am, $p<0.05$, and pm, $p<0.001$. Time series FeNO displayed exponential decay:

ACQ significantly improved exceeding the minimal important difference (>0.5) with values in keeping with controlled asthma (<0.75) after each dose: FP100=0.48, $p=0.004$; FP500=0.37, $p=0.001$. All other secondary inflammatory related outcomes showed significant improvements from baseline but no dose separation. CONCLUSION: There is significant, dose-response of diurnal FeNO to ICS in patients with a high FeNO phenotype, also associated with well controlled asthma.