suggesting an altered inflammatory phenotype, at least in these models, to these stimuli.

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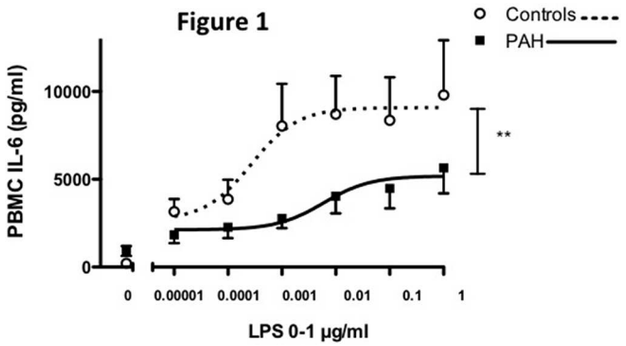

Abstract P159 Figure 1.

P160 RETROSPECTIVE STUDY ANALYSING WHETHER OPTIMIZATION OF PULMONARY VASCULAR ENHANCEMENT INFLUENCES DIAGNOSTIC OUTCOME IN THE INTERPRETATION OF CT PULMONARY ANGIOGRAMS (CTPA)

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Introduction and Objectives Pulmonary embolism (PE) is a common cardiovascular emergency and is the most common preventable cause of hospital deaths. Various factors can impact on the diagnostic accuracy of CTPA, which is now considered the 1st line investigation for PE diagnosis. Mis-timing of contrast medium administration or cardiac impairment can result in an indeterminate scan through hidden or mimicked emboli. This study focuses on the accuracy of CTPAs in excluding a diagnosis of PE.

Method This is a single centre study looking at all inpatient and outpatient CTPAs carried out over a 12-month period with matched CTPA and lower limb ultrasound Doppler events selected. Of these matched studies, all positive CTPAs for PE were excluded. Of the remainder, only those studies done within 6 months of the original CTPA were included in the study. CT pulmonary arterial (PA) opacification with intravenous contrast medium was objectively measured in Hounsfield units (HU) using an oval region of interest in the main pulmonary trunk. PA opacification was categorised as very poor (<100 HU), suboptimal (< 200 HU) and optimal (= 200HU) as measured at the PA trunk based on the estimation that a minimal opacification of 100 HU is required for identification of acute emboli and 200 HU is required for identification of chronic emboli.

Results From the 32 CTPAs included in the study, 28 had a negative initial CTPA with subsequent negative CT or US follow-up. 4 of these cases had an initial negative CTPA with a subsequent positive CTPA or lower limb US Doppler study. Of these latter cases only one initial CTPA was deemed poorly suboptimal (average 174HU) with optimal pulmonary arterial opacification in all other three initial CTPAs.

Conclusion This study demonstrates that despite a large number of initially negative CTPAs undergoing subsequent follow-up imaging due to presumed persistent or recurring patient symptoms, the majority (87.5%) of these negative scans were still negative and only 12.5% were positive for PE. No major pitfall has been identified in local CTPA acquisition technique that may have led to subsequent misses of potentially life-threatening PEs.

Clinical trials in asthma

P161 A RANDOMISED CONTROLLED TRIAL OF SINGLE COMBINATION BUDESONIDE/FORMOTEROL INHALER AS MAINTENANCE AND RELIEVER THERAPY IN ASTHMA PATIENTS AT RISK OF SEVERE EXACERBATIONS

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Introduction The Single budesonide/formoterol inhaler Maintenance And Reliever Therapy (SMART) regimen reduces severe asthma exacerbations, but it is uncertain whether it increases the risk of adverse effects due to high beta-agonist and corticosteroid doses with both short-term and cumulative exposure.

Objectives Our hypothesis was that treatment with the SMART regimen would reduce the risk of beta-agonist overuse but that when such episodes occurred, patients were less likely to seek medical review and, that any reduction in severe exacerbations would be at the cost of a higher systemic corticosteroid burden.

Methods This was a 24-week, open-label, parallel group trial in 303 asthma patients with a recent exacerbation, conducted at four primary healthcare practices and one secondary care hospital. Participants were randomised to 200/6 g budesonide/formoterol metered dose inhaler according to the SMART regimen (two actuations twice daily maintenance with one extra actuation as-needed) or a fixed-dose regimen (two actuations twice daily maintenance) with one to two actuations of 100 g salbutamol as-needed ('Standard'), with electronic monitoring of actual inhaler use. The primary outcome was the proportion of participants with at least one high beta-agonist use episode (>12 budesonide/formoterol actuations/day in SMART or >16 salbutamol actuations/day in Standard).

Results There was no significant difference between groups in the proportion of participants with at least one high use episode: SMART 84/151 (56%) vs Standard 68/152 (45%) participants; relative risk (95% CI) 1.24 (0.99–1.56), p = 0.058. There were fewer days of high use [mean (SD) 5.1 days (14.3) vs 8.9 days (20.9), relative rate (RR) (95% CI) 0.58 (0.39–0.88), p = 0.01] and days of high use without medical review [8.5 days (17.8) vs 18.3 days (24.8) per high use patient, RR 0.49 (0.31–0.75), p = 0.001] in the SMART group. The SMART regimen resulted in higher average daily inhaled corticosteroid exposure, but reduced oral corticosteroid exposure, with no difference in composite systemic corticosteroid exposure [ratio of means (95% CI) 1.03 (0.86–1.22), p = 0.76]. SMART participants had fewer severe asthma exacerbations [35 vs 66, RR 0.54 (0.36–0.82), p = 0.004].

Conclusions The SMART regimen has a favourable risk/benefit profile in patients at risk of severe asthma exacerbations.

P162 EFFECT OF ADDING PROPRANOLOL OR INCREASED INHALED CORTICOSTEROID DOSE IN PERSISTENT ASTHMA

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Introduction and Objectives Chronic propranolol does not improve airway hyper-responsiveness (AHR) in persistent asthmatics taking medium dose inhaled corticosteroid (ICS), 440 g/day[1]. We wished to assess for any putative corticosteroid-sparing effect of propranolol added to low dose ICS versus higher dose ICS, on histamine AHR.

Methods We conducted a randomised double-blind placebo-controlled crossover trial in mild-moderate persistent asthmatics. Patients were run-in for 2 weeks on hydrofluoroalkane-beclometasone dipropionate (HFA-BDP) 100 g/day. Patients were then randomised to either: propranolol 80mg/day plus HFA-BDP 100 g/day; or placebo plus HFA-BDP 400 g/day, each for 4 weeks. Propranolol was up-titrated to 80mg/day for the second 2 weeks of treatment. Patients received tiotropium 18 g/day during run-in and both treatments, which was subsequently discontinued 5 days prior to histamine challenge (primary outcome).

Results 16 patients completed, mean: age 38yr; FEV_1 86.4%; Histamine PC_{20} 1.39mg/ml; ICS 406 g/day. Histamine PC_{20} remained unchanged adding propranolol to HFA-BDP100 compared to baseline (HFA-BDP100): 0.17 doubling dilution (dd) difference (95%CI -0.58–0.92), but there was a significant improvement with HFA-BDP400 compared to both baseline 1.05dd (95%CI 0.43–1.66), P = 0.02; and propranolol 0.88dd (95%CI 0.45–1.30), P = 0.006 (Figure 1a). Significant improvements from baseline were observed with HFA-BDP400 for exhaled nitric oxide, blood eosinophils (Figure 1b) and Asthma Quality of Life Questionnaire (AQLQ) symptom score (Figure 1c), but not with propranolol. Salbutamol recovery time post-challenge was partially blunted by propranolol (median prolongation 5min compared to both baseline and HFA-BDP400, P = 0.002). Domiciliary evening FEV_1 also fell with propranolol (mean reduction from baseline 0.22L [95%CI 0.10–0.34L], P = 0.012) while Asthma Control Questionnaire (ACQ) showed no significant changes with either treatment compared to baseline.

Conclusions In mild-moderate persistent asthmatics, propranolol produced no additive effects on top of low dose ICS, while further significant improvements in AHR and inflammation were seen with a higher dose of ICS. Propranolol attenuated salbutamol recovery and reduced evening FEV_1, but not ACQ or AQLQ.

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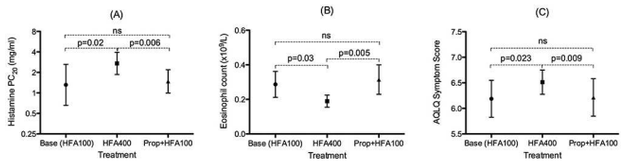

Abstract P162 Figure 1 (A) Histamine provocative concentration causing 20% fall in FEV1. Geometric means with 95% confidence intervals (CI). (B) Blood eosinophil count. Means with 95% CI. (C.) Asthma Quality of Life Questionnaire (AQLQ) symptom component score. Means with 95% CI. HFA = hydrofluoroalkane beclometasone dipropionate. Base = post run-in baseline measurements. HFA100 = 100 g/day. HFA400 = 400 g/day. Prop = Propranolol 80mg/day.

P163 TIOTROPIUM DECREASES THE RISK OF EXACERBATIONS IN PATIENTS WITH SYMPTOMATIC ASTHMA REGARDLESS OF BASELINE CHARACTERISTICS INCLUDING MARKERS OF ALLERGIC STATUS

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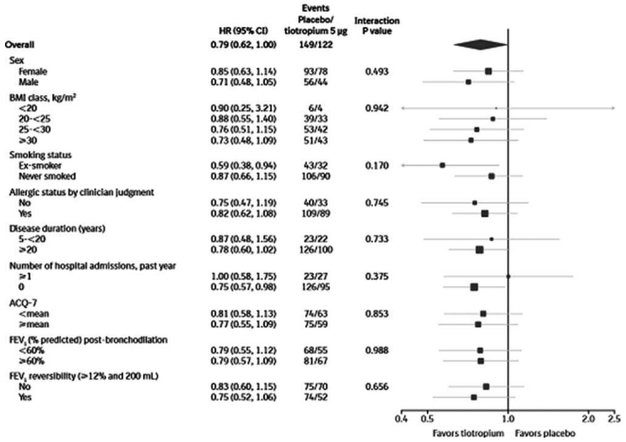
Rationale The addition of tiotropium provides bronchodilation and reduces exacerbations in patients with severe asthma (Kerstjens *et al*. NEJM 2012). Subgroup analyses were performed to determine whether this positive effect was limited to definable subgroups.

Methods Eligible patients: were aged 18–75 years; had a ≥5-year history of asthma; were diagnosed before the age of 40; scored ≥1.5 on Asthma Control Questionnaire 7; and were life-long non-smokers or ex-smokers (<10 pack-years) who quit smoking ≥1 year before study enrolment. Patients had experienced ≥1 exacerbation in the previous year. Time to first severe exacerbation from the pooled data after 48 weeks was one of three primary end points. Secondary end points included time to first episode of asthma worsening. Subgroup analyses of time to first severe exacerbation were performed in groups defined by baseline characteristics, including age, allergic status, smoking status and reversibility.

Results 912 patients were randomised: 456 received 5 g tiotropium via Respimat Soft Mist Inhaler and 456 received placebo once daily for 48 weeks. In the total study group, the time to first severe exacerbation was increased by the addition of tiotropium (risk reduction 21%; hazard ratio 0.79; p = 0.03). The time to first episode of asthma worsening was increased in the tiotropium group compared with placebo (risk reduction 31%; hazard ratio 0.69; p < 0.001). Subgroup analyses showed that neither the time to first severe exacerbation (Figure) nor the time to first episode of asthma worsening was dependent on baseline characteristics (no significant interactions).



Abstract P163 Figure. Analysis of the time to severe asthma exacerbation by subgroups defined at baseline.