GLA activity intracellularly in IS than peripheral blood, p=0.001 (see Abstract P179 Figure 1), and extracellularly in IS supernatant versus plasma in males alone (p<0.05).

Conclusions Sputum GLA activity is lower in male AFD patients than controls. However AFD subjects had significantly higher GLA activity in lung than blood. Measured airway obstruction in AFD was mild, though common. We speculate that the higher levels of lung enzyme found in AFD patients, on or off enzyme replacement, may contribute to the relative preservation of pulmonary function compared to other organ systems.

P180 SPUTUM EOSINOPHIL POSITIVITY TO TAILOR STEROID MANAGEMENT OF SEVERE ASTHMATICS

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The use of sputum eosinophil count in asthma clinics is rapidly expanding as it has been reported as being a useful indicator of the worsening of asthma symptoms and that its normalisation reduces asthma exacerbations and admissions. Without additional steroids, levels of sputum eosinophils have been shown to be highly variable in severe asthmatic patients. Furthermore, precise patient phenotyping is increasingly becoming important as our understanding of the physiopathology of severe asthma widens. We introduced sputum differential cell counting in our severe asthma clinic, with a view to first reducing sputum eosinophils below 3% by augmenting anti-inflammatory therapy, and attempting steroid withdrawal once patients became sputum eosinophil negative (E−). To date, 264 patients have been investigated for sputum eosinophils, using induction with nebulised sodium chloride if necessary and suitable. This paper presents our yearly update of the anti-inflammatory (steroid) therapy of the first successive patients with at least two successful sputum counts (current n=71), specifically investigating patients' management in the light of their positive sputum eosinophil levels at baseline assessment. Twenty patients were sputum eosinophil positive (E+) on their initial visit and 25 had reduced eosinophil levels (p=0.001) on a subsequent visit, including 14 becoming E−. Nineteen were offered a trial of steroid augmentation:
11 patients with a trial of IM triamcinolone (all patients had subsequent reduced eosinophils levels, 9 becoming E−, p=0.003);
5 patients with increased oral prednisolone treatment (four patients with reduced eosinophils levels, one becoming E−);
3 with increased inhaled steroid therapy (all with reduced eosinophil levels, 1 becoming E−).

66% of patients with uncontrolled sputum eosinophilia were treated with an increase in anti-inflammatory maintenance therapy. Sputum eosinophil levels decreased for 95% of these as already reported, but only 11/19 achieved full control of sputum eosinophilia with 2/11 failing to normalise eosinophils despite IM triamcinolone (representing a population of confirmed steroid resistance. Sputum eosinophil negativity used as a surrogate marker for asthma control has been shown to be an essential tool in identification and management of patients with asthma at risk of deterioration and admission.

P181 BETTER ASTHMA CONTROL WITH MONTELUKAST THAN SALMETEROL IN ARG-16 HOMOZYGOUS CHILDREN WITH ASTHMA

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Introduction and Objectives Diminished efficacy of salmeterol for improving asthma control is increased in children with asthma homozygous for arginine-16 (Arg16) allele of the *ADRB2*. Concerns have been raised regarding the efficacy and safety of long-term salmeterol use in patients with asthma. We investigated whether there is a genotype-specific difference in long-term asthma control with montelukast compared to salmeterol in individuals homozygous for Arg16 of *ADRB2*.

Methods In this pragmatic randomised controlled trial, 62 children (5−18 years) with asthma, carrying Arg/Arg16 genotype and exacerbation of asthma at least once within the previous year, were randomly assigned to receive Flixotide® (fluticasone propionate) via accuhaler (Diskus) dry powder inhaler device plus oral montelukast (Group I); or Seretide® (salmeterol plus equivalent dose of fluticasone) via accuhaler dry powder inhaler device plus placebo for montelukast (Group II). No effort was made to blind the prescribed inhaler. The primary end point was school absence, prospectively measured as individual events over the period of 1 year.

Results No significant difference was observed in school absences (p=0.097) between the treatment groups. The use of reliever medication was significantly decreased in Group I compared to Group II (p=0.004). Total exacerbations were reduced in Group 1 compared to Group 2 (p=0.049). Self-reported symptoms were significantly improved in Group I compared to Group II (morning cough p=0.018; morning wheeze p=0.001; morning dyspnoea p=0.008; night wheeze: p=0.004; night dyspnoea: p=0.001). A significant improvement in quality of life as per the Juniper paediatric asthma quality of life questionnaire was observed in Group I compared to Group II (activity limitation score (p=0.004), symptom score (p=0.009), emotional function score (p=0.002)).

Conclusion In individuals homozygous for Arg16 of the *ADRB2* locus, montelukast is an effective step up medication compared with salmeterol. Montelukast, as an asthma controller added on to inhaled steroid, improved asthma symptoms and quality of life, while reducing the use of reliever medication, in comparison to salmeterol. A larger randomised controlled trial is required, comparing asthma control with salmeterol versus montelukast in the genotypic subgroups in *ADRB2*, and to explore the cost-effectiveness of genotype-specific controller therapies in children with asthma.

P182 ADENOSINE POTENTIATES HUMAN MAST CELL FIBRINOLYTIC ACTIVITY

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We investigated whether adenosine, a potent contributor to the regulation of pulmonary function, can modulate human lung mast cell (HLMC) fibrinolytic activity. Tissue plasminogen activator (tPA) activity and tPA transcript expression levels from a human mast cell line (HMC-1) and HLMC were monitored following adenosine application. Adenosine potentiated mast cell tPA activity and tPA gene expression in a dose-dependent manner. Adenosine effects were abolished in the presence of adenosine deaminase. HMC-1 cells predominantly expressed adenosine A_{2A} and A_{2B} receptor transcripts ($A_{2A}>>A_{2B}>A_3>>A_1$). In addition to A_{2A} and A_{2B}, A_3 receptor transcripts were also abundantly found in HLMC ($A_{2A}>>A_{2B}>>A_3>>A_1$). Pharmacological and signalling studies