from baseline to Week 12 (FP/FORM: +0.196 L; FP/SAL: +0.257 L). The LS mean difference in change in pre-dose FEV_1 was −0.061 L between treatments (95% CI −0.161 to 0.040). Non-inferiority of FP/FORM to FP/SAL was demonstrated (the lower limit of the 95% CI exceeded the acceptance limit of −0.2 L). In total, 72.3% (73/101) patients started on FP/FORM 250/10 μg and 75.2% (76/101) on FP/SAL 250/50 μg. Eight patients (FP/FORM: n=5; FP/SAL: n=3) required an increase in dose. Similar numbers of patients treated with FP/FORM and FP/SAL discontinued due to lack of efficacy (FP/FORM: n=1; FP/SAL: n=2). Twenty-three patients (11.4%) experienced mild or moderate asthma exacerbations. Four patients (2.0%) experienced severe exacerbations (FP/FORM: n=3; FP/SAL: n=1; p=0.621). Overall, 23.8% of patients experienced at least one AE. The rate was the same in both treatment groups (24/101). Most AEs were mild or moderate. No clinically important changes in laboratory results, vital signs or ECGs were observed.

Conclusion FP/FORM and FP/SAL had similar efficacy and safety profiles.

Abstract P177 Table 1 Pre-dose FEV_1 at Week 12—per protocol set

		Pre-dose FEV_1 (L)				
		Week 12		Difference FP/FORM − FP/SAL		
	n	LS mean	95% CI	LS mean	95% CI	*P* value
FP/FORM	96	2.402	2.324 to 2.481	−0.061	−0.161 to 0.040	0.007
FP/SAL	95	2.463	2.384 to 2.543			

P178 VALIDATION OF A NOVEL SYNTHETIC ABSORPTIVE MATRIX (SAM) FOR SAMPLING NASAL MUCOSAL LINING FLUID

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Introduction An improved method for sampling nasal mucosal lining fluid (MLF), termed nasosorption, utilises a synthetic absorptive matrix (SAM) (Accuwick Ultra, Pall). Conventionally, Whatman's filter paper has been used for absorption of nasal MLF, but this natural cellulose source has the capacity to bind mediators, causing eluted fluid to have decreased and variable detectable levels of mediators. Nasal lavage has the problem of diluting MLF and this also causes detectable levels of mediators to be low. Strips of Accuwick are effective for nasosorption in adults following nasal allergen challenge and for sampling children with active rhinitis. However, Accuwick is no longer manufactured and we wished to validate an alternative SAM (Leukosorb, Pall).

Methods Sputum supernatant (40 μl) from a subject with COPD as well as a standard preparation of cytokines was spiked onto Accuwick and Leukosorb strips. Following elution by spin filter centrifugation, the MesoScale Diagnostics (MSD) multi-immunoassay platform was used to assess levels of IFN-γ, IL-10, IL-12 p70, IL-6, IL-8, and TNFα. After absorption to Accuwick and Leukosorb, elution was compared with and without buffer (PBS with BSA (1%) and Triton X (1%)), prior to immunoassay of the recovered sample.

Results Without buffer the recovery of 7 cytokines after the sputum supernatant was applied to Accuwick was a mean of 17.6% (range 1—100%), while recovery was a mean of 20.2% (range 2.9—92.5%) using Leukosorb. Addition of the buffer prior to elution of the fluid increased mean recovery to 61.8% when employing the Leukosorb system. Finally, in a direct comparison when employing Leukosorb and Accuwik for nasosorption in different nostrils after nasal allergen challenge in a single subject, Leukosorb resulted in higher detectable IL-5 levels in MLF.

Conclusion Leukosorb appears to be a superior alternative to Accuwick Ultra for nasosorption in terms of recovery of cytokines. Addition of a buffer containing detergent and protein prior to elution significantly increases recovery. SAM has the potential to be employed in the upper and lower respiratory tract to sample undiluted MLF.

P179 LUNG-BASED ASSESSMENT IN ANDERSON FABRY DISEASE (AFD) DEMONSTRATES DIFFERENTIAL α GALACTOSIDASE A ENZYME (GLA) ACTIVITY AT BLOOD AND TISSUE SITES

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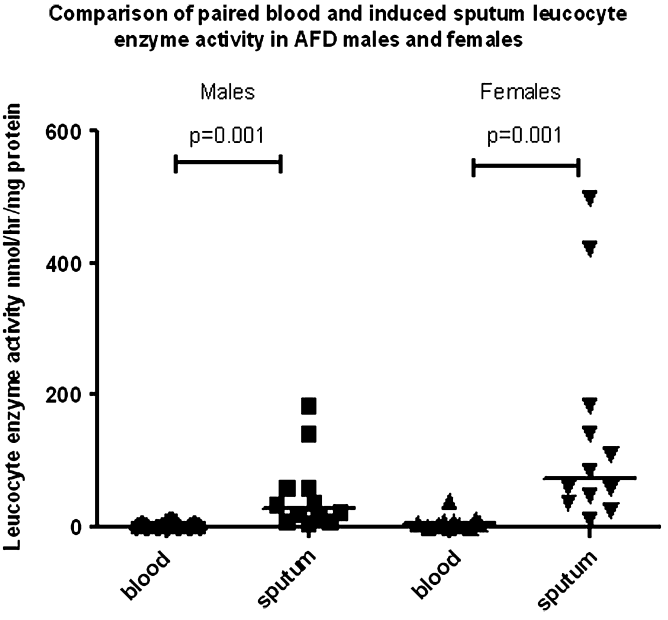
Introduction and Objectives AFD is an X-linked lysosomal storage disorder caused by mutations of the GLA gene. Lack of enzyme results in storage material accumulation within lysosomes, leading to multi-organ pathology. Airflow obstruction has been reported, though there has been no systematic assessment of lung enzyme activity in affected individuals. We therefore undertook a controlled cohort review of UK AFD patients focussing in particular on the relationship between airway and blood intra- and extracellular GLA, and lung pathology.

Methods Study subjects and controls were recruited following local Ethics Committee approval. All underwent systematic pulmonary investigation, including lung function testing and sputum induction with 40 ml of 4% hypertonic saline over 20 min via an ultrasonic nebuliser. GLA activity was measured from AFD patients and healthy controls in induced sputum (IS) cells and supernatant using a fluorometric assay. In addition, in AFD patients, GLA activity was measured simultaneously in blood leucocytes and plasma.

Results 45 AFD patients with variable severity extra-pulmonary disease were recruited (20 males, 10 smokers). The population had a mean FEV1 of 89% predicted. 20 of 45 (44%) (13 males, 6 smokers) had evidence of airflow obstruction with FEV1/FVC ratio <70%. IS intra- and extracellular GLA activity was lower in AFD affected males compared to controls (n=18 and 13, median enzyme activity 18.8 vs 41.7 nmol/h/mg protein and 0.9 vs 10.0 nmol/h/ml, p<0.001 and p<0.01, respectively). No similar difference was found in females. Paired blood and sputum data from 22 AFD patients (13 males, 18 on enzyme replacement therapy) demonstrated greater



Abstract P179 Figure 1 Comparison of paired blood and induced sputum leucocyte enzyme activity in AFD males and females.