influential proteins from this PCA were further examined. Within the entire CF cohort (n=37), seven of these ten proteins significantly correlated ($p<0.05$) with baseline lung function, with triosephosphate isomerase showing the greatest correlation ($r_s=-.594$, $p<0.001$). When comparing those with the greatest (n=5) and least (n=5) FEV1% decline, the PCA showed no separation and only one protein, proteasome activator complex subunit 1, showed a significant difference.

Discussion These data confirm findings from previous smaller studies that differences in the sputum proteome relate to baseline severity of lung disease. However, it does not appear to relate to longitudinal changes in lung function over 12 months. A biomarker might be only able to inform over shorter time periods, potentially because the proteome is in a state of flux. Further work is required to evaluate if longitudinal assessment of the proteome allow prediction of FEV1% decline, or if proteome changes are predictive of a pulmonary exacerbation.

S19 PEAK NASAL INSPIRATORY FLOW AND NASAL CYTOKINES ARE USEFUL BIOMARKERS OF NASAL INFLAMMATION IN CYSTIC FIBROSIS GENE THERAPY

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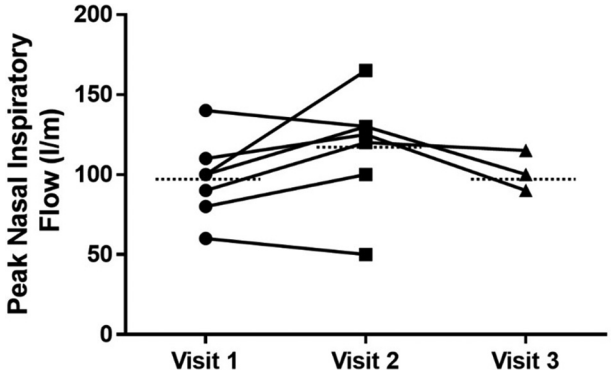
Introduction The UK Cystic Fibrosis Gene Therapy Consortium has developed a programme of gene therapy for cystic fibrosis (CF). Studies include administration in the nasal respiratory epithelium to confirm molecular efficacy and safety in advance of lung trials. The aim of this study is to validate the measurement of peak nasal inspiratory flow (PNIF) and cytokines in nasal secretions from stable CF subjects and controls, for use as safety outcome measures to detect immune inflammatory responses.

Methods Study participants were asked to perform a short maximal sniff manoeuvre using an In-Check device (Clement Clarke) and the best of 2 proficient attempts was used. PNIF was measured in 19 subjects with stable CF and 23 healthy controls. Smokers and subjects with significant nasal pathology or steroid use were excluded. Repeat visits were performed in 7 patients with CF to assess intra-subject variability. Nasal secretions were obtained from 12 CF subjects and 6 healthy controls within the cohort using open cell polyurethane sponges. Cytokines correlating with innate (IL-1β, IL-8, TNFα, IFNα and CXCL11) and adaptive (IL-4, IL-6, IL-10, RANTES and IFNγ) viral immune responses were analysed using a MagPix bead assay.

Results PNIF was not significantly different in between healthy subjects and those with CF and there was no significant difference between male and female subjects overall. PNIF was stable between visits 1 and 2 in CF (%CV 16.6). IL-1β, IL-8, IL-6, IFNγ, TNFα, CXCL11 and RANTES were detectable in most samples. Nasal IFNγ was higher in nasal secretions from subjects with CF (5.8 (0–10.75) pg/ul) compared with healthy controls (0 (0–0), p=0.002) whereas differences were non-significant for other cytokines. In CF subjects, median cytokine level did not vary significantly between visit 1 and 2 for any cytokine. However, mean coefficient of variation for all cytokines was 63%.



Abstract S19 Figure 1 Peak nasal inspiratory flow result for repeat measurements in subjects with cystic fibrosis. No significant differences in group medians between visits(dotted lines)

Conclusions We show for the first time that peak inspiratory nasal flow and detection of cytokines can be rapidly undertaken and are well-tolerated measurements in CF. Group medians for PNIF and all nasal cytokines were stable on repeat visits. These biomarker assays are suitable for safety outcome measures reporting nasal inflammation at clinical trial.

S20 INHALED AZTREONAM LYSINE RECOVERS LUNG FUNCTION AND IMPROVES QUALITY OF LIFE IN ACUTE PULMONARY EXACERBATIONS OF CYSTIC FIBROSIS

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Background Pulmonary exacerbations cause significant morbidity in people with cystic fibrosis, but treatment with extended courses of intravenous antibiotics may also result in systemic side-effects, adverse reactions and co-morbid complications. Treatment through the inhaled route, where the lungs are targeted directly with less systemic exposure may be more appropriate. The AZTEC-CF study investigated the efficacy of inhaled aztreonam lysine (AZLI) in the treatment of acute pulmonary exacerbations.

Methods AZTEC-CF was an open-label randomised crossover study designed and conducted at a regional adult cystic fibrosis centre in the UK (*ClinicalTrials.gov:* NCT02894684). Inclusion criteria included age > 16 years, *P. aeruginosa* infection and no prior use of AZLI. Exclusion criteria included *Burkholderia cepacia* complex infection and solid-organ transplant. During two consecutive exacerbations requiring hospitalisation for intravenous antibiotics, subjects received 14 days AZLI plus intravenous colistimethate (AZLI+IV) or standard dual intravenous antibiotics (IV+IV). Primary outcome was recovery of% predicted FEV1 (ppFEV1) at 14 days. Key secondary outcomes included health-related quality of life outcomes, sputum bacterial load, systemic inflammatory markers, aztreonam resistance and safety outcomes.

Results Sixteen adults with CF were consented and randomised, and by March 2019 (censorship date) 28/32 (87.5%) exacerbations were completed. At 14 days, improvement in $ppFEV_1$ was greater for AZLI +IV compared to IV+IV (mean +13.5% versus +8.3%; paired differences [95% CI] +4.6%