therapy trial. Serum markers also appear to be of limited use is assessing efficacy but will still be useful for toxicology and safety studies.

Abstract P106 Table 1

Assay	Visit 1 (median (range))	Visit 2 (median (range))	Visit 3 (median (range))	Visit 4 (median (range))	Intra-individual CV (%)(median (range))
Total cell counts (cells/g sputum)	1.0 (0.1 -7.6)	1.1 (0.1-15.2)	1.0 (0.2-7.4)	1.1 (0.2-7.2)	56 (1-129)
Sputum Neutrophil (%)	97.3 (36-100)	98.3 (71-100)	99.0 (77.3-100)	98.3 (90.7-100)	1.3 (0-12.8)
Sputum IL8 (ng/ml)	14.9 (2.3-57.2)	14.6 (3.2-37.2)	13.2 (2.4-49.5)	15.5 (2.3- 48.0)	30 (5-80)
Sputum Calprotectin (mg/ml)	1.48 (0.19-4.77)	1.63 (0.11-5.29)	1.26 (0.20-4.38)	1.69 (0.20-5.25)	30 (4-86)
Sputum Neutrophil Elastase (mU)	868 (32-3788)	884 (32-4104)	947 (32-4104)	1010 (95-4261)	34 (0-97)
Sputum Myeloperoxidase (µg/ml)	19.9 (3.6-78.8)	18.7 (1.8-69.4)	20.9 (3.3-53.3)	22.4 (5.2 -73.4)	32 (2-85)
Sputum Extracellular DNA (µg/ml)	29.8 (1.8-128.8)	28.0 (2.5-154.4)	26.9 (1.6-96.9)	34.1 (0.6-171.2)	33 (5-101)
24hr sputum weight (g)	7.65 (0.10-143.3)	6.16 (0.53-127.99)	7.07 (0.04-128.64)	8.33 (0.19-117.48)	45 (4-134)
Serum IL8 (pg/ml)	2.9 (0.6-40.3)	2.7 (0.6-49.0)	2.5 (0.5-44.7)	2.8 (0.8-44.5)	26 (2-95)
Serum calprotectin (µg/ml)	12.1 (1.9-72.5)	10.8 (1.6-60.1)	8.4 (0.8-61.8)	8.3 (1.1-56.2)	36 (2-153)

P107 PULMONARY IMAGING TECHNIQUES TO IDENTIFY SUITABLE PATIENTS AND ACT AS OUTCOME MEASURES IN THE UK CF GENE THERAPY CONSORTIUM CLINICAL PROGRAMME

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We are conducting a large, longitudinal study to assess outcome measures and identify optimal patients for a multidose trial of CF gene therapy. Two imaging modalities are being employed: radioisotope deposition scans and high resolution CT. Subjects have undergone these scans on a single occasion, whilst clinically stable. The purpose was: *Deposition scan*—to determine which patients would be most optimal for topical drug delivery and *CT*—to assess the suitability of various parameters as efficacy measures. Following inhalation of ^{99m}Tc-labelled human serum albumin, planar gamma camera images and SPECT were used to assess 3-D deposition. Images were scored both digitally and visually (I- no defects; II- patchy deposition; III- patchy deposition with large defects; IV- grossly abnormal). HRCT scans were scored by two radiologists on a lobar basis for the following: bronchiectasis (extent/severity), airway wall thickening, mucus plugging and gas trapping. 147 deposition scan were available; digital indices (DI) ranged from 34 (best) to 150 (severely abnormal). Visual scores correlated well with DI (R2 0.63; $p<0.001$) and both were significantly negatively correlated with FEV_1% ($p<0.01$). Nine Grade IV subjects had a mean (SD) FEV_1 of 43.9(4.3)%, significantly lower than groups I-III ($p<0.01$). On the basis of very poor deposition, this group is considered unsuitable to progress to the trial. Others have deposition scans which suggest that the gene therapy product could be delivered at least moderately well; they will be filtered through other inclusion/exclusion criteria. Potentially reversible components of the HRCT scores are being considered as efficacy outcome measures. As an example, power calculations suggest that our anticipated group size (n=100) would have 80% power to detect a change in wall thickness half that seen with intravenous antibiotics in a previous study. In conclusion, lung imaging techniques have both aided us in the identification of patients to take through into our multi-dose trial and are currently under consideration as efficacy outcomes.

P108 PHENOTYPIC CHANGES IN PSEUDOMONAS AERUGINOSA (PSA) POPULATIONS DURING EXACERBATIONS IN ADULT CYSTIC FIBROSIS PATIENTS INFECTED WITH NON-EPIDEMIC STRAINS

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Background Chronic infection with Psa in most CF patients is due to single unique strains, which over time accumulate mutations resulting in mucoid conversion, loss of motility, auxotrophy and increased antibiotic resistance, in turn leading to multiple phenotypes. However, changes in Psa population morphology related to short term pressures (eg, during IV antibiotic-treated exacerbations), have not previously been studied. We therefore looked at Psa population structure during exacerbations.

Methods Sputum samples from four CF patients chronically infected (for at least 4 years) with unique single Psa strains were analysed at the beginning and end of an intravenous antibiotic-treated exacerbation, where every patient had subjective and spirometric improvement. From each sample, 40 single Psa colonies were selected (with every morphological type proportionately represented), and colony morphology, susceptibility to six antibiotics (ciprofloxacin, ceftazidime, colomycin, meropenem, tobramycin, tazocin), hypermutability (rate of spontaneous mutation to rifampicin resistance) and auxotrophy (ability to grow on glucose M9 media) determined. Additionally, the density of Psa (colony forming units (CFU) per ml) in sputum samples was measured.

Results Although the predominant colony morphology changed from green, non-mucoid and smooth (mean 67%, range 43–98) to straw-coloured, non-mucoid and smooth (57%, 5–95) ($p=0.001$), there was no change in mean antibiotic resistance to all antibiotics (21.5% vs 20.3%, $p=0.9$), prevalence of hypermutable isolates (38% vs 25%, $p=0.48$) and auxotrophic mutants (66% vs 98%, $p=0.17$). However, there was an increase in Psa sputum density (mean CFU/ml 1.3×10^5 vs 2.0×10^6, $p<0.001$), despite the use of relevant antimicrobial therapy.

Conclusion The changes in prevalent population composition following antibiotic pressure, associated with clinical improvement, might suggest that some morphotypes alone are responsible for the adverse clinical features. Conversely, the increase in sputum density of Psa despite objective clinical improvement implies that the exacerbation has occurred independently of the presence of the organism, supporting the observation that clinical improvement is often seen in CF patients even where the Psa seems resistant to the administered antibiotics. Further work need to be done to tease out the role of Psa in clinical exacerbations of CF patients with chronic infection.

P109 EXERCISE CAPACITY AND PHYSICAL ACTIVITY IN PATIENTS WITH CF: DATA FROM THE UK CF GENE THERAPY CONSORTIUM (UKCFGTC) 'RUN-IN' STUDY

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Introduction Exercise capacity is predictive of mortality in CF. Objective measurement of daily physical activity may be related to exercise capacity and both may be useful outcome measures in