**Conclusion** In the TOMORROW trial, the effect of nintedanib on slowing disease progression in patients with IPF was maintained up to week 76. No relevant changes in the safety and tolerability of nintedanib were observed with treatment up to week 76 compared with week 52.

## S111 DOES RATE OF DECLINE IN LUNG FUNCTION PREDICT RESPONSE TO PIRFENIDONE THERAPY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS?

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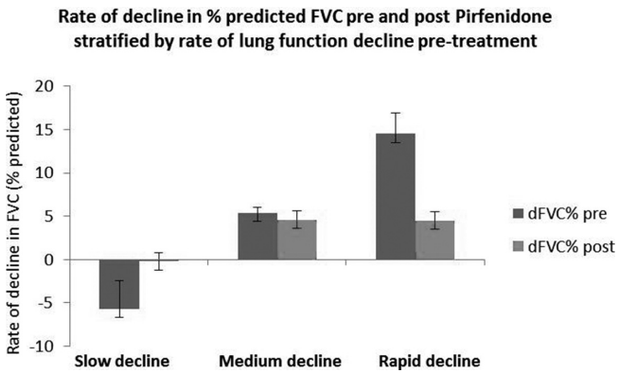
10.1136/thoraxjnl-2015-207770.117

**Introduction and objectives** Idiopathic pulmonary fibrosis (IPF) is a progressive, irreversible interstitial lung disease with a poor prognosis. Randomised, placebo-controlled clinical trials have shown that treatment of IPF patients with pirfenidone reduces disease progression. Published studies used incident forced vital capacity (FVC) values for study inclusion. Our objective was to determine whether the rate of decline in lung function predicts response to therapy.

**Methods** The clinical records of 68 patients with IPF who started pirfenidone treatment between June 2013 and March 2015 at a UK tertiary referral centre were reviewed. 34 patients had lung function sufficient for a full evaluation.

**Results** The mean (+/-SE) rate of decline in FVC per year pre-treatment was 196.0+/-66.1 ml versus 135.0+/-61.8 ml post treatment (p = 0.512). The decline in percent predicted FVC per year pre-treatment was 4.4+/-1.9% vs. 3.0+/-1.9% post treatment (p = 0.572). The decline in absolute total gas transfer (TLco) per year pre-treatment was 0.6+/-0.2 compared to 0.4 +/-0.2 post treatment (p = 0.472). The decline in percent predicted TLco per year pre-treatment was 6.7+/-2.8% compared to 4.4 +/-2.0% post treatment (p = 0.504). Pirfenidone showed a trend towards positive benefit in all parameters measured. Patients were stratified into tertiles of slow, medium and rapid rate of FVC decline (pre-treatment). In slow and medium rate decliners (up to FVC decline of approximately 200 ml per year or 5.4% per year) no effect was seen (p = NS). In fast decliners (FVC decline 576.1+/-97.8 ml and FVC percent predicted decline 14.5+/-2.4% per year) a statistically significant effect was seen, reducing decline to 199.1+/-99.6 ml and 4.5+/-2.4% respectively (p = 0.022; 0.015).

16.2% of the patients died with a mean survival of 239 days post pirfenidone.




**Abstract S111 Figure 1**

**Conclusions** Pirfenidone treatment reduced disease progression (decline in FVC and TLco) in our total cohort. Our results indicate that patients with rapid decline in FVC may benefit most from pirfenidone. Those declining at less than 200 ml per year may not benefit. These results suggest that further clinical studies are warranted, including patients with evidence of rapid lung function decline with FVC >80% predicted.

# Pseudomonas: digging for gold or search and destroy?

## S112 VARIABILITY IN SUSCEPTIBILITY TO ANTIBIOTICS AND BACTERIOPHAGES BETWEEN INDIVIDUAL COLONIES OF PSEUDOMONAS AERUGINOSA FROM CYSTIC FIBROSIS SPUTUM SAMPLES: IMPLICATIONS FOR FUTURE CLINICAL TRIAL DESIGN

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10.1136/thoraxjnl-2015-207770.118

Antimicrobial resistance is a growing problem. As part of the Cystic Fibrosis (CF) Trust-funded Strategic Research Centre for research into *Pseudomonas aeruginosa* (Pa) (http://www.cysticfibrosis.org.uk/research-care/research/about-cystic-fibrosis-research/how-we-invest-in-research/strategic-research-centres/src-1), we are exploring the therapeutic potential of bacteriophages. To date, we have a) identified a mix of 4 bacteriophages to which >80% of our CF isolates appear sensitive; b) confirmed efficacy in an acute murine model and c) confirmed compatibility with clinically relevant nebulisers. In the clinical trial, patients will be selected on the basis of confirmed sensitivity of their Pa strain (s) to the bacteriophage mix. Significant variability has previously been reported when multiple, morphologically indistinguishable colonies were tested against antibiotics; here, we explored whether a similar phenomenon occurs with bacteriophages.

CF sputum (n = 6 patients) was cultured on Pa-specific agar. Up to 10 individual morphologically identical colonies were inoculated separately into broth. After overnight culture each was subjected to disc diffusion (12 antibiotics) and phage testing (standard plaque assays).

Reproducibility (repeat testing of same broth) was excellent for susceptibility/resistance to antibiotics (97.2% within 3 mm) and bacteriophages (93.3% within one log dilution). Variability in antibiotic susceptibility was lower than anticipated: in no samples were there both completely resistant and fully sensitive colonies and although zone sizes did vary, these crossed break points in only 12.5% of assessable samples. There was more variability in phage sensitivity. Colonies from two subjects displayed <1 log dilution differences between them and were therefore reasonably consistent. The other 4 subjects displayed >1 log differences between the most and least sensitive; in one, colonies clearly fell into two groups (highly sensitive/less so with a 4 log dilution difference) and on subculture, differences in pigment production were apparent. Susceptibility may not be predicted by testing a mix of colonies.

As described previously for antibiotics, individual, apparently morphologically similar colonies of Pa in a CF sputum sample display inconsistent susceptibility profiles to anti-pseudomonal bacteriophages. The potential role of genetic variability to