



Abstract S106 Figure 1

p-value was not significant for the primary endpoint ( $p = 0.81$ ) or for the key secondary endpoints of time to first acute exacerbation ( $p = 0.37$ ) or change from baseline in St George's Respiratory Questionnaire total score ( $p = 0.67$ ), indicating that the treatment effect of nintedanib was not statistically significantly different between the subgroups.

**Conclusion** Decline in FVC in placebo arms was virtually identical in patients with A) the presence of honeycombing and/or biopsy confirmation of UIP; and B) the absence of both, but features of "possible UIP" on HRCT. Nintedanib slowed FVC decline equally in both sub-groups. These findings have major implications for diagnosis and clinical trial design.

**S107 DISEASE PROGRESSION MODELLING IN IDIOPATHIC PULMONARY FIBROSIS: A PREDICTION OF TIME TO DISEASE PROGRESSION AND LIFE EXPECTANCY WITH PIRFENIDONE**

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**Objectives** Currently, clinical trials in idiopathic pulmonary fibrosis (IPF) are not designed to estimate disease progression and survival over a long period. The objective of this study was to develop a disease progression model in IPF to predict the extent to which treatment with pirfenidone could extend the time to disease progression and improve life expectancy versus best supportive care (BSC) over a patient's lifetime.

**Methods** A disease progression model was developed categorising disease progression into four health states: progression free;

progressed ( $\geq 10\%$  decline in FVC or  $\geq 50$  m decrease in 6-minute walking distance); lung transplant; and dead. Two cohorts entered the model in the progression-free state: one cohort received pirfenidone ( $n = 1000$ ), the other received BSC ( $n = 1000$ ). The proportion of patients in each health state was calculated every 3 months based on parametric survival distributions fitted to data from clinical trials and registries. Distributions calculating progression-free survival (PFS) and overall survival (OS) for pirfenidone were fitted to data from randomised controlled trials (RCTs; Studies 004, 006, 016) and a long-term open-label extension study (Study 012). Distributions calculating PFS and OS for BSC were fitted to data from the RCTs and a US-based IPF registry. Mean PFS and OS were determined for pirfenidone and BSC. Uncertainty was explored by deterministic and probabilistic sensitivity analysis.

**Results** The model calculated mean PFS as 3.28 years and 2.18 years with pirfenidone and BSC, respectively (Figure). Hence, pirfenidone extended the estimated mean time to disease progression by 1.10 years. Mean OS was calculated as 9.29 years and 6.10 years with pirfenidone and BSC, respectively (Figure 1). Therefore, pirfenidone improved estimated life expectancy by 3.19 years. The extent to which pirfenidone improved PFS and OS was sensitive to choice of parametric survival distribution and method of extrapolation.

**Conclusions** This disease progression model suggests that treatment with pirfenidone extends the time to disease progression and improves life expectancy, thus preventing early morbidity and deaths in IPF. These conclusions are consistent with expectations for a therapy that has been shown to reduce disease progression and mortality, as measured by a pooled analysis of outcomes in Phase 3 clinical trials.