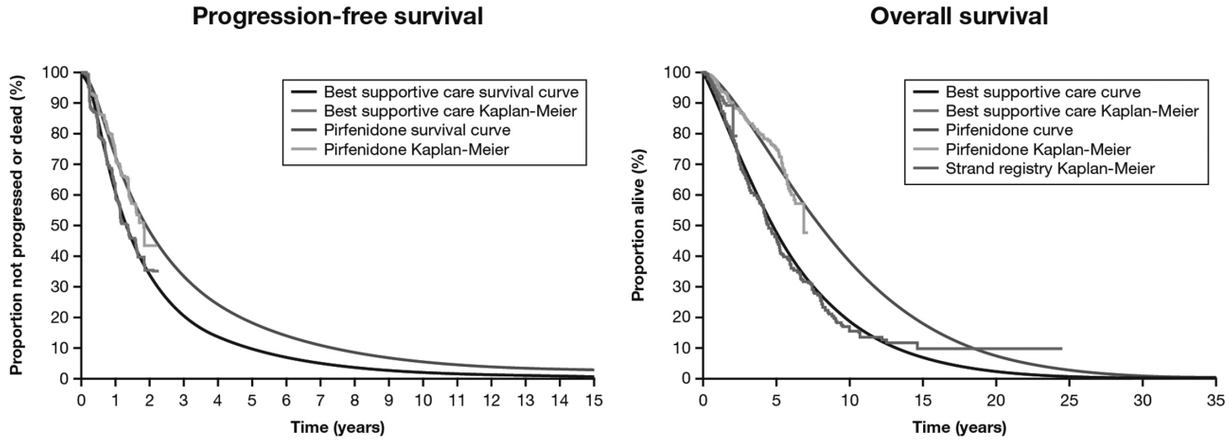

Abstract S107 Figure 1 Progression-free and overall survival Kaplan-Meier and curves

S108 EFFECT OF BASELINE FVC ON DECLINE IN LUNG FUNCTION WITH NINTEDANIB IN PATIENTS WITH IPF: RESULTS FROM THE INPULSIS® TRIALS

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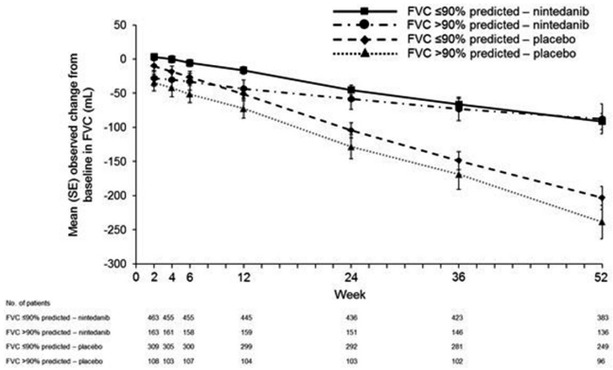
10.1136/thoraxjnl-2015-207770.114

Introduction The two replicate, randomised, placebo-controlled, 52-week Phase III INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily (bid) in patients with idiopathic pulmonary fibrosis (IPF). Patients with forced vital capacity (FVC) ≥50% predicted were included. The primary endpoint, the annual rate of decline in FVC, was significantly reduced in the nintedanib group compared with placebo in both trials, consistent with a slowing of disease progression. Key secondary endpoints were time to first acute exacerbation and change from baseline in St. George's Respiratory Questionnaire total score, both over 52 weeks. In a pre-specified subgroup analysis of patients with baseline FVC ≤70% versus >70% predicted, the treatment effect of nintedanib on decline in FVC was consistent in both subgroups.

Methods A *post-hoc* subgroup analysis of patients with baseline FVC >90% versus ≤90% predicted was undertaken using pooled data from the INPULSIS® trials to investigate whether patients with marginally impaired FVC receive the same benefit from nintedanib.

Results 274 patients (nintedanib 166, placebo 108) had baseline FVC >90% predicted and 787 patients (nintedanib 472, placebo 315) had baseline FVC ≤90% predicted. There was no significant treatment-by-subgroup interaction for the primary endpoint (p = 0.5300); in patients with baseline FVC >90% predicted, the adjusted annual rate of decline in FVC was -91.5 mL/year with nintedanib and -224.6 mL/year with placebo (difference: 133.1 mL/year [95% CI: 68.0, 198.2]) while in patients with baseline FVC ≤90% predicted, it was -121.5 mL/year with nintedanib and -223.6 mL/year with placebo (difference: 102.1 mL/year [95% CI: 61.9, 142.3]). Consistent results were observed for changes from baseline in FVC over time (Figure 1). No significant treatment-by-subgroup interaction was observed for the key secondary endpoints. The frequency of adverse events and serious adverse events was comparable between the treatment arms of each subgroup.



Abstract S108 Figure 1

Conclusion In a subgroup analysis of pooled data from the INPULSIS® trials, nintedanib 150 mg bid slowed the decline in lung function in patients with IPF independent of degree of lung function impairment at baseline, suggesting that patients with marginally impaired FVC also benefit from treatment with nintedanib.

S109 EFFECT OF CONTINUED TREATMENT WITH PIRFENIDONE FOLLOWING A CLINICALLY MEANINGFUL DECLINE IN PERCENT PREDICTED FORCED VITAL CAPACITY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF)

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10.1136/thoraxjnl-2015-207770.115

Introduction and objectives The clinical course in patients with IPF is characterised by substantial inter- and intra-subject variability in the rates of disease progression, thereby confounding clinical assessments of therapeutic responses in individual patients. We pooled data from three Phase 3 trials to assess the potential benefit of continued treatment with pirfenidone in patients who experienced a ≥10% decline in percent predicted forced vital capacity (%FVC) during the first 6 months of treatment.

Methods Source data included all patients randomised to treatment with pirfenidone 2403 mg/d or placebo in the Phase 3 ASCEND or CAPACITY studies (N = 1247). We selected patients with a ≥10% absolute decline in%FVC by the month 3 or 6 study visit and compared the proportion of patients in the pirfenidone and placebo groups who experienced any of the following during the subsequent 6-month interval: (1) ≥10% absolute decline in%FVC or death; (2) no further decline in%FVC; or (3) death. Observed data were used in the analysis.

Results 34 (5.5%) and 68 (10.9%) patients in the pooled pirfenidone and placebo groups, respectively, experienced a ≥10% absolute decline in%FVC between baseline and month 6 (relative difference, 49.5%). Analysis of outcomes during the subsequent 6-month interval demonstrated that fewer patients in the pirfenidone group compared with placebo experienced a ≥10% decline in%FVC or death (pirfenidone, 2/34 [5.9%] vs. placebo, 19/68 [27.9%]). More patients in the pirfenidone group compared with placebo had no further decline in%FVC (20/34 [58.8%] vs. 26/68 [38.2%]; Table 1). Additionally, there were fewer deaths in the pirfenidone group (1/34 [2.9%]) compared with placebo (14/68 [20.6%]).

Abstract S109 Table 1 Outcomes during the 6-month period following an initial decline in percent predicted FVC ≥10% during the first 6 months of treatment

Outcome, n (%)	Pirfenidone (n = 34)	Placebo (n = 68)	Relative difference*	*P* value†
≥10% decline in FVC or death	2 (5.9)	19 (27.9)	–78.9%	0.009
Death	1 (2.9)	14 (20.6)	–85.7%	0.018
>0% to <10% decline in FVC	12 (35.3)	23 (33.8)	4.3%	ND
No further decline in FVC‡	20 (58.8)	26 (38.2)	53.8%	0.059

FVC = forced vital capacity.
*Relative difference calculated using the following formula: 100 × [pirfenidone – placebo]/[placebo].
†Fisher's exact test.
‡Either no decline or an increase in FVC.

Conclusions Among patients who experienced a ≥10% decline in%FVC during the first 6 months of treatment, continued treatment with pirfenidone resulted in a lower risk of%FVC decline or death during the subsequent 6 months. These findings suggest a potential benefit to continued treatment with pirfenidone despite an initial decline in FVC.

S110 EFFICACY AND SAFETY OF NINTEDANIB IN PATIENTS WITH IPF BEYOND WEEK 52: DATA FROM THE PHASE II TOMORROW TRIAL

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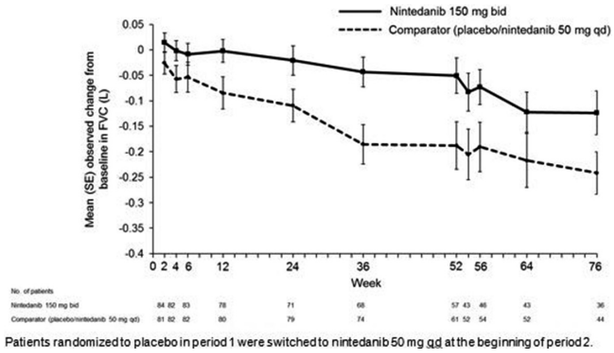
10.1136/thoraxjnl-2015-207770.116

Introduction Period 1 of the TOMORROW trial was a phase II, randomised, placebo-controlled trial of four doses of nintedanib (50 mg qd, 50 mg bid, 100 mg bid, 150 mg bid) in patients with idiopathic pulmonary fibrosis (IPF) over 52 weeks. Results suggested that nintedanib 150 mg bid was associated with a reduced decline in forced vital capacity (FVC) and fewer acute exacerbations versus placebo. After completing period 1, patients could continue treatment in a further blinded treatment phase (period 2).

Methods In period 2, patients treated with nintedanib in period 1 continued their dose, and placebo-treated patients switched to nintedanib 50 mg qd. Here we present descriptive data on FVC, acute exacerbations, mortality and adverse events for the nintedanib 150 mg bid and comparator (placebo/nintedanib 50 mg qd) groups during periods 1 and 2.

Results Of 428 patients treated in period 1 (nintedanib 150 mg bid n = 85, placebo n = 85), 316 patients completed period 1 and 286 patients (nintedanib 150 mg bid n = 48, comparator n = 54) continued treatment in period 2. Mean total duration of exposure was 14.2 months for nintedanib 150 mg bid and 16.8 months for comparator. The mean observed change from baseline in FVC over time was consistently lower in the nintedanib 150 mg bid group compared with comparator across periods 1 and 2 (Figure 1). The incidence of acute exacerbations was lower in the nintedanib 150 mg bid group compared with comparator (3.2 vs. 13.4 per 100 patient-years). Overall, 14 patients (16.3%) died in the nintedanib 150 mg bid group and 19 patients (21.8%) died in the comparator group. The safety and tolerability of nintedanib 150 mg bid was similar between periods 1 and 2. The proportion of patients reporting an adverse event across periods 1 and 2 was similar in the nintedanib 150 mg bid and comparator groups (97.6% and 94.1%, respectively).



Abstract S110 Figure 1