Introduction The INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily in patients with idiopathic pulmonary fibrosis. Nintedanib significantly reduced the annual rate of decline in forced vital capacity (FVC) compared with placebo in both trials. Patients who completed the 52-week treatment period and follow-up visit 4 weeks later (n = 807) could receive open-label nintedanib in an extension trial.
Aim To assess the long-term efficacy and safety of nintedanib.
Methods Patients treated with placebo in the INPULSIS® trials initiated treatment with nintedanib in the extension; patients treated with nintedanib continued to receive nintedanib.
Results 734 patients were treated in the extension trial (430 continuing nintedanib; 304 initiating nintedanib). Baseline characteristics were similar between groups. For patients initiating nintedanib, mean (SD) duration of exposure was 16.0 (7.3) months; for patients continuing nintedanib, mean (SD) duration of exposure in the extension was 17.2 (6.6) months, resulting in a mean (SD) duration of exposure across the parent and extension trial of 29.2 (6.6) months. Among all patients treated in the extension, mean (SD) change in FVC from the start of the extension to week 48 was -87 (240) mL (-1.95 [7.09]% FVC predicted). In total, 92.8% of patients continuing nintedanib and 96.7% initiated on nintedanib had ≥1 adverse event during the extension. The most frequent adverse event was diarrhoea, reported in 63.3% of patients continuing nintedanib and 64.1% of patients initiated on nintedanib.
Conclusion An interim analysis of data from the INPULSIS®-ON extension trial confirmed the efficacy and safety observed in the INPULSIS® trials.

P8 POOLED ANALYSIS OF DATA FROM THE TOMORROW AND INPULSIS® TRIALS OF NINTEDANIB IN IPF

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10.1136/thoraxjnl-2015-207770.145

Background The 52-week, Phase II TOMORROW trial and two replicate 52-week, Phase III INPULSIS® trials investigated the efficacy and safety of nintedanib 150 mg twice daily (bid) versus placebo in patients with idiopathic pulmonary fibrosis (IPF).
Aim A pooled analysis of data from the TOMORROW and INPULSIS® trials was conducted to obtain a more precise estimate of the treatment effect of nintedanib.
Methods Results for annual rate of decline in forced vital capacity (FVC), time to first investigator-reported acute exacerbation, change from baseline in St George's Respiratory Questionnaire (SGRQ) total score and mortality over 52 weeks were analysed.
Results 1231 patients (nintedanib 150 mg bid n = 723, placebo n = 508, reflecting the 3:2 randomisation in the INPULSIS® trials) were included. Baseline characteristics were comparable between treatment groups and across trials. The overall adjusted annual rate of decline in FVC was −112.4 mL/year with nintedanib and −223.3 mL/year with placebo (difference: 110.9 mL/year [95% CI: 78.5, 143.3]; p < 0.0001). The overall hazard ratio for time to first acute exacerbation was 0.53 (95% CI: 0.34, 0.83; p = 0.0047) in favour of nintedanib. The overall adjusted mean change from baseline in SGRQ total score at week 52 was 2.92 with nintedanib and 4.97 with placebo (difference: −2.05 [95% CI: −3.59, −0.50; p = 0.0095]). Hazard ratios for time to all-cause and on-treatment mortality were 0.70 (95% CI: 0.46, 1.08; p = 0.0954) and 0.57 (95% CI: 0.34, 0.97; p = 0.0274), respectively, in favour of nintedanib.
Conclusion Pooled data from the TOMORROW and INPULSIS® trials confirm a significant beneficial effect of nintedanib on reducing disease progression in patients with IPF.

P9 NINTEDANIB FOR THE TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS – INITIAL CLINICAL EXPERIENCE IN A UK COHORT

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10.1136/thoraxjnl-2015-207770.146

Introduction and objectives Nintedanib (OFEV®) is the second drug licensed for the treatment of Idiopathic Pulmonary Fibrosis (IPF). Evidence from the INPULSIS study demonstrated that it reduced annual FVC decline by approximately 50%. Nintedanib has been available in the UK from October 2014 through the Individual Patient Supply Programme (IPSP); initially for those with FVC >50% predicted, latterly available for all with a diagnosis of IPF regardless of FVC. We present preliminary findings of clinical experience with nintedanib in routine UK clinical practice.
Methods A multi-centre, cohort review was undertaken across 6 NHS Trusts. Data were collected from clinical records of individuals receiving nintedanib for the treatment of IPF from October 2014 to July 2015.
Results 210 patients (161 male) had consented to nintedanib IPSP by July 2015. Mean age (±S. D.) at diagnosis was 70.0 ± 7.7 years. Reasons for starting nintedanib included ineligibility for pirfenidone (FVC >80% predicted: 67 (31.9%) and FVC <50% predicted: 12 (5.7%)), intolerance to pirfenidone 63 (30%), patient preference 54 (25.7%), and clinical progression on pirfenidone 8 (3.8%). Pre-treatment lung function was FVC 72.2 ± 19.0% and DL_{CO} 40.1 ± 17.2% predicted (Domiciliary oxygen was administered to 66 (31.4%) of the cohort.

Mean duration of treatment was 2.4 months (range 0 – 8 months) and 78 patients had completed 3-month follow up. Of these 14/78 patients (17.9%) had discontinued nintedanib due to diarrhoea (5 patients), other GI side effects (3), death/lung transplant (2/1), miscellaneous reasons (3). The commonest potential adverse drug reaction (ADR) was diarrhoea occurring in 21/78 (26.9%), which required a dose reduction in 11 patients. Other common ADRs included nausea 11/78 (14.1%), abdominal pain 11/78 (14.1%), decreased appetite 7/78 (9.0%), and weight loss 5/78 (6.4%).
Conclusions These data demonstrate that at 3 months follow up, Nintedanib is generally well tolerated when used in routine UK practice in patients with IPF across a wide range of FVC's. The incidence of diarrhoea at 3 months is much lower than the 12 month reported rate in the INPULSIS study. Ongoing longitudinal follow up of this cohort will further inform our understanding of the use of nintedanib for the treatment of IPF.