Introduction Idiopathic pulmonary fibrosis (IPF) is characterised by a progressive loss of lung function. Intervention with an anti-fibrotic, such as pirfenidone, as early as possible in the disease course may be the most appropriate strategy to preserve lung capacity.¹ In this analysis, data from the pivotal CAPACITY (004/006; NCT00287716/NCT00287729) trials and subsequent RECAP (012; NCT00662038) rollover trial were used to investigate the impact of deferring pirfenidone treatment on annual decline in lung function (forced vital capacity [FVC]) in patients with IPF.

Methods The annual rate of lung function (FVC; mL) decline was calculated for all treated patients who completed CAPACITY and RECAP. Weeks 0–120 included all patients randomised in CAPACITY to pirfenidone 2,403 mg/day or placebo. Weeks 72–120 included data for the transition period, when patients either continued pirfenidone or switched to pirfenidone in RECAP. After Week 120, only data for patients in RECAP were included. Patients randomised to pirfenidone in CAPACITY were compared with those who received placebo in CAPACITY before initiating pirfenidone in RECAP.

Results From Week 0 to 120, the annual rate of lung function decline (FVC) was -142.0 mL ($n=345$) in patients who received pirfenidone in CAPACITY and -182.3 mL ($n=347$) in those who received placebo. During the transition period (Weeks 72–120), these values were -155.2 mL ($n=236$) and -151.9 mL ($n=249$) in patients who continued and switched to pirfenidone, respectively. In RECAP ($\geq$ Week 120), the annual rate of lung function decline in patients who received pirfenidone in both trials was -145.3 mL ($n=219$) and -140.9 mL ($n=218$) in those who switched from placebo to pirfenidone.

Conclusions These data show that loss of lung function during CAPACITY was not recovered during RECAP. Therefore, failure to initiate pirfenidone treatment in IPF as early as possible may lead to an irrecoverable loss of lung volume during the period without treatment.

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REFERENCE

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M29

FVC DECLINE OVER 1 YEAR PREDICTS MORTALITY BUT NOT SUBSEQUENT FVC DECLINE IN PATIENTS WITH IPF

¹L Richeldi, ²M Kolb, ³A Azuma, ⁴W Stansen, ⁵M Quaresma, ^{4S} Stowasser, ⁶B Crestani. ¹Catholic University of the Sacred Heart, Rome, Italy; ²McMaster University, Hamilton, Ontario, Canada; ³Department of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan; ⁴Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim am Rhein, Germany; ⁵Center for interstitial and rare lung diseases, Pneumology, Thoraxklinik, University of Heidelberg, and Translational Lung Research Centre Heidelberg, German Centre for Lung Research, Germany; ⁶Hôpital Bichat, Pneumologie, Paris, France

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Introduction In the INPULSIS trials, nintedanib reduced disease progression by reducing FVC decline vs placebo in patients with IPF. Patients who completed an INPULSIS trial could receive open-label nintedanib in the extension trial INPULSIS-ON.

Aim To assess the impact of FVC decline in INPULSIS on FVC decline and mortality in INPULSIS-ON.

Methods Descriptive analysis of the proportions of nintedanib-treated patients who had FVC decline $<10\%$ or $\geq 10\%$ predicted (pred) from baseline to week 52 of INPULSIS and the proportions of patients in these groups who had FVC decline $<10\%$ pred, $\geq 10\%$ pred, or died in the first year of INPULSIS-ON.

Results 430 patients received nintedanib in both INPULSIS and INPULSIS-ON. Of these, 89.1% had FVC decline $<10\%$ pred from baseline to week 52 of INPULSIS. FVC decline from baseline to week 52 in patients treated with nintedanib in INPULSIS did not predict FVC decline in the first year of INPULSIS-ON. Most patients (77.2%) had FVC decline $<10\%$ pred in the first year of INPULSIS-ON. Patients who had

Abstract M28 Figure 1 Annual rate of decline in lung volume in CAPACITY and RECAP.

FVC decline $\geq 10\%$ pred in INPULSIS had higher mortality in INPULSIS-ON than patients with FVC decline $< 10\%$ pred.

Conclusion Independent of FVC decline in the first year, most patients had FVC decline $< 10\%$ pred with continued nintedanib for a second year. FVC decline $\geq 10\%$ pred over 1 year did not predict subsequent FVC decline, but was associated with higher mortality.

Please refer to page A261 for declarations of interest in relation to abstract M29.

Abstract M29 Table 1

Absolute decline in FVC from baseline to week 52 of INPULSIS in patients treated with nintedanib (first year of treatment)	Outcome in the first year of INPULSIS-ON (second year of treatment)*	n (%)
$< 10\%$ predicted (n=383)	Absolute decline in FVC $< 10\%$ predicted [†]	301 (78.6)
	Absolute decline in FVC $\geq 10\%$ predicted	64 (16.7)
	Death	18 (4.7)
$\geq 10\%$ predicted (n=47)	Absolute decline in FVC $< 10\%$ predicted [†]	31 (66.0)
	Absolute decline in FVC $\geq 10\%$ predicted	8 (17.0)
	Death	8 (17.0)

*Patients who discontinued INPULSIS-ON without having an absolute decline in FVC $\geq 10\%$ predicted or having died were counted in the category "absolute decline in FVC $< 10\%$ predicted". [†]Includes patients with an increase, no decline, or an absolute decline in FVC $> 0\%$ but $< 10\%$ predicted in the first year of INPULSIS-ON.

M30

EFFECT OF DOSE REDUCTIONS AND/OR INTERRUPTIONS ON THE EFFICACY OF NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF): SUBGROUP ANALYSIS OF THE INPULSIS TRIALS

¹TM Maher, ²Y Inoue, ³AH Case, ⁴W Sakamoto, ⁵S Stowasser, ⁶WA Wuyts. ¹National Institute for Health Research Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust, and National Heart and Lung Institute, Imperial College, London, UK; ²Clinical Research Centre, National Hospital Organisation Kinki-Chuo Chest Medical Centre, Osaka, Japan; ³Piedmont Healthcare, Atlanta, Georgia, US; ⁴Nippon Boehringer Ingelheim Co. Ltd, Tokyo, Japan; ⁵Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim am Rhein, Germany; ⁶Department of Respiratory Medicine, University Hospitals Leuven, Leuven, Belgium

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Introduction and Aim The efficacy and safety of nintedanib in patients with IPF were assessed in two replicate Phase III placebo-controlled INPULSIS trials. In both trials, nintedanib reduced disease progression by reducing decline in FVC. The recommended dose of nintedanib was 150 mg bid, but dose reductions to 100 mg bid and treatment interruptions were allowed for the management of adverse events. Following dose reduction, the dose could be re-escalated to 150 mg bid. We assessed whether dose reductions and/or treatment interruptions influenced the effect of nintedanib on reducing FVC decline.

Methods We assessed change from baseline in FVC (mL) at week 52 in subgroups of patients by their last dose (150 mg bid or 100 mg bid) and whether they had experienced a dose reduction and/or treatment interruption using pooled data from both INPULSIS trials. Patients who prematurely

discontinued trial medication but had an FVC value at week 52 were included in the analysis. Analyses were descriptive and based on observed cases.

Results A total of 864 patients were included in the analysis (519 treated with nintedanib, 345 with placebo). Most (75%) patients did not have a dose reduction or treatment interruption. Mean (SD) changes from baseline in FVC at week 52 in subgroups by dose are shown in the Table. In patients who took nintedanib 150 mg bid as their last dose, absolute mean changes from baseline in FVC at week 52 were -118 mL and -90 mL in patients who did and did not have any prior dose reduction and/or treatment interruption, respectively. In patients who took nintedanib 100 mg bid as their last dose, mean change from baseline in FVC at week 52 was -74 mL. These changes were consistent with the decline in FVC observed in the whole nintedanib group (-89 mL).

Conclusion Pooled data from the INPULSIS trials show that decline in FVC was similar in patients treated with nintedanib irrespective of whether they had dose reductions and/or treatment interruptions. These Results suggest that the dosing regimen used in the INPULSIS trials was effective at reducing disease progression in patients with IPF.

Please refer to page A261 for declarations of interest in relation to abstract M30.

Abstract M30 Table 1 Change from baseline in FVC (mL) at week 52 by dose subgroups in INPULSIS

	Nintedanib		Placebo	
	N	Mean (SD)	N	Mean (SD)
All patients	519	-89 (264)	345	-203 (293)
Patients who did not have a dose reduction or treatment interruption	340	-90 (265)	309	-200 (292)
Patients who took 150 mg bid as last dose and had ≥ 1 dose reduction and/or treatment interruption	56	-118 (251)	31	-203 (273)
Patients who took 100 mg bid as last dose after ≥ 1 dose reduction and/or treatment interruption	123	-74 (269)	5	-391 (422)

M31

SAFETY OF COMBINED PIRFENIDONE AND NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

¹KR Flaherty, ²CD Fell, ³JT Huggins, ⁴H Nunes, ⁵R Sussman, ⁶C Valenzuela, ⁷U Petzinger, ⁸JL Stauffer, ⁹F Gilberg, ¹⁰M Bengus, ¹¹M Wijsenbeek. ¹University of Michigan, Ann Arbor, US; ²University of Calgary, Calgary, Canada; ³Medical University of South Carolina, Charleston, US; ⁴Hôpital Avicenne, Paris, France; ⁵Atlantic Health System, Overlook Medical Centre, Summit, US; ⁶Hospital Universitario de La Princesa, Instituto de Investigación Princesa, Madrid, Spain; ⁷Clinipace-Accovion GmbH, Eschborn, Germany; ⁸Genentech Inc., South San Francisco, US; ⁹F. Hoffman-La Roche Ltd, Basel, Switzerland; ¹⁰Erasmus University Medical Centre, Rotterdam, The Netherlands

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Background Safety data on combined pirfenidone and nintedanib use are limited.

Methods A single-arm, open-label study (NCT02598193) assessed safety and tolerability of 24 weeks' pirfenidone (1602–2403 mg/day) and nintedanib (200–300 mg/day) in patients with idiopathic pulmonary fibrosis (IPF) with forced vital capacity (FVC) $\geq 50\%$ and diffusing capacity of the lung for carbon monoxide (DLco) $\geq 30\%$. Before initiating nintedanib, patients had received pirfenidone for ≥ 16 weeks and tolerated a stable dose