ILD highlights from the ERS international congress 2019

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Boehringer Ingelheim

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ERS, European Respiratory Society; ILD, interstitial lung disease

Contents

FVC, forced vital capacity; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; SSc, systemic sclerosis

Risk factors for diagnostic delay in a prospective IPF cohort

(Hoyer N *et al.;* Roche-supported)

- This study used data from patients included in the prospective multicenter Danish pulmonary fibrosis biomarker cohort to determine the duration, cause, and risk factors for diagnostic delay in IPF[1,2]
- Of the 204 included patients, 158 (77.5%) were male, 52 (25.6%) were never smokers and the mean (SD) age at diagnosis was 73.7 (7.8) years; mean (SD) values for FVC and DLco (% predicted) at diagnosis were 88.9% (19.0%) and 52.6% (13.6%), respectively
- Dates of important time points (eg onset of symptoms, first hospital contact, etc) leading to an IPF diagnosis were recorded at the time of diagnosis and used to divide the total diagnostic delay into specific patient- and healthcare-related delays
- The median (IQR) total diagnostic delay from the onset of symptoms to an IPF diagnosis was 2.1 (0.9–5.0) years (Figure 1); delays were primarily attributable to the patient, general practitioner and non-specialized (ie community) hospitals
- Male sex was a risk factor for a prolonged patient delay, age was a risk factor for a prolonged healthcare delay, and previous use of inhalation medicine was a risk factor for prolonged total delay (Table 1)
- Overall, 41% of patients reported being misdiagnosed before a final diagnosis of IPF was established

Conclusion: There is a significant diagnostic delay of 2.1 years in patients with IPF, with age, sex, and treatment of alternative diagnoses identified as risk factors for delay.

Figure 1. Total delay in IPF diagnosis (box represents the median delay and the IQR)

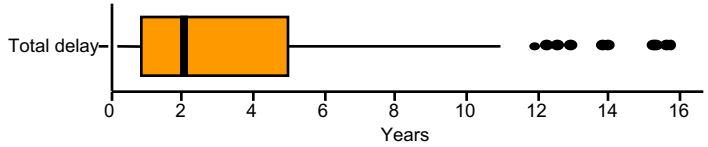


Table 1. IRR of risk factors for patient delay, healthcare delay, and total delay in IPF diagnosis

	Patient delay		Healthcare delay		Total delay	
	IRR (95% CI)	*P* value	IRR (95% CI)	*P* value	IRR (95% CI)	*P* value
Patient characteristics						
Age	0.97 (0.92–1.02)	0.24	1.03 (1.01–1.06)	0.004	1.01 (0.98–1.03	0.59
Male sex	3.84 (1.17–11.36)	0.006	1.01 (0.68–1.49)	0.95	0.99 (0.66–1.48)	0.97
Ever smoker	1.34 (0.48–3.35)	0.51	0.78 (0.54–1.11)	0.18	0.79 (0.54–1.14)	0.19
Higher education	2.16 (0.91–5.18)	0.06	1.28 (0 91–1.81)	0.14	1.15 (0.83–1.60)	0.39
Inhalation therapy use	4.68 (1.77–13.37)	0.0004	1.98 (1.38–2.90)	<0.0001	1.99 (1.40–2.88)	<0.0001
Clinical characteristics at diagnosis						
DLco	1.05 (1.02–1.08)	0.005	1.02 (1.01–1.03)	0.006	1.02 (1.00–1.03)	0.02
FVC	1.02 (0.99–1.05)	0.06	1.00 (0.99–1.01)	0.96	1.00 (0.99–1.01)	0.67
Airway obstruction	1.10 (0.23–3.86)	0.89	1.57 (0.86–2.66)	0.11	1.61 (0.94–2.61)	0.07
SGRQ total score	1.03 (1.01–1.07)	0.004	1.01 (1.00–1.03)	0.003	1.02 (1.01–1.03)	0.001
UIP pattern on HRCT	0.84 (0.30–2.11)	0.71	1.32 (0.89–1.95)	0.16	1.47 (1.01–-2.11)	0.04

CI, confidence interval; DLco, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity; HRCT, high resolution computed tomography; IPF, idiopathic pulmonary fibrosis; IQR, interquartile range; IRR, incidence rate ratio; SD, standard deviation; SGRQ, St George's Respiratory Questionnaire; UIP, usual interstitial pneumonia

1. Hoyer N *et al.* ERS international congress 2019; abstract PA1724; 2. Hoyer N *et al. Respir Res* 2019;20:103

Transbronchial lung cryobiopsy for ILD diagnosis: results of the COLDICE Study (Troy L *et al.*)

- Transbronchial lung cryobiopsy (TBLC) is a novel technique for sampling lung tissue for ILD diagnosis; despite increasing use, the diagnostic accuracy of TBLC compared with surgical lung biopsy (SLB) remains unclear
- The aim of this prospective, multicenter study was to investigate the agreement between TBLC and SLB (n=65)[1,2]
- ILD patients referred for lung biopsy after central screening underwent sequential TLBC and SLB, under one anesthetic
  - Blinded analysis of samples was conducted by three pathologists, individually and by consensus; at MDD, de-identified cases were discussed twice with either TBLC or SLB along with clinical and radiology data, in random non-consecutive order
- Primary endpoints were agreement of TBLC and SLB for 1) 'definite/probable UIP', 'indeterminate for UIP' and 'alternative diagnosis' histopathologic patterns; and for 2) MDD diagnoses
  - Histopathological agreement between TBLC and SLB was 70.8%, weighted κ 0.70 (95% CI: 0.55–0.86); agreement at MDD was 76.9%, κ 0.62 (95% CI: 0.47–0.78)
  - For TBLC with high/definite diagnostic confidence at MDD (39/65, 60% of cases), 94.9% were concordant with SLB diagnoses; in the 26 with low-confidence/unclassifiable TBLC diagnoses, SLB reclassified only 6 to alternative high/definite MDD diagnoses

Figure 1: Comparison of TBLC and SLB diagnoses of guideline-refined histopathological patterns

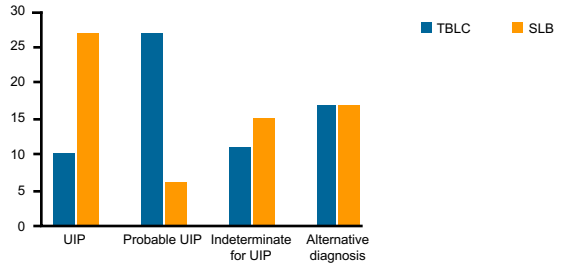
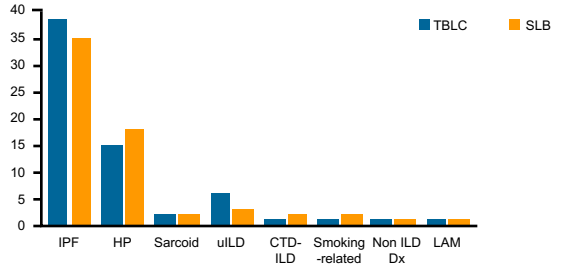


Figure 2: Comparison of TBLC and SLB ILD diagnoses following MDD



Conclusion: High agreement between TBLC and SLB for pathologic and MDD diagnoses support the clinical utility of TBLC in ILD diagnostic algorithms.

CI, confidence interval; CTD-ILD, connective tissue disease-associated interstitial lung disease; Dx, diagnosis; ILD, interstitial lung disease; HP, hypersensitivity pneumonitis; IPF, idiopathic pulmonary fibrosis; LAM, lymphangioeiomyomatosis; MDD, multidisciplinary discussion; SLB, surgical lung biopsy; TBLC, transbronchial lung cryobiopsy; uILD, unclassifiable interstitial lung disease; UIP, usual interstitial pneumonia

1. Troy L *et al.* ERS international congress 2019; abstract RCT1886; 2. Troy L *et al. Lancet Respir Med* 2019; doi: 10.1016/S2213-2600(19)30342-X

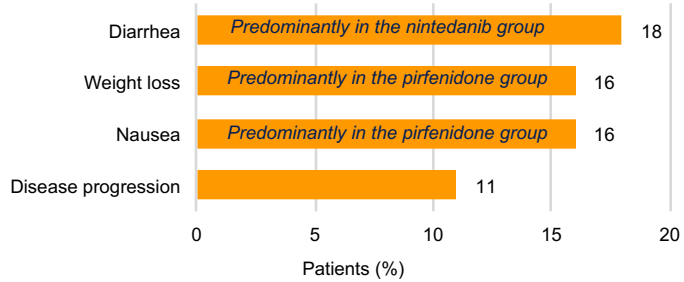
What proportion of patients with IPF fall outside UK prescribing criteria for antifibrotic treatment? A UK specialist center review (Brereton C *et al.*)

- This was a retrospective specialist-center cohort study that evaluated the proportions of patients with IPF who (i) did not meet UK NICE prescribing criteria for antifibrotic treatment (ie an FVC of 50–80% predicted) and (ii) who discontinued antifibrotic treatment because of disease progression
  - Included patients (n=194) had a diagnosis of IPF on the basis of multidisciplinary discussions and were followed up for ≥12 months
  - Of the included patents, 150 (77%) were male, 120 (65%) were ex-smokers and the mean (SD) age at diagnosis was 73 (8) years; mean (SD) values (% predicted) for FVC and TLco at diagnosis were 75% (20%) and 47% (16%), respectively
- Just over one-quarter of patients (n=51) were ineligible for antifibrotic therapy
  - Of the ineligible patients, 29 (15%) patients had an FVC that was outside the NICE prescribing criteria; 20 patients (10%) had an FVC that was >80% predicted, while nine patients (5%) had an FVC that was <50% predicted (other reasons for ineligibility included age, frailty and comorbidities)
- An antifibrotic was prescribed in 117 patients (60%)
  - The use of nintedanib and pirfenidone as the first prescribed antifibrotic was almost identical; however, the rate of subsequent discontinuation was lower for nintedanib (Table 1)
  - Discontinuation of either agent because of disease progression was uncommon (Figure 1)

Table 1. Antifibrotic treatment uptake and discontinuation

	Nintedanib	Pirfenidone	Total
Received antifibrotic treatment	58	59	117/194 (60%)
Discontinued antifibrotic treatment*	12	26	38/117 (32%)
*For reasons other than death			

Figure 1. Reasons for discontinuation of antifibrotic treatment (n=38)



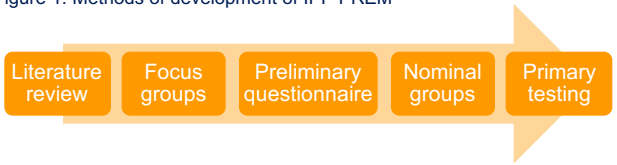
Conclusion: Overall, 15% of patients with IPF who were referred for specialist care were ineligible for antifibrotic treatment per NICE FVC criteria. In those patients who received an antifibrotic, the most common reasons for stopping treatment were diarrhea, nausea and weight loss; treatment cessation because of disease progression was uncommon.

FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; NICE, The National Institute for Health and Care Excellence; SD, standard deviation; TL_{CO}, transfer capacity of the lung for carbon monoxide
Brereton C *et al.* ERS international congress 2019; abstract PA1348

Development of a patient reported experience measure for IPF (Russell A *et al.*)

- This project aimed to develop an IPF-PREM informed by patients' perceptions of their healthcare experiences
- Four focus groups were created at three academic referral centers in the UK and US; 29 patients completed the IPF-PREM after an outpatients clinic visit at a UK ILD center (Figure 1)
  - Of these patients, 22 were male, with a median age of 71 years and a range of ethnicities (18 Caucasian, six British Asian and five other) and disease severities (based on GAP score)

Figure 1. Methods of development of IPF-PREM



- A nominal group of ILD clinical specialists rated and ranked emerging themes; themes were mapped to eight domains, each associated with approximately five statements:
  1. Respect for patient values, eg 'I feel like I am treated with sensitivity and care at the ILD service'
  2. Communication, eg 'I have access to electronic healthcare record and/or digital resources with the ILD team'
  3. Information and understanding, eg 'I understand my diagnosis and the course it is likely to take'
  4. Physical comfort, eg 'I feel that my symptoms are managed well'
  5. Access to the right ILD pathway of care, eg 'I have contact with an ILD doctor/nurse every 3-6 months
  6. Emotional well-being, eg 'I have been offered counselling/peer support/talking therapy
  7. Involvement of family and friends, eg 'My family/informal carers have access to the necessary information about my condition and evolving needs'
  8. Global experience of health, eg 'Overall my experience of healthcare has been positive in the last 12 months'

Conclusion: Patients valued having a condition-specific questionnaire and were happy with their care overall. The IPF-PREM will provide a valuable quality indicator for IPF service delivery at all stages of the disease trajectory, complementing existing IPF patient reported outcome measures. Further analyses and a validation study will determine reliability.

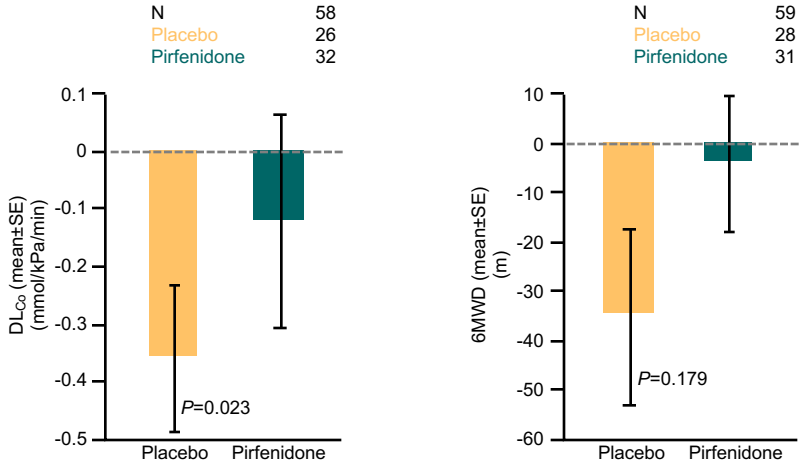
GAP, gender, age and physiology index; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; IPF-PREM, idiopathic pulmonary fibrosis patient-reported experience measure

Russell A *et al.* ERS international congress 2019; abstract PA1320

Exploring efficacy and safety of oral pirfenidone for progressive, non-IPF lung fibrosis: the RELIEF trial (Guenther A *et al.*; Roche-supported)

- The aim of the Phase II RELIEF trial was to assess the efficacy and safety of pirfenidone (2403 mg/day) vs placebo in patients with four types of progressive fibrosing ILD: fNSIP, CVD-LF, cHP and ALF
- Included patients had progressive disease despite previous therapy, with progression defined as FVC decline of >5% predicted per year, calculated using three PFTs performed 6–24 months prior to screening; other inclusion criteria were specific to each disease type
- A sample size of 374 patients was planned; however, the trial was terminated prematurely in December 2018 due to futility (low recruitment rates)
  - Final cohort: n=127; cHP n=57, CVD-LF n=37, fNSIP n=27, ALF n=6
- At baseline, mean FVC% predicted was ~62% and DL_{CO}% predicted was ~38%
- The primary endpoint was the change in FVC% predicted from baseline to week 48; with imputation of missing values by rank ANCOVA, an improvement was observed with pirfenidone. Analysis of secondary endpoints showed less deterioration of DL_{CO} (Figure 1), TLC and 6MWD and improved progression-free survival in pirfenidone-treated patients vs placebo
- The safety data were consistent with previous trials of pirfenidone

Figure 1. Relative change in DL_{CO} in patients treated with pirfenidone vs placebo*



Conclusion: The study ended prematurely due to slow recruitment; with imputation of missing data, pirfenidone appeared to reduce decline in FVC % predicted vs placebo over the course of the trial. Had the study reached completion, it may have shown a favorable effect of pirfenidone in patients with progressive fibrosing ILDs.

*Wilcoxon two-sided test, no imputation, deceased patients excluded

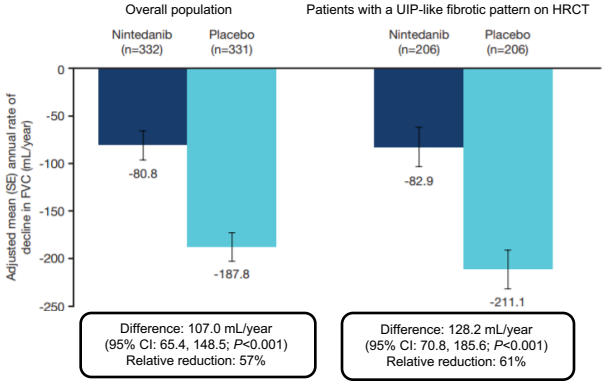
6MWD, 6-minute walk distance; ALF, asbestos-related lung fibrosis; ANCOVA, analysis of covariance; cHP, chronic hypersensitivity pneumonitis; CVD-LF, collagen vascular disease associated with lung fibrosis; DL_{CO}, diffusing capacity of the lung for carbon monoxide; fNSIP, fibrotic non-specific interstitial pneumonia; FVC, forced vital capacity; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; PFT, pulmonary function test; SE, standard error; TLC, total lung capacity

Guenther A *et al.* ERS international congress 2019; abstract RCT1879 (ALERT ILD session)

Nintedanib in patients with chronic fibrosing ILDs with the progressive phenotype: the INBUILD trial (Flaherty K *et al.*; Sponsor: BI)

- The Phase III INBUILD trial investigated the efficacy and safety of nintedanib in patients with fibrosing ILDs with a progressive phenotype, excluding IPF (n=663)[1,2]
- Eligible patients had >10% extent of fibrotic ILD on HRCT, and met defined criteria for progression 24 months prior to screening, based on relative FVC decline, fibrosis extent on HRCT, and/or symptoms; at baseline across both treatment arms, mean FVC was 68% predicted, mean DL_{CO} was ~46% predicted, and ~62% of patients has the UIP-like fibrotic pattern on HRCT
- Clinical ILD diagnoses were similar in the overall population across both treatment groups, and included hypersensitivity pneumonitis, autoimmune ILDs, idiopathic NSIP, unclassifiable IIP and other ILDs
- **Primary endpoint:** Annual rate of decline in FVC (mL/year) over 52 weeks; a) in the overall population; b) in patients with a UIP-like fibrotic pattern of HRCT
  - Nintedanib reduced the annual rate of decline in FVC over 52 weeks compared with placebo, both in the overall population and in patients with UIP-like fibrotic pattern on HRCT (Figure 1)
- **Main secondary endpoint:** change from baseline in K-BILD questionnaire total score over 52 weeks[1,2]
  - In the overall population, changes from baseline at week 52 were small in both treatment groups (*P*=0.11)
- **Main secondary endpoints:** time to first acute exacerbation of ILD or death; time to death (over 52 weeks)
  - In the overall population, using data up to first database lock, nintedanib was associated with a numerically reduced risk of acute exacerbation of ILD or death, and of death
- The adverse event profile of nintedanib was consistent with that observed in patients with IPF

Figure 1. Annual rate of decline in FVC (mL/year) over 52 weeks



Conclusion: Nintedanib slowed the progression of ILD in patients with the progressive fibrosing phenotype, as demonstrated by a lower rate of decline in FVC, with a consistent effect between patients with a UIP-like fibrotic pattern and other fibrotic patterns on HRCT. Nintedanib was associated with a numerically reduced risk of acute exacerbation of ILD or death, and of death. The adverse event profile of nintedanib was consistent with that observed in previous trials.

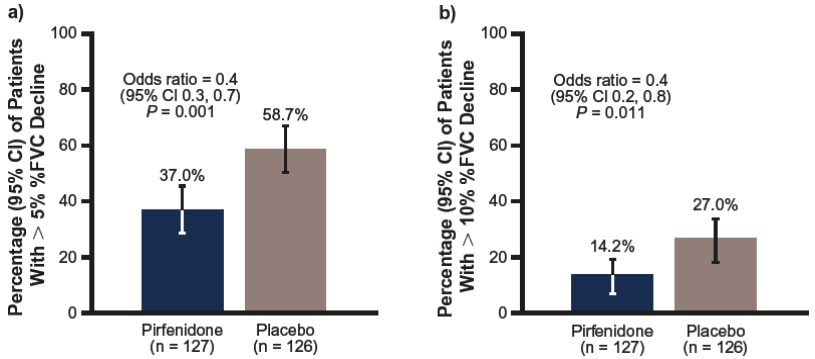
CI, confidence interval; DL_{CO}, diffusing capacity of the lung for carbon monoxide FVC, forced vital capacity; HRCT, high resolution computed tomography; IIP, idiopathic interstitial pneumonia; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; K-BILD, King's brief interstitial lung disease questionnaire; NSIP, non-specific interstitial pneumonia; PF-ILD, progressive fibrosing interstitial lung disease; SE, standard error; UIP, usual interstitial pneumonia

1. Flaherty K *et al.* ERS international congress 2019; abstract RCT1881 (ALERT ILD session); 2. Flaherty K *et al. N Engl J Med* 2019; doi: 10.1056/NEJMoa1908681

Phase II trial of pirfenidone in patients with progressive fibrosing unclassifiable ILD (Maher T *et al.;* Sponsor: Roche)

- This international, randomized, double-blind, placebo-controlled Phase II trial investigated the efficacy and safety of pirfenidone (2403 mg/day) vs placebo over 24 weeks in patients with fibrotic uILD[1,2]
  - Eligible patients showed progression, defined as >10% fibrosis on HRCT within the previous 12 months and progressive disease within the previous 6 months (>5% absolute decline in %FVC or significant symptomatic worsening not due to cardiac, pulmonary, vascular or other causes)
- 253 patients were randomized to receive either pirfenidone (n=127) or placebo (n=126). The primary endpoint was to evaluate the efficacy of pirfenidone vs placebo using change in FVC (mL) measured by daily home spirometry over 24 weeks
  - Analysis was impacted by high intra-variability in home spirometry values meaning the planned statistical model could not be applied
  - Decline in FVC was significantly lower in patients treated with pirfenidone (*P*=0.002) by study site spirometry (secondary endpoint)
  - Absolute declines of >5% and >10% in %FVC were reported less frequently in patients receiving pirfenidone vs placebo (Figure 1)
  - In subgroup analyses, a treatment benefit was observed regardless of age, gender, lung function and presence/absence of IPAF

Figure 1. Percentage of patients with categorical declines of (a) >5% and (b) >10% for %FVC (ITT population)



Conclusion: Results support the conclusion that pirfenidone was effective in patients with progressive fibrotic uILD over 24 weeks, with an acceptable safety and tolerability profile. Further studies are required before daily home spirometry can be used as a primary outcome measure.

CI, confidence interval; FVC, forced vital capacity; HRCT, high resolution computed tomography; ILD, interstitial lung disease; IPAF, interstitial pneumonia with autoimmune features; ITT, intention to treat; PF-ILD, progressive fibrosing interstitial lung disease; uILD, unclassifiable interstitial lung disease

1. Maher T *et al.* ERS international congress 2019; abstract RCT1880 (ALERT ILD session); 2. Maher TM *et al. Lancet Respir Med* 2019; doi: 10.1016/S2213-2600(19)30341-8

Home and clinic spirometry for FVC measurements

Correlation between home and clinic spirometry: the INMARK trial[1]
(Maher T *et al.*; Sponsor: BI)

- In patients with IPF and well-preserved lung function, home and clinic measurements of FVC and FEV_6 at individual visits over 52 weeks were strongly correlated
- However, there was only a weak correlation between home and clinic measurements of changes from baseline and rates of decline in these lung function measures, apparently due to variability in changes from baseline in FVC measured using home spirometry

Disease outcomes using home monitoring devices: the STARMAP trial[2]
(Belloni P *et al.*; Sponsor: Roche)

- In patients with IPF enrolled in the STARMAP study, the ability of home-based mobile health tools to monitor disease progression and capture PROs was analyzed over 26 weeks
- Correlations between home and clinic FVC measurements did not translate to correlation with clinical endpoints, including change from baseline in FVC or linear trends in FVC over time (Figure 1)

Phase II trial of pirfenidone in patients with progressive fibrosing unclassifiable ILD[3,4]
(Maher T *et al.*; Sponsor: Roche)

- The primary endpoint of this trial was median predicted FVC change from baseline at week 24; analysis was impacted by high intra-variability in home spirometry values, meaning that the planned statistical model could not be applied (Figure 2)

Figure 1. Slopes of best-fit lines to the home vs in-clinic measurements*

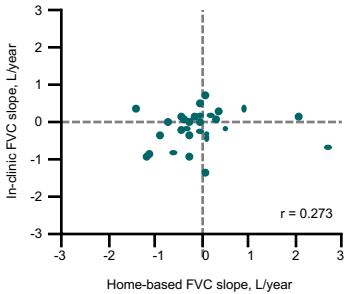
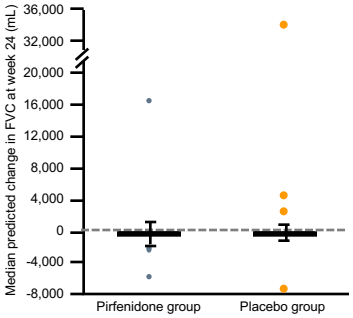


Figure 2. Median predicted FVC change from baseline at week 24 measured using daily home spirometry (n=253)†



*n=31 patients with available data; †the whiskers show the minimum and maximum values, excluding outliers; the circles show the outliers

FEV, forced expiratory volume; FVC, forced vital capacity; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; PF-ILD, progressive fibrosing interstitial lung disease; PRO, patient-reported outcome

1. Maher T *et al.* ERS international congress 2019; abstract PA1318; 2. Belloni P *et al.* ERS international congress 2019; abstract PA1333; 3. Maher T *et al.* ERS international congress 2019; abstract RCT1880; 4. Maher TM *et al. Lancet Respir Med* 2019; doi: 10.1016/S2213-2600(19)30341-8

Analyses from the SENSCIS trial of patients with SSc-ILD (Sponsor: BI)

Details of the primary SENSCIS results can be found in Distler *et al.* publication[1]

Effects of nintedanib on FVC decline over 52 weeks[2] (Highland K *et al.*)

- Over 52 weeks, the proportions of patients with any decline in FVC, and with FVC decline >5% predicted (*P*=0.01) and >10% predicted (*P*=0.68), were lower in the nintedanib group than in the placebo group
- In patients with a decline in FVC >5% predicted, there was a greater proportion of ATA-positive patients and a lower proportion of patients taking mycophenolate at baseline

Effects of nintedanib in patients with differing FVC at baseline[3] (Maher T *et al.*) (Figure 1)

- Nintedanib reduced the rate of decline in FVC both in patients with FVC <80% and ≥80% predicted at baseline
- The treatment effect of nintedanib vs placebo on the rate of FVC decline was numerically more pronounced in patients with FVC ≥80% than <80% predicted at baseline, but was not statistically significant

Effects of nintedanib in patients with differing extents of lung fibrosis[4] (Raghu G *et al.*) (Figure 2)

- In this subgroup comparison of patients with extent of fibrosis on HRCT <20% vs ≥20% at baseline, there were no significant subgroup differences regarding the effect of nintedanib on the rate of decline in FVC over 52 weeks, or the proportions of patients with an absolute decline in FVC >5% or >10% predicted
- An increase (worsening) in SGRQ total score with nintedanib vs placebo was observed in patients with extent of fibrotic ILD <20% at baseline but not in those with extent of fibrotic ILD ≥20% at baseline

Dose adjustments[5] (Highland K *et al.*)

- The annual rate of decline in FVC was similar in nintedanib-treated patients irrespective of dose adjustments
- Most patients remained on therapy, suggesting that dose adjustments minimized treatment discontinuations

Figure 1: Rate of decline in FVC (mL/year) by baseline FVC % predicted

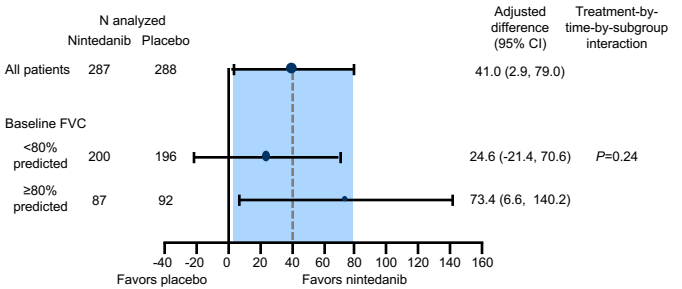
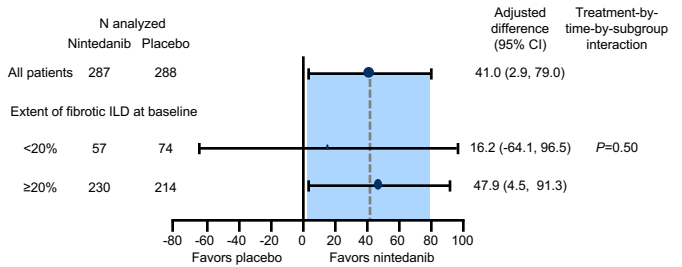


Figure 2: Rate of decline in FVC over (mL/year) by extent of fibrotic ILD at baseline



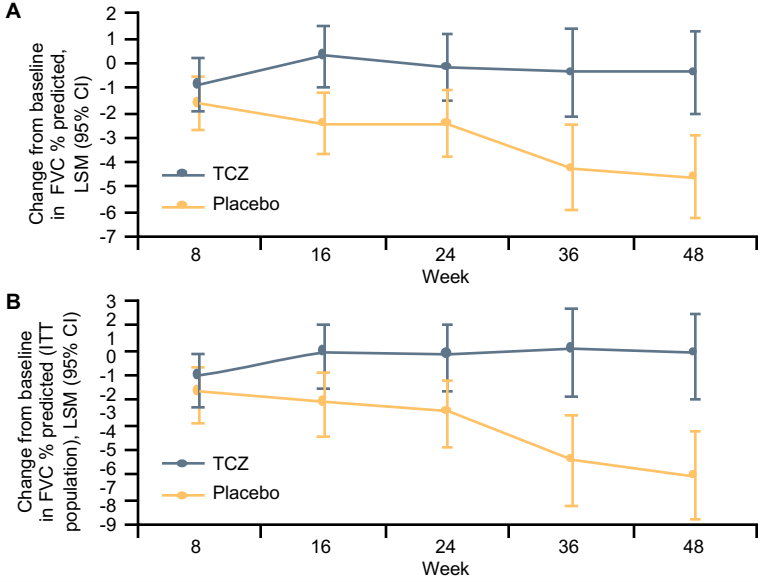
ATA, antitopoisomerase antibody; CI, confidence interval; FVC, forced vital capacity; HRCT, high resolution computed tomography; ILD, interstitial lung disease; SGRQ, St George's Respiratory Questionnaire; SSc-ILD, systemic sclerosis-associated interstitial lung disease;

1. Distler O *et al. N Engl J Med* 2019;380:2518–28; 2. Highland K *et al.* ERS international congress 2019; abstract RCT1882; 3. Maher T *et al.* ERS international congress 2019; abstract OA3599; 4. Raghu G *et al.* ERS international congress 2019; abstract PA5193; 5. Highland K *et al.* ERS international congress 2019; abstract PA4731

Lung function preservation in a Phase III trial of tocilizumab in SSc (Denton C *et al.*; Sponsor: Roche)

- Randomized, double-blind, placebo-controlled Phase III trial in patients with SSc (≤60 months from first non-Raynaud symptom, n=212)[1,2]
- Primary endpoint of change from baseline to week 48 in mRSS was not met
- Clinically meaningful difference in cumulative distribution of FVC % predicted change from baseline to week 48 was observed between the tocilizumab and placebo-treated groups
  - Pulmonary function was preserved during 48 weeks of tocilizumab treatment vs placebo
  - Proportion of patients with FVC decline >10% was lower with tocilizumab treatment vs placebo
- In patients with SSc-ILD (n=111), the difference between the treatment groups in change from baseline in FVC % predicted was greater compared with the SSc cohort (Figure 1)
- HRCT scans were obtained at baseline and at week 48, from which a computer-aided QLF score was derived; patients receiving tocilizumab had significantly lower QLF scores vs placebo (P<0.001), thereby supporting the FVC results
- The time to treatment failure showed a hazard ratio in favor or tocilizumab vs placebo, whereas HAQ-DI, patient VAS and clinician VAS did not show any significant treatment effects
- No new safety signals were identified

Figure 1. Change from baseline to week 48 in FVC % predicted in patients with A) SSc overall and B) SSc-ILD



Conclusion: The primary endpoint of change from baseline to week 48 in mRSS was not met. FVC results were clinically meaningful, particularly in the SSc-ILD cohort, and supported by HRCT data. No new safety signals were identified.

CI, confidence interval; FVC, forced vital capacity; HAQ-DI, Health Assessment Questionnaire Disability Index; ITT, intention to treat; LSM, least squares mean; mRSS, modified Rodnan skin score; QLF, quantitative lung fibrosis; SSc, systemic sclerosis; SSc-ILD, systemic sclerosis-associated interstitial lung disease; TCZ, tocilizumab; VAS, visual analog scale

1. Denton C *et al.* ERS international congress 2019; abstract RCT1883; 2. NCT02453256. www.clinicaltrials.gov (accessed October 2019)