THE ANNUAL MEETING OF THE
LEBANESE PULMONARY SOCIETY
2023
LE CONGRÈS ANNUEL DE LA SOCIÉTÉ
LIBANAISE DE PNEUMOLOGIE

PPF Guidelines: From Theory to Clinical Practice

Moussa RIACHY, MD, FCCP

Beirut, April 2023

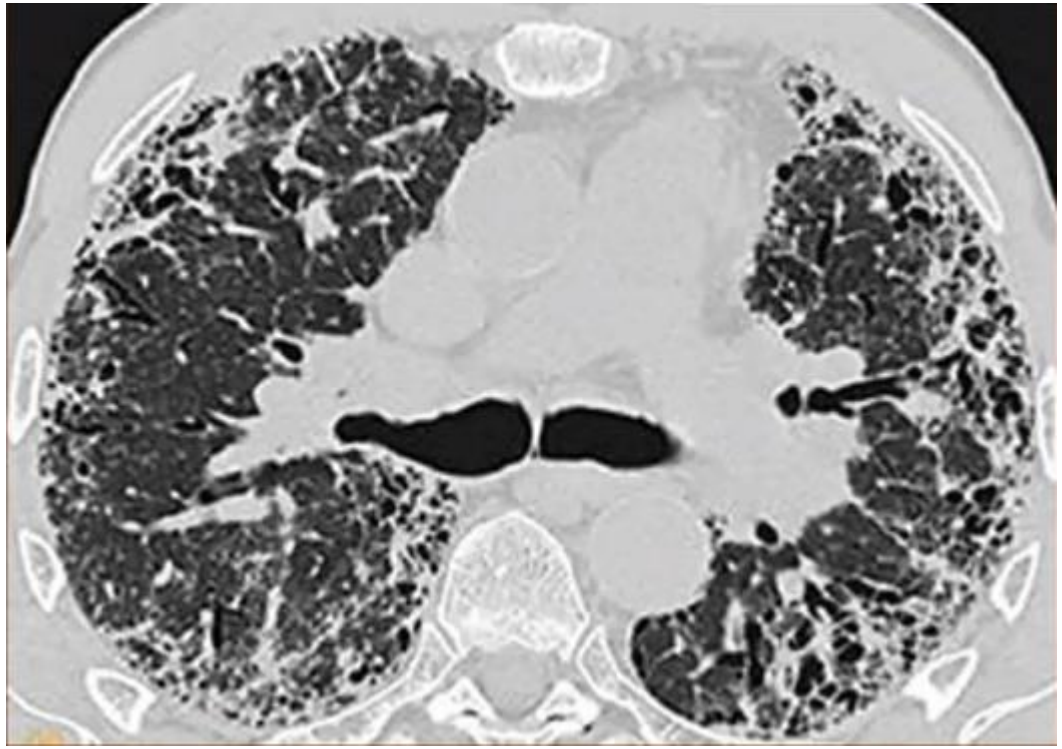
OUTLINE: PPF Guidelines

- Pulmonary Fibrosis
- Methodology
- Definition
- Diagnostic criteria
- Biomarkers
- Outcome
- Treatment

Fibrotic Lung Diseases

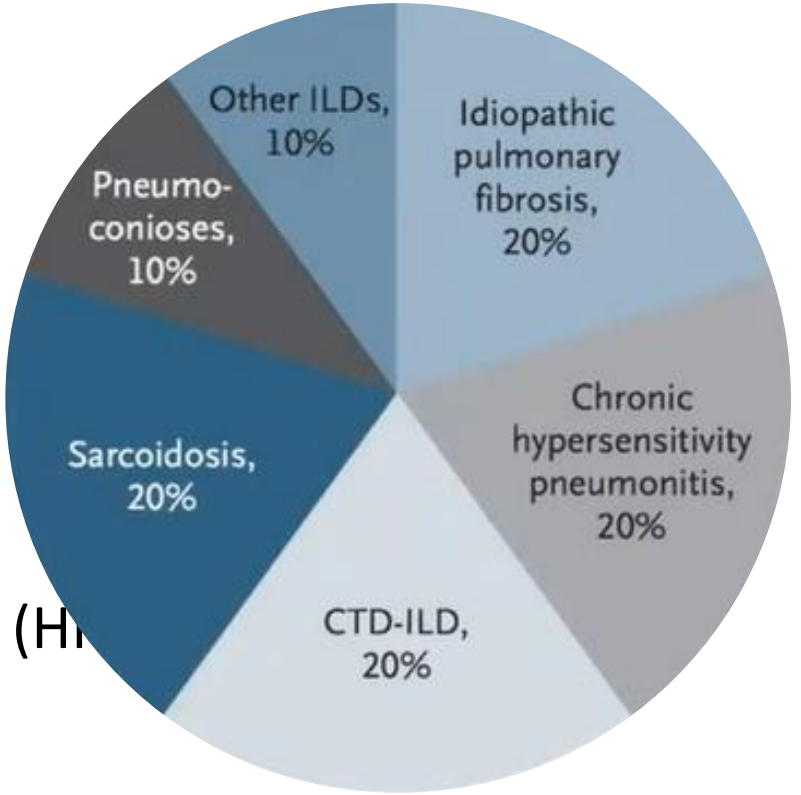
- Diffuse parenchymal lung diseases with alveolar inflammation/fibrosis which results in impairment of gas exchange

- Pulmonary fibrosis is characterized by parenchymal scarring with or without inflammation (interstitial lung disease).

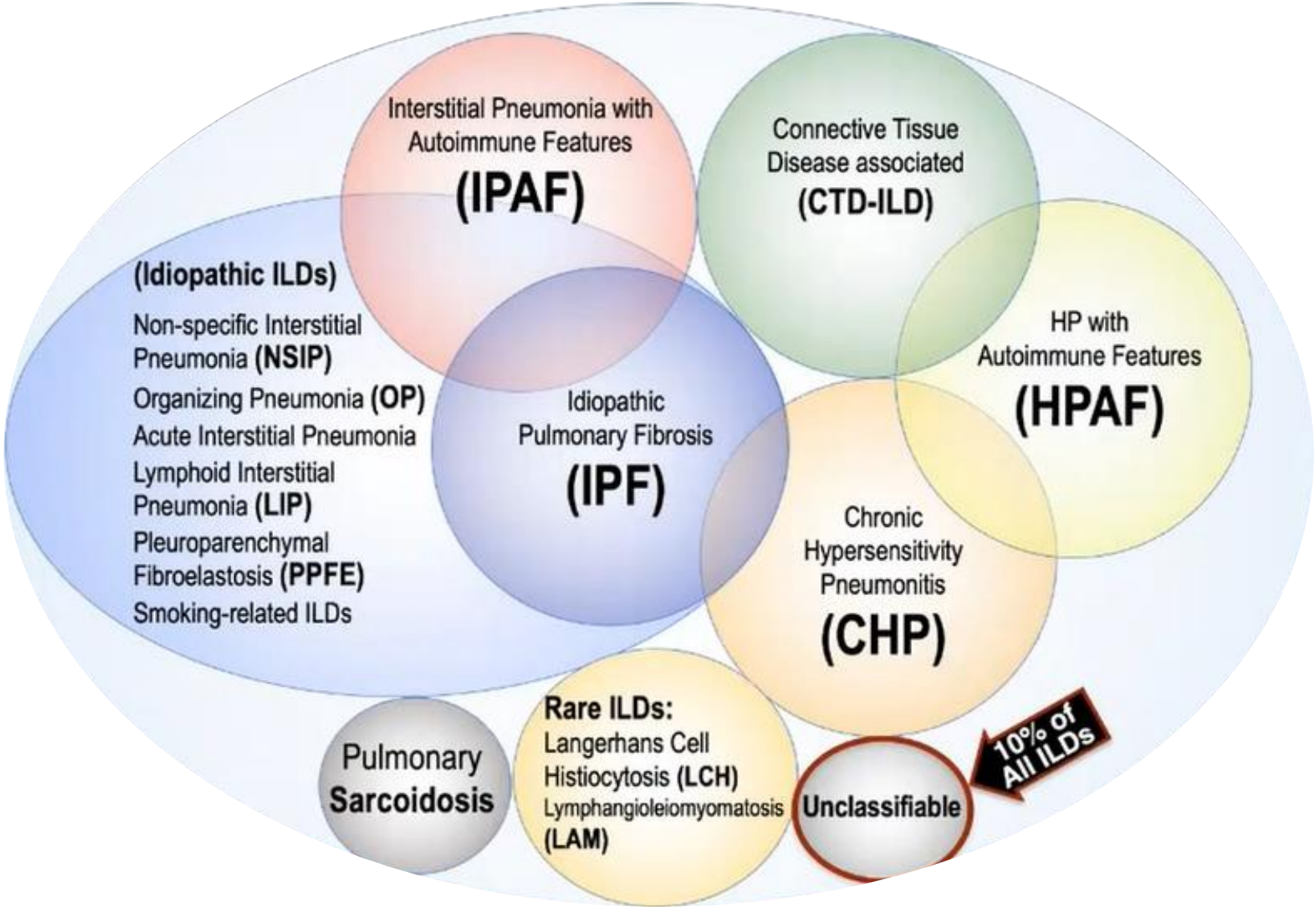


Pulmonary Fibrosis - Epidemiology

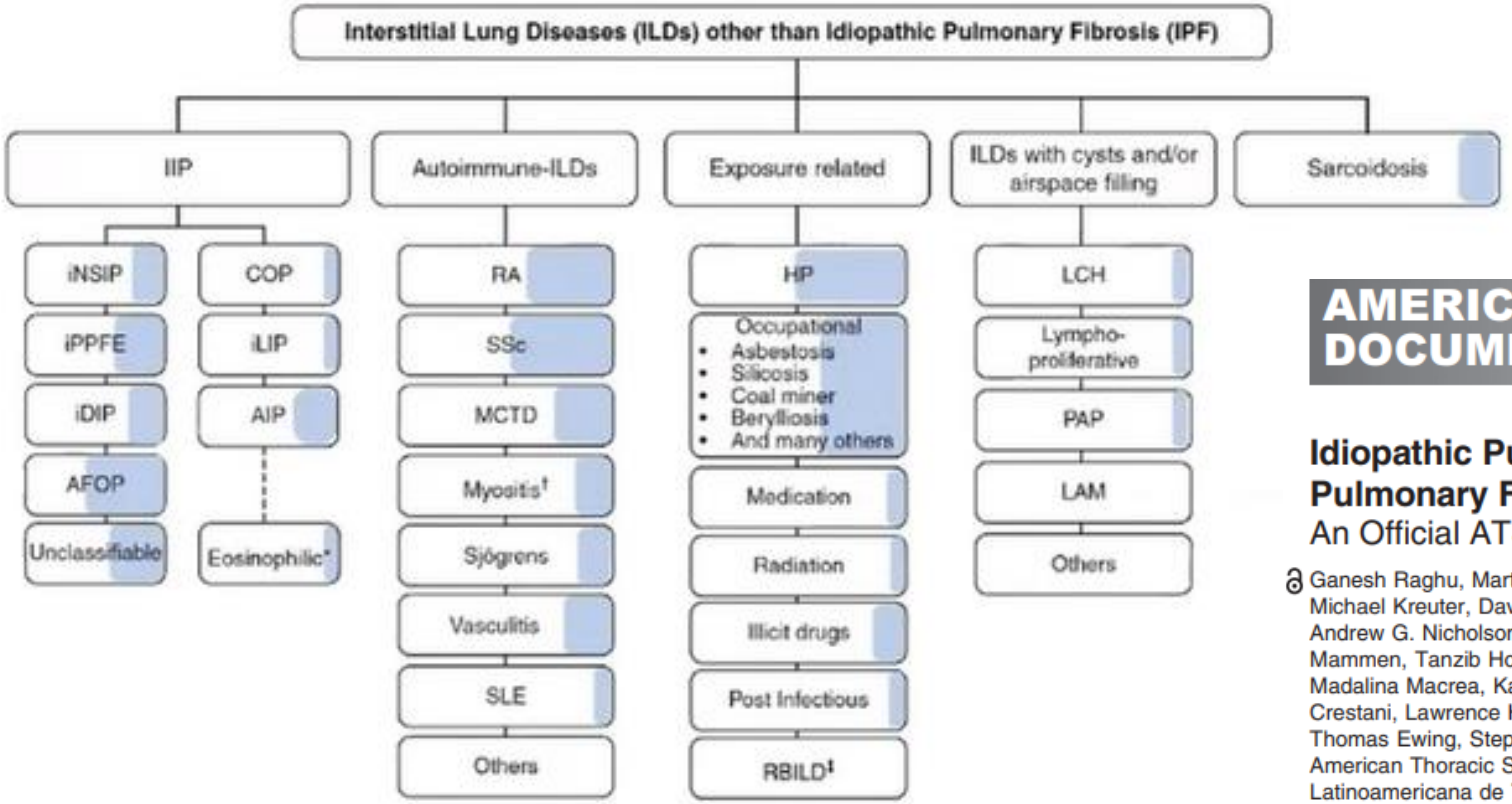
- 81/100.000 population in USA
- IPF seems to be increasing in Western nations
- Etiologies:
  - Connective tissue diseases (CTD)
  - Environmental exposurese.g. Hypersensitivity pneumonitis (H
  - Unknown e.g. idiopathic pulmonary fibrosis (IPF)
  - Familial/Genetic factors
  - Sarcoidosis
  - Pneumoconiosis
  - Others…



Pulmonary Fibrosis Phenotypes



Progressive Pulmonary Fibrosis



AMERICAN THORACIC SOCIETY DOCUMENTS

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

Ganesh Raghu, Martine Remy-Jardin, Luca Richeldi, Carey C. Thomson, Yoshikazu Inoue, Takeshi Johkoh, Michael Kreuter, David A. Lynch, Toby M. Maher, Fernando J. Martinez, Maria Molina-Molina, Jeffrey L. Myers, Andrew G. Nicholson, Christopher J. Ryerson, Mary E. Strek, Lauren K. Troy, Marlies Wijsenbeek, Manoj J. Mammen, Tanzib Hossain, Brittany D. Bissell, Derrick D. Herman, Stephanie M. Hon, Fayez Kheir, Yet H. Khor, Madalina Macrea, Katerina M. Antoniou, Demosthenes Bouros, Ivette Buendia-Roldan, Fabian Caro, Bruno Crestani, Lawrence Ho, Julie Morisset, Amy L. Olson, Anna Podolanczuk, Venerino Poletti, Moisés Selman, Thomas Ewing, Stephen Jones, Shandra L. Knight, Marya Ghazipura, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

This official clinical practice guideline was approved by the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax February 2022

Shading represents the estimated proportion of patients who manifest PPF (no data)

The ATS/ERS/JRS/ALAT clinical practice guideline methodology

Narrative portions (eg radiological criteria, physiological criteria and definitions) were developed using **consensus by discussion**

Questions about pirfenidone and nintedanib were informed by **systematic reviews** and answered with **evidence-based recommendations** using the GRADE approach

>70% agreement* was required for a recommendation to be made

Strong recommendation: the vast majority of patients should receive the recommended course of action†

Conditional recommendation: different choices will be appropriate for different patients, and the clinician must help each patient arrive at an appropriate management decision†

>20% abstentions indicated an insufficient quorum for decision-making

If the primary reason for the abstentions was insufficient evidence, a research recommendation was also made

*With <20% abstentions; †Further detail on the implications and interpretation of strong and conditional recommendations is provided in the back-up section

Raghu G *et al. Am J Respir Crit Care Med* 2022;205:e18–47

Progressive Pulmonary Fibrosis (PPF): Definition

- ILD patient of known or unknown etiology (other IPF) who has radiological evidence of pulmonary fibrosis.
- At least two of the following 3 criteria occurring within the past year (no alternative explanation):

1. Worsening respiratory symptoms

2. Physiologic evidence of disease progression

3. Radiological evidence of disease progression

Progressive Pulmonary Fibrosis (PPF)

- Guideline adopts the new "**progressive pulmonary fibrosis (PPF)**" instead of using the established term "progressive fibrosis ILD"

➔ Why was this new term necessary?

Disease progression is the result of PPF beyond the interstitial space in the lung parenchyma

Disease progression causes a clinical course similar to IPF

PPF is simple and compatible with the broadly used term that is well-known and currently used by both clinicians and patients: 'pulmonary fibrosis'

PF-ILD: No known genotype !!!

Raghu 2022

Progressive Pulmonary Fibrosis (PPF): Criteria

In a patient with ILD of known or unknown etiology (other than IPF) who has radiological evidence of pulmonary fibrosis, PPF is defined as **at least two of the following three criteria** occurring **within the past year** with no alternative explanation:

1. Worsening respiratory symptoms
2. Physiological evidence of disease progression
3. Radiological evidence of disease progression

Progressive Pulmonary Fibrosis (PPF)

Outcome	AUC	Sensitivity (70% specificity)	Cutt off For FVC%	Sensitivity (90% specificity)	Cutt off FVC%
Increased dyspnea	0.71	0.62	5.2	0.35	11.1
Increased ILD on HRCT	0.72	0.67	5.0	0.36	10.7
New O_2 use	0.68	0.57	6.25	0.36	12.0
Death	0.67	0.61	6.5	0.32	13.5
Exacerbation	0.61	0.48	6.9	0.22	13.9

1. Worsening respiratory symptoms
2. Physiological evidence of disease progression
3. Radiological evidence of disease progression

Sahec 2018

Progressive Pulmonary Fibrosis (PPF)

- Physiological evidence of disease progression is based on an absolute decline in FVC and/or DLCO within 1 year of follow-up

Progressive Pulmonary Fibrosis (PPF)

- Radiological evidence of disease progression is based on the appearance or increase extent of fibrotic features on CT appearance

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis
B. New ground-glass opacity with traction bronchiectasis
C. New fine reticulation
D. Increased extent or increased coarseness of reticular abnormality
E. New or increased honeycombing
F. Increased lobar volume loss

1. Worsening respiratory symptoms
2. Physiological evidence of disease progression
3. Radiological evidence of disease progression

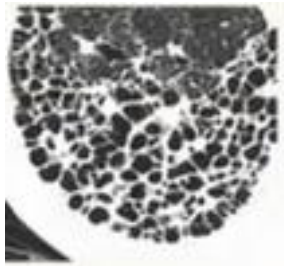
Optimal imaging for assessing CT change

2011 Guidelines[1]	2018 Guidelines[2]

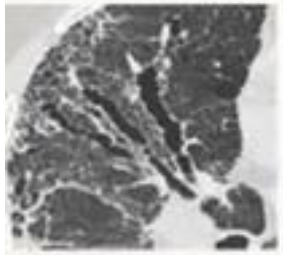
• Non contrast supine inspiratory CT
  • Interspaced OR volumetric
  • Collimation <2mm
• Expiratory CT optional
  • Interspaced
• Prone CT if ?dependent change?
	• Non contrast supine inspiratory CT
	  • Volumetric
	  • Collimation <1mm
	• Expiratory supine CT recommended
	  • Interspaced or volumetric
	• Prone CT if ?dependent change?
	• Dose reduction techniques (1-3mSv)
	  • But not ultra-low dose CT (<1mSv)
	• CTPA +/- non-contrast CT
	  • Interspaced or volume

Raghu 2011
Raghu 2018

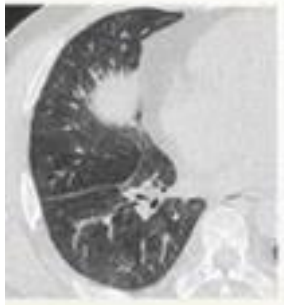
Diagnosis & Judging disease severity can be tricky



- Honeycomb pattern



- Traction bronchiectasis



- Volume loss

Radiologic evidence of disease progression (1)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

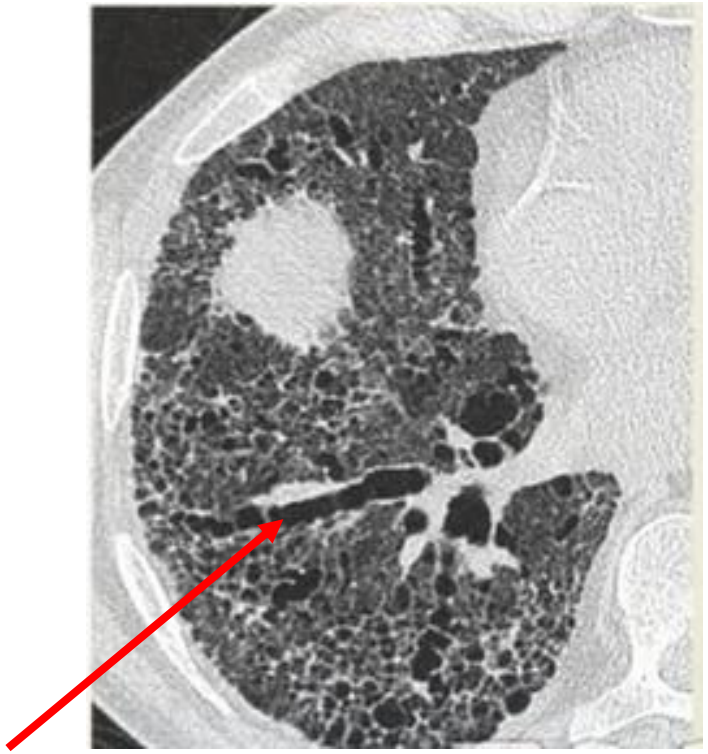
B. New ground-glass opacity with traction bronchiectasis

C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

E. New or increased honeycombing

F. Increased lobar volume loss



Radiologic evidence of disease progression (2)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

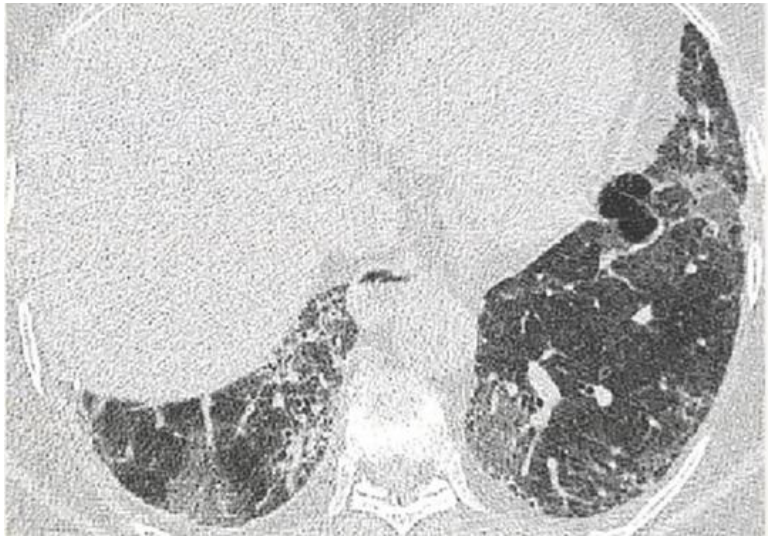
B. New ground-glass opacity with traction bronchiectasis

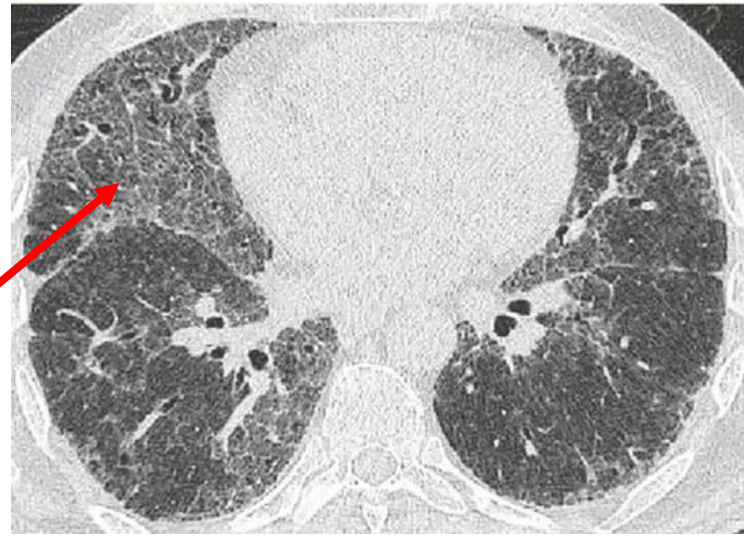
C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

E. New or increased honeycombing

F. Increased lobar volume loss





Radiologic evidence of disease progression (4)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

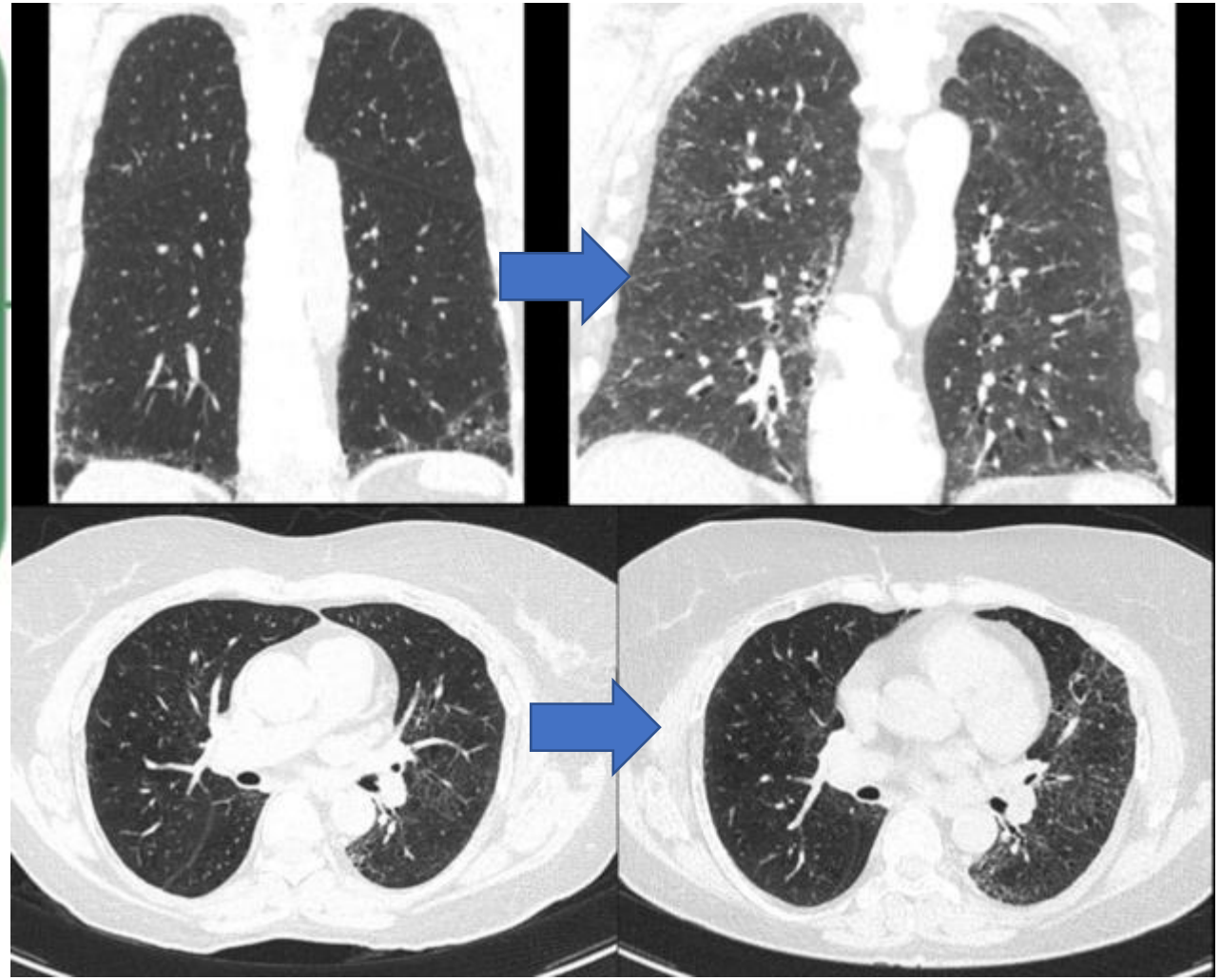
B. New ground-glass opacity with traction bronchiectasis

C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

E. New or increased honeycombing

F. Increased lobar volume loss



Radiologic evidence of disease progression (3)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

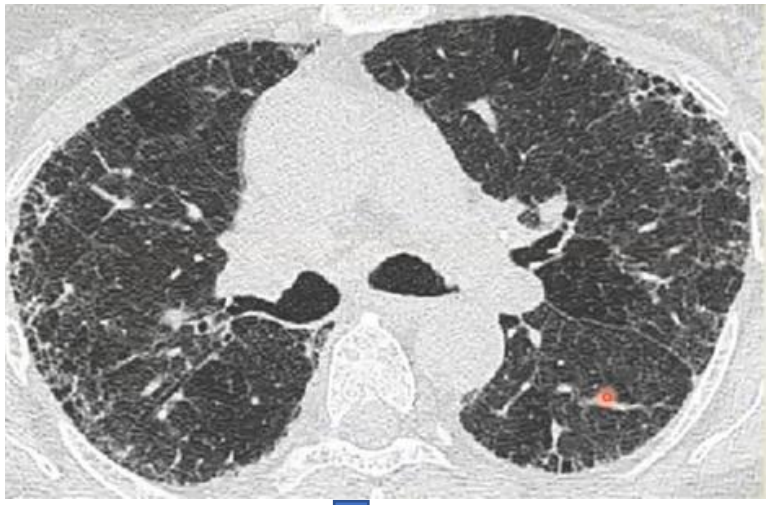
B. New ground-glass opacity with traction bronchiectasis

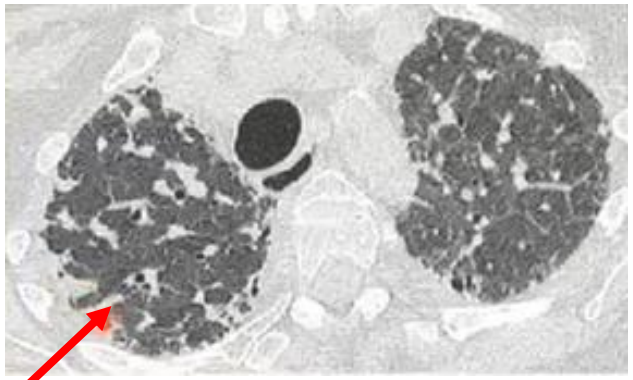
C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

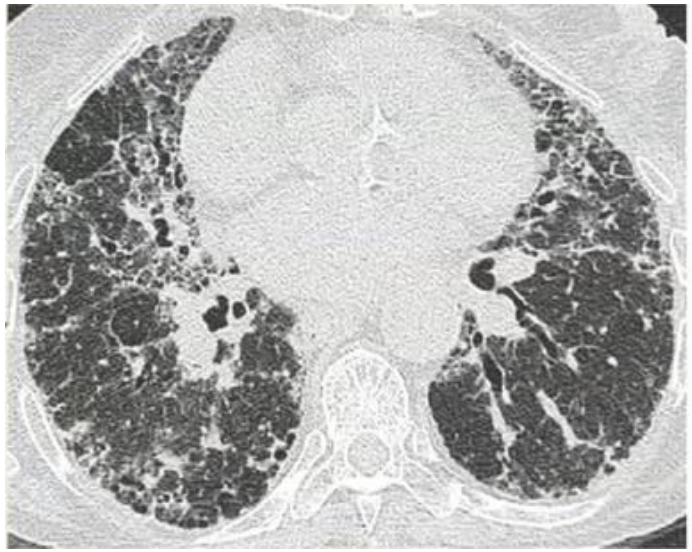
E. New or increased honeycombing

F. Increased lobar volume loss





PPFE



Radiologic evidence of disease progression (5)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

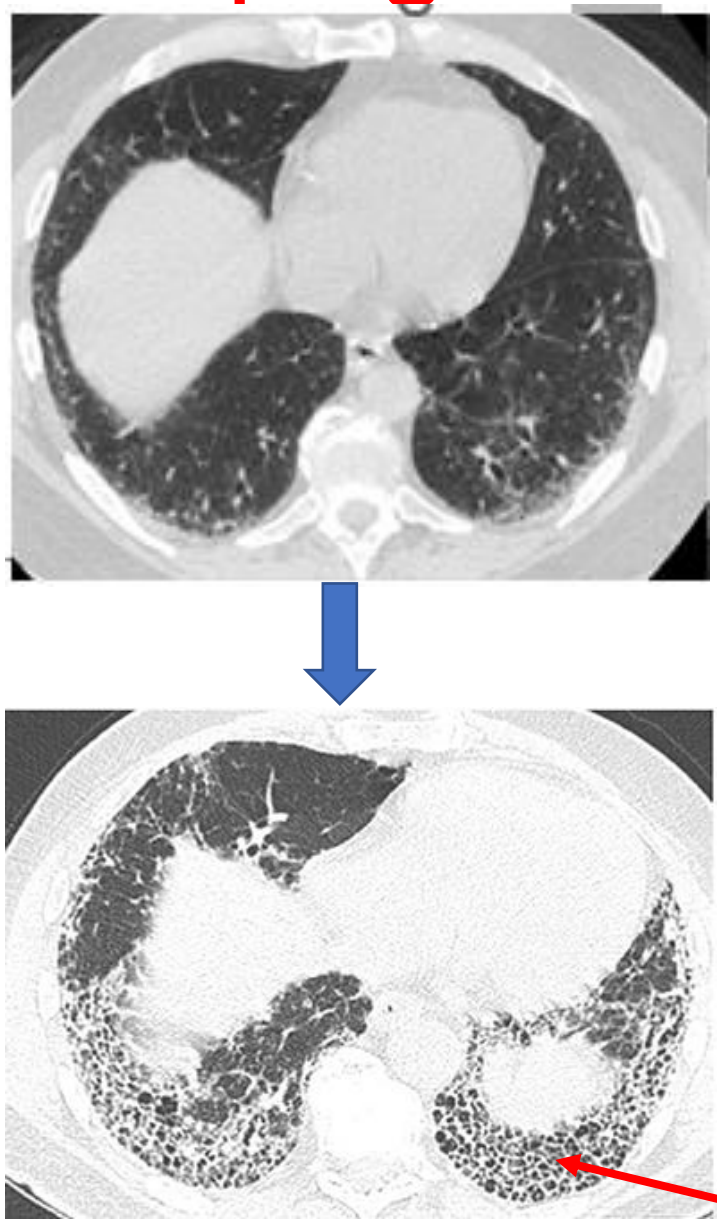
B. New ground-glass opacity with traction bronchiectasis

C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

E. New or increased honeycombing

F. Increased lobar volume loss



Radiologic evidence of disease progression (6)

One or more of:

A. Increased extent or severity of traction bronchiectasis and bronchiolectasis

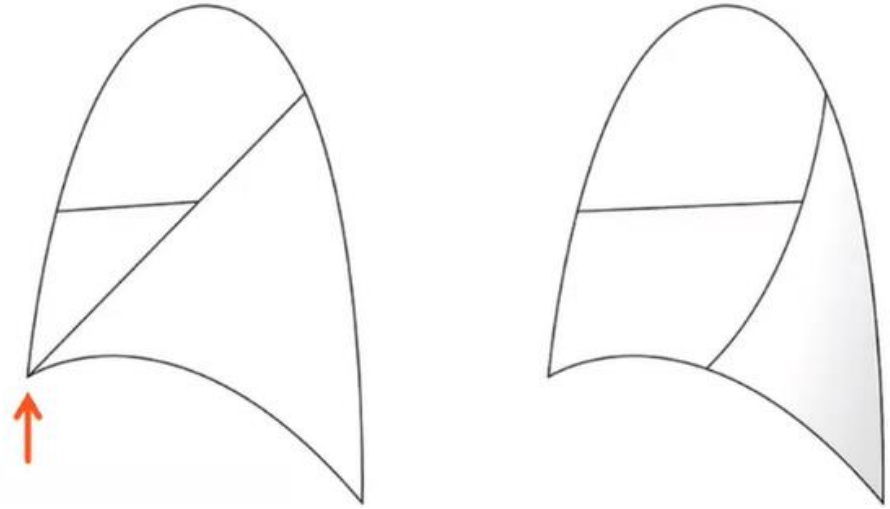
B. New ground-glass opacity with traction bronchiectasis

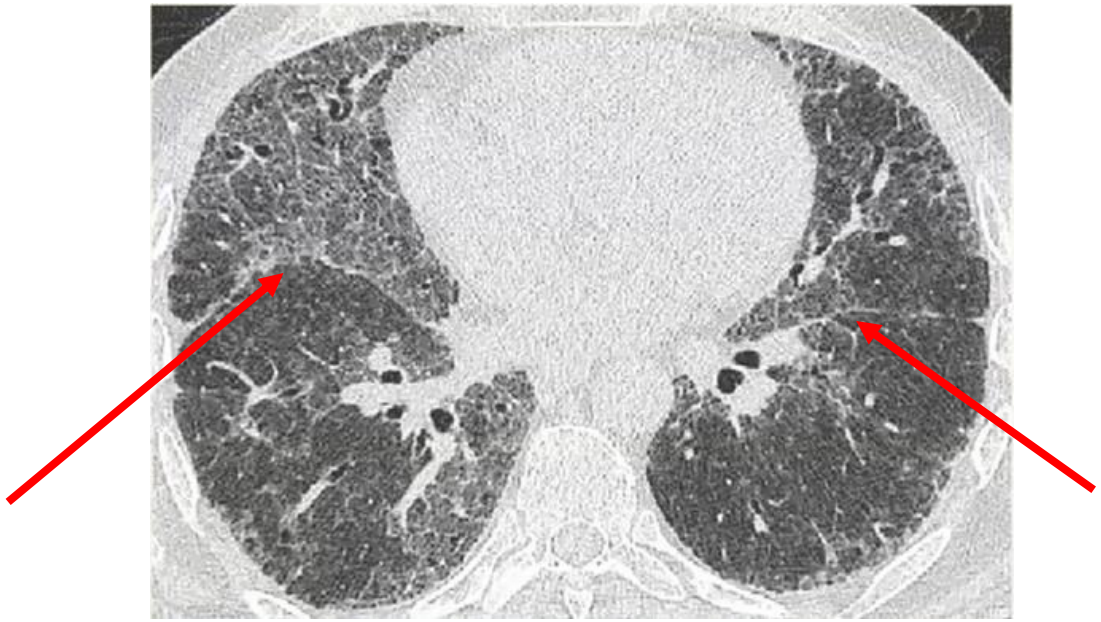
C. New fine reticulation

D. Increased extent or increased coarseness of reticular abnormality

E. New or increased honeycombing

F. Increased lobar volume loss





Progressive Pulmonary Fibrosis

- Context on agreed criteria for disease progression:

Absolute decline in FVC of ≥5% within 1 year of follow-up

The guideline committee chose an absolute decline in FVC of ≥5% over 1 year as a criterion for disease progression, a value that was extrapolated from the IPF literature

Absolute decline in DL_{CO} of ≥10% within 1 year of follow-up

Change in DL_{CO} (corrected for Hb) is a consistent and strong predictor of mortality in patients with a variety of fibrotic lung diseases

Radiological evidence of disease progression

CT is routinely used to follow progression of pulmonary fibrosis. However, criteria for assessment may vary in individual diseases and need to be carefully evaluated

- Worsening respiratory symptoms and decline in DL_{CO} are considered to have lower specificity for PPF compared with FVC and chest CT
- Criteria based on walk distance, acute exacerbations, hospitalizations, pulmonary hypertension, and quality of life were rejected as they were considered too highly variable or may be altered by the clinical context

Progressive Pulmonary Fibrosis (PPF): Criteria

- Criteria for PPF is consistent with the PF-ILD criteria for progression defined in INBUILD trial;

INBUILD® criteria[1]

Meeting **≥1 measure of progression 24 months before screening**, despite management:

- Relative decline in FVC ≥10% predicted
- Relative decline in FVC ≥5–<10% predicted and worsening respiratory symptoms
- Relative decline in FVC ≥5–<10% predicted and increased extent of fibrosis on HRCT
- Worsening of respiratory symptoms and increased extent of fibrosis on HRCT

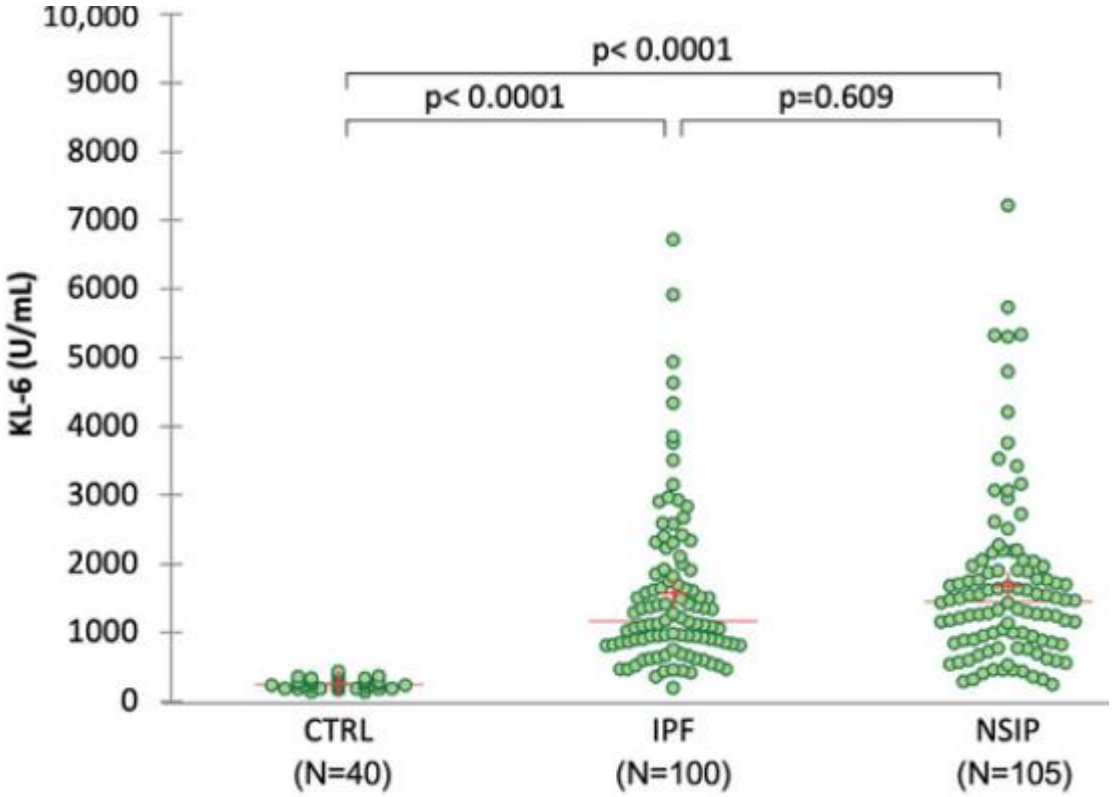
PPF guideline criteria[2]

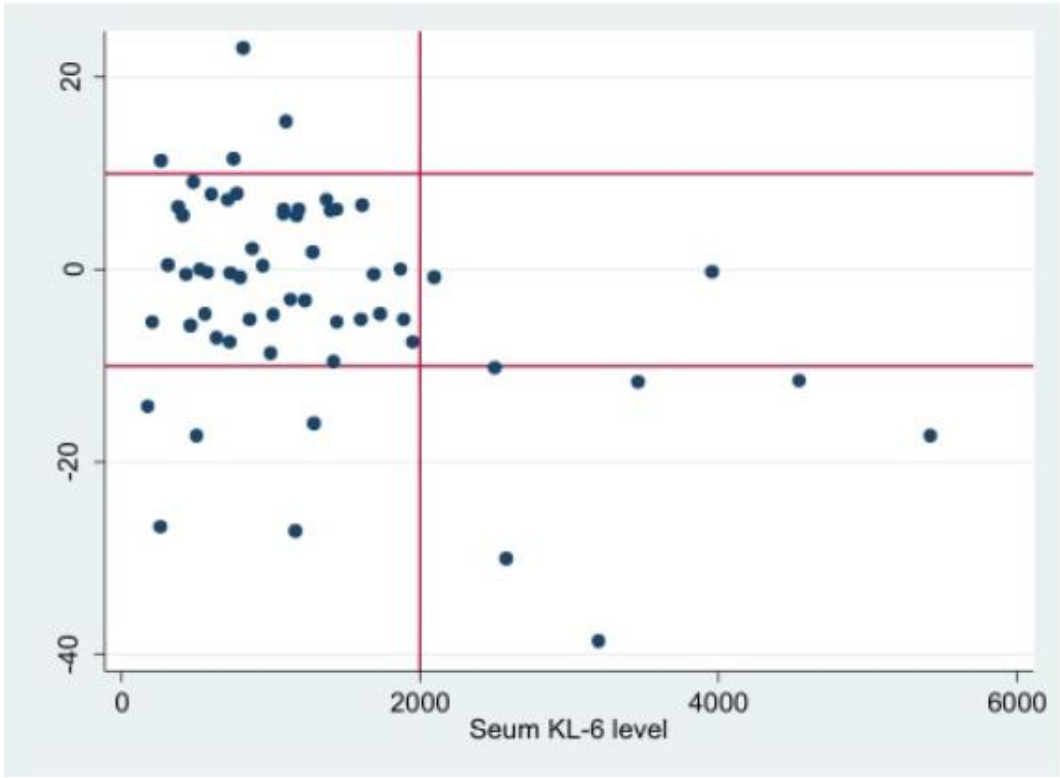
Clinical, physiological and radiological criteria to identify PPF (**≥2 of the following occurring within the past year**, with no alternative explanation):

- ★ Worsening respiratory symptoms
- ★ Physiological evidence of disease progression
  - Absolute FVC decline ≥5% predicted within 1 year of follow-up
  - Absolute DL_{CO} decline ≥10% predicted within 1 year of follow-up
- ★ Radiological evidence of disease progression

Biomarkers for Progressive Pulmonary Fibrosis?

KL-6 marker of epithelial damage





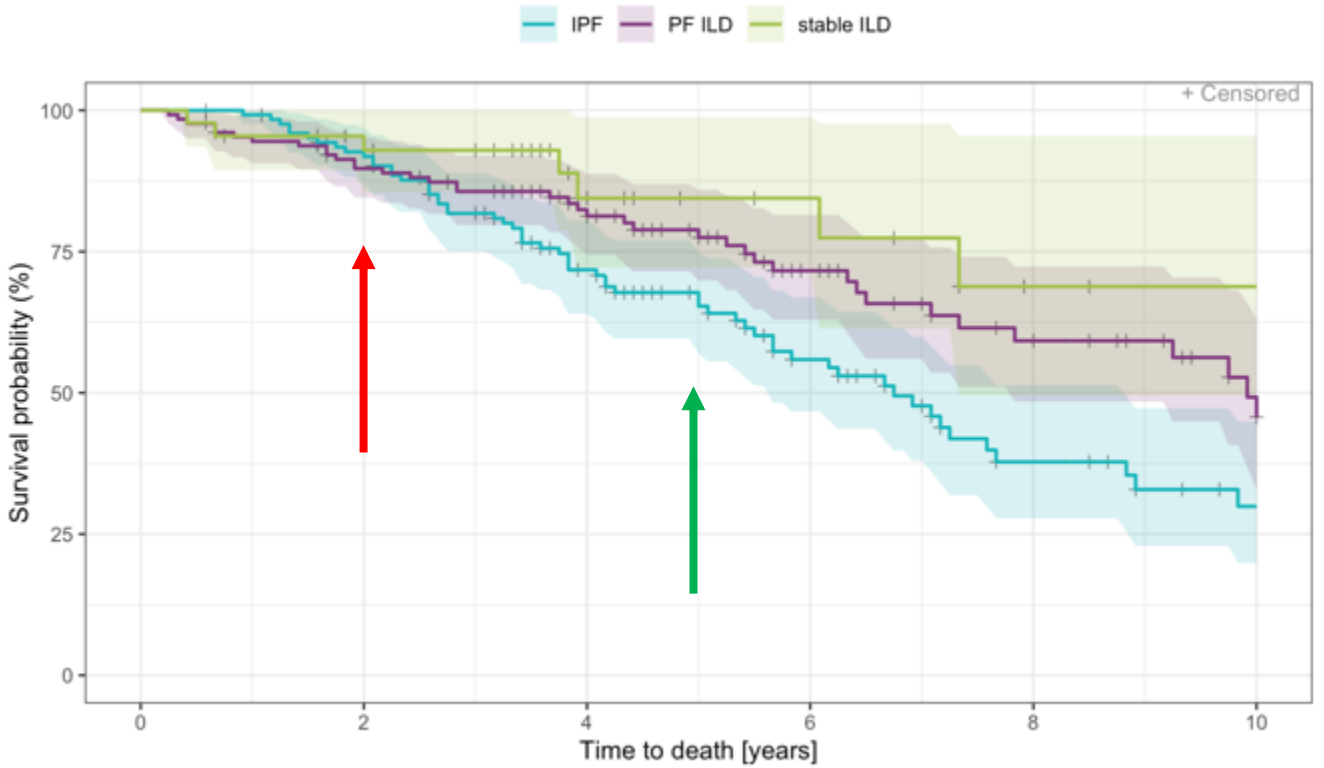
Cutoff ≥ 425 U/mL: excellent Se & Sp ILDs
Billi 2018

Cutoff ≥2000 U/ml : Progressive pulmonary fibrosis
Kokosi 2020

Progressive Pulmonary Fibrosis: Outcome

	Probability of survival [95% CI] at:	
	Year 2	Year 5
IPF	91.8 [87.1; 96.8]	64.4 [55.9; 74.1]
PF ILD	89.7 [84.6; 95.2]	75.7 [67.9; 84.4]
stable ILD	92.9 [85.5; 100]	84.5 [72.2; 98.8]

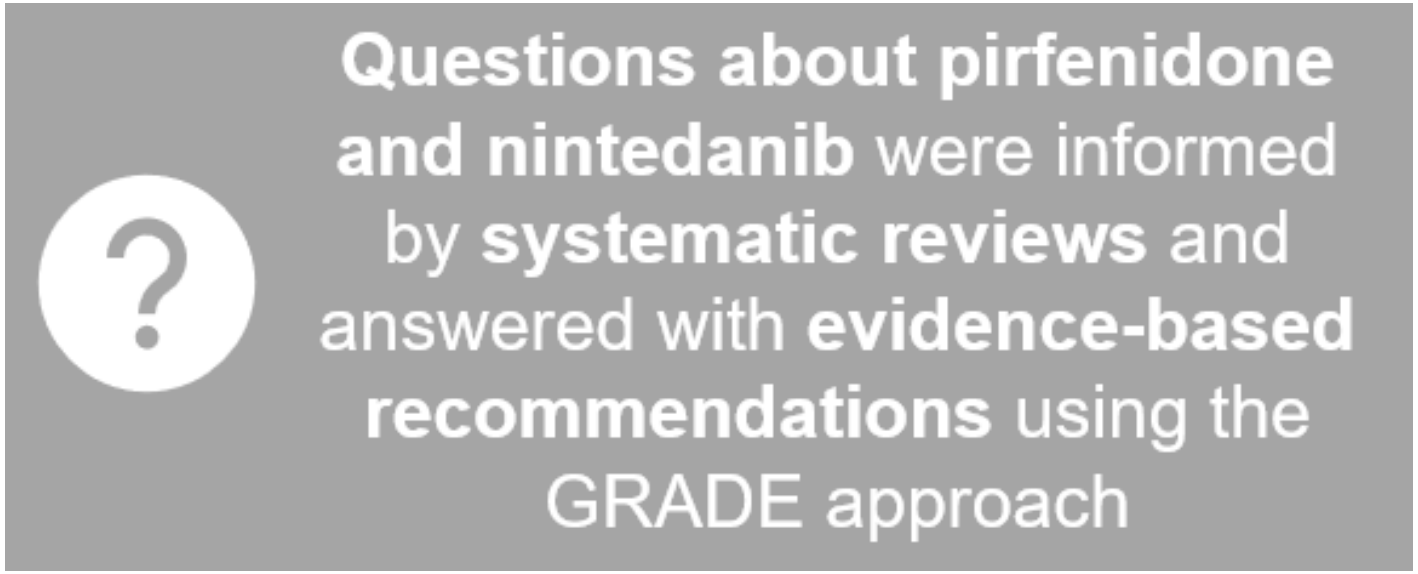
N=601



	HR [95% CI]	p value (Wald test)
PF ILD vs. IPF	0.64 [0.44, 0.93]	0.021
stable ILD vs. IPF	0.28 [0.13, 0.62]	0.002
Overall p-value (Log-rank test): 0.001		

EXCITING ILD registry in Germany

Progressive Pulmonary Fibrosis: Treatment



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

K.R. Flaherty, A.U. Wells, V. Cottin, A. Devaraj, S.L.F. Walsh, Y. Inoue, L. Richeldi, M. Kolb, K. Tetzlaff, S. Stowasser, C. Coeck, E. Clerisme-Beaty, B. Rosenstock, M. Quaresma, T. Haeufel, R.-G. Goeldner, R. Schlenker-Herceg, and K.K. Brown, for the INBUILD Trial Investigators*

- RCT phase III trial
- Efficacy and safety of nintedanib PPF (other than IPF).
- N=663 patients
- 153 sites in 15 countries
- CTD-ILD, HP, Sarcoidosis, Others ILD

- Primary endpoint:

Annual rate of decline in FVC (52-week)

Characteristic	Nintedanib (N=332)	Placebo (N=331)
Male sex — no. (%)	179 (53.9)	177 (53.5)
Age — yr	65.2±9.7	66.3±9.8
Former or current smoker — no. (%)	169 (50.9)	169 (51.1)
UIP-like fibrotic pattern on high-resolution CT — no. (%)	206 (62.0)	206 (62.2)
Criteria for disease progression in previous 24 mo — no. (%)		
Relative decline in FVC of ≥10% of predicted value	160 (48.2)	172 (52.0)
Relative decline in FVC of 5% to <10% of predicted value plus worsening of respiratory symptoms or increased extent of fibrosis on high-resolution CT	110 (33.1)	97 (29.3)
Worsening of respiratory symptoms and increased extent of fibrosis on high-resolution CT	62 (18.7)	61 (18.4)
FVC		
Mean value — ml	2340±740	2321±728
Percent of predicted value	68.7±16.0	69.3±15.2
Diffusing capacity for carbon monoxide†		
Mean value — mmol/min/kPa	3.5±1.2	3.7±1.3
Percent of predicted value	44.4±11.9	47.9±15.0
Total score on K-BILD questionnaire‡	52.5±11.0	52.3±9.8

N Engl J Med 2019

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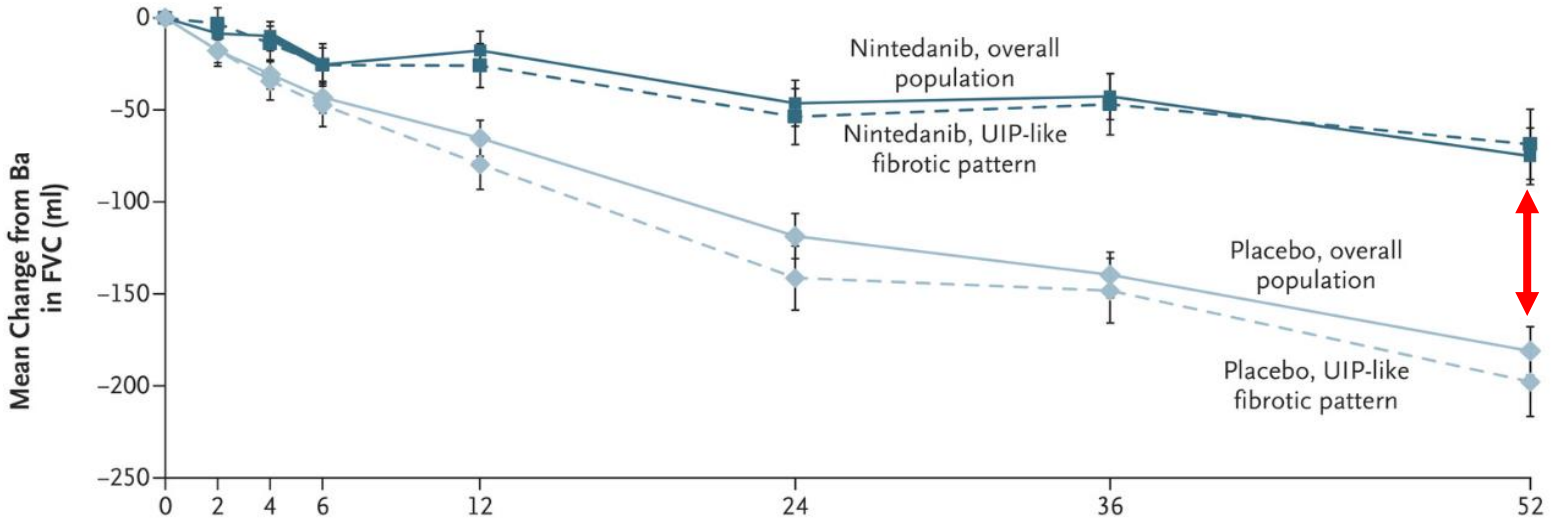

End Point	Nintedanib (N=332)	Placebo (N=331)	Difference (95% CI)
Primary end point			
Rate of decline in the FVC at 52 wk — ml/yr†			
Overall population	−80.8±15.1	−187.8±14.8	107.0 (65.4 to 148.5)‡
Patients with a UIP-like fibrotic pattern	−82.9±20.8	−211.1±20.5	128.2 (70.8 to 185.6)‡
Patients with other fibrotic patterns	−79.0±21.6	−154.2±21.2	75.3 (15.5 to 135.0)§

~ INPULSIS with IPF:
Overall between-group : 107.0 ml
UIP-like fibrotic pattern : 128.2 ml

Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial

Toby M Maher, Tamera J Corte, Aryeh Fischer, Michael Kreuter, David J Lederer, Maria Molina-Molina, Judit Axmann, Klaus-Uwe Kirchgaessler, Katerina Samara, Frank Gilberg, Vincent Cottin

- Phase 2 trial
- Efficacy and safety of pirfenidone

  with progressive fibrosing unclassifiable ILD
- N= 253 patients were randomly assigned

- <u>Primary outcome:</u>

Mean predicted change in FVC from baseline over 24 weeks (home spirometry)

	Pirfenidone (n=127)	Placebo (n=126)
Age at screening, years	70·0 (61·0–76·0)	69·0 (63·0–74·0)
Sex		
Men	70 (55%)	69 (55%)
Women	57 (45%)	57 (45%)
Race		
White	120 (94%)	123 (98%)
Black	1 (1%)	2 (2%)
Asian	5 (4%)	0
Native American or Alaskan Native	1 (1%)	0
Other	0	1 (1%)
Body-mass index, kg/m²	28·6 (26·5–32·9)	29·3 (26·2–32·7)
Previous surgical lung biopsy	40 (31%)	48 (38%)
Percent predicted FVC	71·0% (59·0–87·3)	71·5% (58·0–88·0)
Percent predicted DLco	44·6% (36·9–53·5)	48·0% (38·4–59·0)
Percent predicted FEV_1	75·0% (62·0–88·0)	76·0% (62·0–92·7)
FEV_1/FVC ratio	0·82 (0·78–0·86)	0·84 (0·78–0·87)
6MWD, m	372·0 (303·0–487·0)	395·0 (325·0–472·0)
Concomitant treatment with mycophenolate mofetil	23 (18%)	22 (17%)
IPAF diagnosis	15 (12%)	18 (14%)
Concomitant treatment with mycophenolate mofetil	6 (5%)	6 (5%)
Unclassifiable ILD diagnosis		
Low-confidence rheumatoid arthritis-ILD	0	0
Low-confidence systemic sclerosis-ILD	0	1 (1%)
Low-confidence undifferentiated connective tissue disease-ILD	3 (2%)	2 (2%)
Low-confidence chronic hypersensitivity pneumonitis-ILD	10 (8%)	9 (7%)
Low-confidence idiopathic non-specific interstitial pneumonia-ILD	4 (3%)	3 (2%)
Low-confidence sarcoidosis-ILD	0	0
Low-confidence myositis-ILD	0	0
Low-confidence other defined ILD	1 (1%)	0
Unclassifiable ILD	93 (73%)	93 (74%)

Lancet Respir Med 2019

Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial

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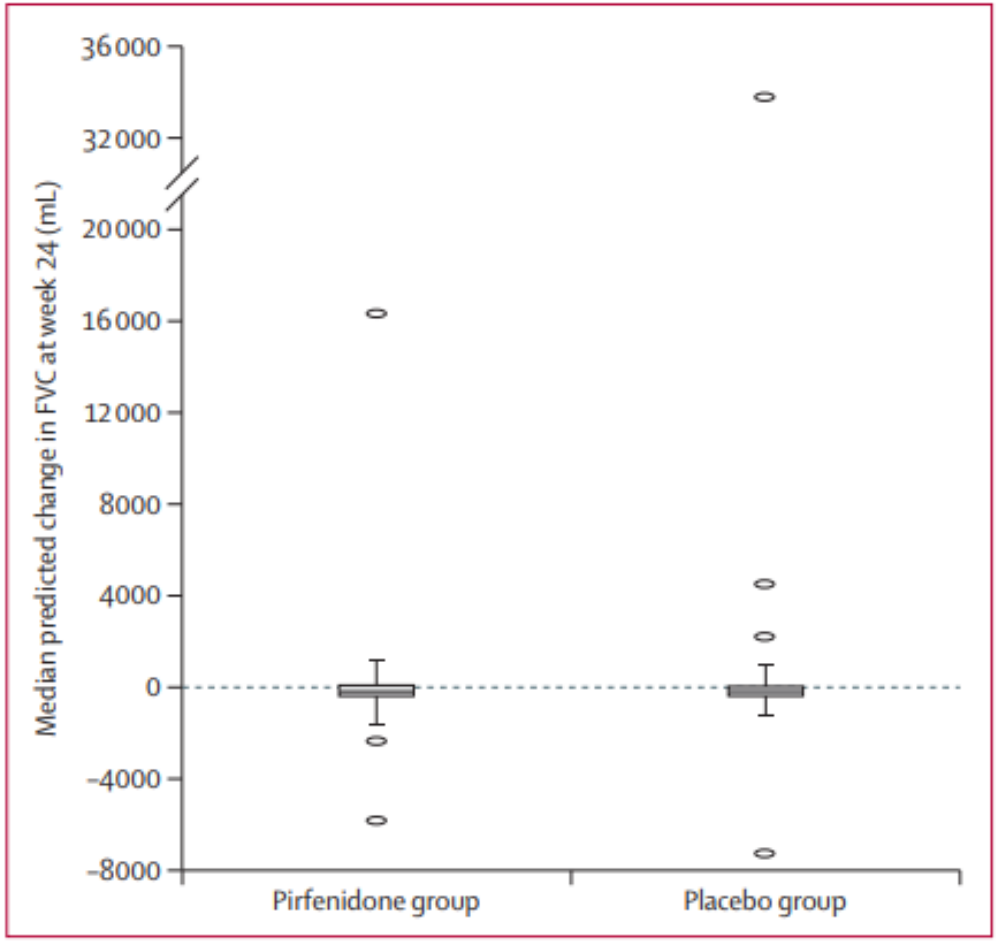
Results

Median change in FVC from baseline was:
–87·7 mL (Q1–Q3 –338·1 to 148·6) in pirfenidone group
–157·1 mL (Q1–Q3 –370·9 to 70·1) in placebo group
(p 0.002)

Analysis of the primary endpoint was affected by intraindividual variability in home spirometry values



Lancet Respir Med 2019

Pirfenidone in patients with progressive fibrotic interstitial lung diseases other than idiopathic pulmonary fibrosis (RELIEF): a double-blind, randomised, placebo-controlled, phase 2b trial

*Jürgen Behr, Antje Prasse, Michael Kreuter, Johannes Johow, Klaus F Rabe, Francesco Bonella, Reiner Bonnet, Christian Grohe, Matthias Held, Heinrike Wilkens, Peter Hammerl, Dirk Koschel, Stefan Blaas, Hubert Wirtz, Joachim H Ficker, Wolfgang Neumeister, Nicolas Schönfeld, Martin Claussen, Nikolaus Kneidinger, Marion Frankenberger, Simone Hummler, Nicolas Kahn, Silke Tello, Julia Freise, Tobias Welte, Petra Neuser, Andreas Günther, on behalf of the RELIEF investigators**

- Phase 2b trial
- Efficacy and safety of pirfenidone

in patients with 4 non-IPF progressive fibrotic ILD

- N=127 patients

- Primary endpoint:

Absolute change in FVC % predicted at to week 48

	Pirfenidone (n=64)	Placebo (n=63)
Age, years	63·2 (10·6)	63·5 (9·1)
Sex		
Men	43 (67%)	32 (51%)
Women	21 (33%)	31 (49%)
Supplemental O_2 at rest	14 (22%)	20 (32%)
Flow rate at rest, L/min	2·2 (0·9)*	2·3 (0·8)†
FVC, % predicted	62·6 (14·5)	62·2 (13·5)
FEV_1, % predicted	68·1 (15·4)	64·4 (14·3)
DLCO, % predicted	38·1 (14·1)	37·7 (14·2)
FEV_1/FVC ratio	86·7 (6·9)	83·8 (7·7)
6MWD, m	357·7 (99·2)	345·2 (110·0)
Any steroid or immunosuppressant therapy	47 (73%)	56 (89%)
Steroid monotherapy	17 (27%)	31 (49%)
Combination therapy with steroids	23 (36%)	22 (35%)
Azathioprine	11 (17%)	11 (18%)
Mycophenolate	7 (11%)	6 (10%)

Lancet Respir Med 2021

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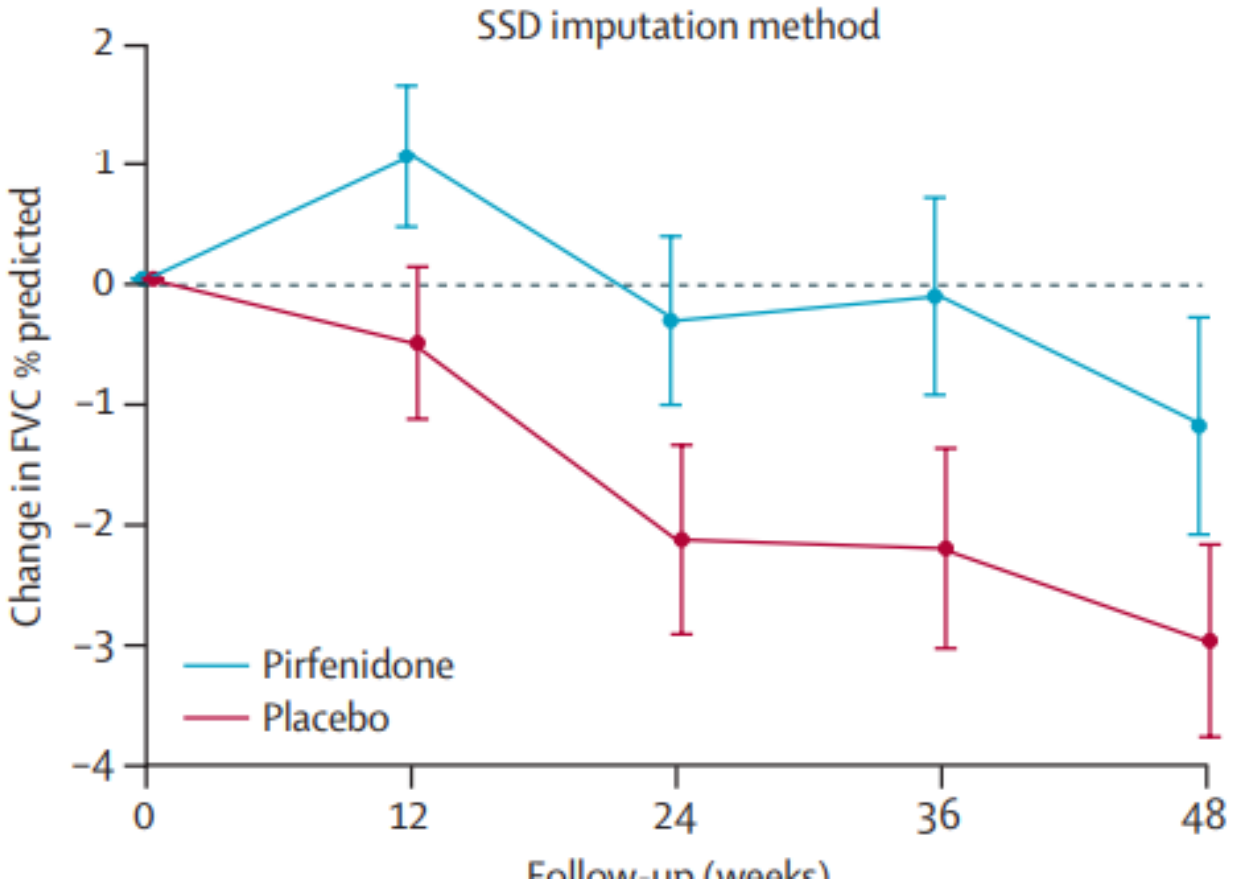
*Jürgen Behr, Antje Prasse, Michael Kreuter, Johannes Johow, Klaus F Rabe, Francesco Bonella, Reiner Bonnet, Christian Grohe, Matthias Held, Heinrike Wilkens, Peter Hammerl, Dirk Koschel, Stefan Blaas, Hubert Wirtz, Joachim H Ficker, Wolfgang Neumeister, Nicolas Schönfeld, Martin Claussen, Nikolaus Kneidinger, Marion Frankenberger, Simone Hummler, Nicolas Kahn, Silke Tello, Julia Freise, Tobias Welte, Petra Neuser, Andreas Günther, on behalf of the RELIEF investigators**

Results

median difference for the primary endpoint was:

1·69 FVC % predicted (95% CI –0·65 to 4·03)



Lancet Respir Med 2021

Recommendations for the treatment of PPF (other than IPF) are based on evidence from randomized clinical trials of nintedanib and pirfenidone

	Nintedanib[1–3]	Pirfenidone[1,4,5]
Studies informing recommendations	• **INBUILD®** 663 patients with PPF randomized to receive nintedanib or placebo for 52 weeks • ***Post hoc* analysis of INBUILD® data** Comparing the effects of nintedanib with placebo in individual ILDs manifesting PPF	• **uILD trial** 253 patients with fibrotic uILD randomized to receive pirfenidone or placebo for 24 weeks • **RELIEF** 127 patients with PPF randomized to receive pirfenidone or placebo for 48 weeks*
Critical outcomes[†‡]	• Mortality • Disease progression (determined by change in FVC)	• Mortality • Disease progression (determined by change in FVC)
Important outcomes[†]	• Respiratory symptoms (determined by changes in the K-BILD questionnaire) • AEs	• Lung function (determined by changes in FEV_1, TLC, DL_{CO} and 6MWD) • Respiratory symptoms (determined by change in SGRQ, LCQ, UCSD-SOBQ or VAS for cough scores) • AEs

*Trial terminated early because of futility triggered by slow recruitment; [†]Outcomes were defined as critical and important based on the opinions of the guideline committee. These definitions do not necessarily align with the primary and secondary endpoints in the studies; [‡]Critical outcomes determine the rating of the quality of evidence

1. Raghu G *et al. Am J Respir Crit Care Med* 2022;205:e18–47; 2. Flaherty KR *et al. N Engl J Med* 2019;381:1718–27; 3. Wells AU *et al. Lancet Respir Med* 2020;8:453–60; 4. Maher TM *et al. Lancet Respir Med* 2020;8:147–57; 5. Behr J *et al. Lancet Respir Med* 2021;9:476–86

The guideline gives a conditional recommendation for nintedanib as a treatment for PPF and suggests additional research into pirfenidone

Nintedanib

We suggest nintedanib for the treatment of PPF in patients who have failed standard management for fibrotic ILD, other than IPF

(conditional recommendation, low-quality evidence)

Pirfenidone

We recommend further research into the efficacy, effectiveness, and safety of pirfenidone in both: 1) non-IPF ILD manifesting PPF in general, and 2) specific types of non-IPF ILD manifesting PPF

Standard management will differ from patient to patient and could be:

- Immunosuppressive treatment in an attempt to stabilize or reverse initial disease
- Antigen remediation
- **Observation**

It should also be acknowledged that in many ILDs, evidence-based guidance for standard of care is lacking; hence, standard of care may vary from region to region

Raghu G *et al. Am J Respir Crit Care Med* 2022;205:e18–47

Over 90% of the guideline committee was in favor of recommending nintedanib for the treatment of PPF

Nintedanib

We suggest nintedanib for the treatment of PPF in patients who have failed standard management for fibrotic ILD, other than IPF

(conditional recommendation, low-quality evidence)

Guideline committee voting

- **Strong recommendation for nintedanib, 10 of 34 (29%); conditional recommendation for nintedanib, 21 of 34 (62%)**
- Conditional recommendation against nintedanib, 0 of 34 (0%); and strong recommendation against nintedanib, 0 of 34 (0%)
- **3 participants (9%) abstained from voting**, 1 citing insufficient evidence to make a recommendation and 2 citing insufficient expertise to render a thoughtful judgment

Pirfenidone

We recommend further research into the efficacy, effectiveness, and safety of pirfenidone in both: 1) non-IPF ILD manifesting PPF in general, and 2) specific types of non-IPF ILD manifesting PPF

Guideline committee voting

- **Strong recommendation for pirfenidone, 0 of 34 (0%); conditional recommendation for pirfenidone, 21 of 34 (62%)**
- Conditional recommendation against pirfenidone, 0 of 34 (0%); and strong recommendation against pirfenidone, 0 of 34 (0%)
- **13 participants (38%) abstained from voting**, 11 citing insufficient evidence to make a recommendation and 2 citing insufficient expertise to render a thoughtful judgment

Raghu G *et al. Am J Respir Crit Care Med* 2022;205:e18–47

The ATS/ERS/JRS/ALAT clinical practice guideline provides evidence-based recommendations for the treatment of PPF (other than IPF)

Nintedanib: recommended for the treatment of patients with PPF

Pirfenidone: not enough evidence to recommend use in PPF

- No other drug is recommended for the treatment of patients with PPF
- A recommendation for further clinical studies is given

Raghu G *et al. Am J Respir Crit Care Med* 2022;205:e18–47

Progressive Pulmonary Fibrosis (PPF) guideline Summary

- The guideline adopted the new term "PPF" instead of PF-ILD
- Acknowledges that PPF occurs in multiple ILDs
- Provides clarity on defining progression and that PPF is not a diagnosis
- PPF criteria overlap but are not identical to the INBUILD trial criteria
- Nintedanib is recommended for the treatment of patients with PPF who have failed standard management
- Further research into pirfenidone is suggested