PROGRESSIVE FIBROSING INTERSTITIAL LUNG DISEASES

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Foreword from guest editor, Jesse Roman, MD, Jane and Leonard Korman Respiratory Institute, Thomas Jefferson University, Philadelphia, PA, USA.

Interstitial lung disease (ILD) afflicts millions of patients globally. The sheer number of ILDs, the varied nature of their presentation and progression, and the fact that many ILDs are idiopathic, make this a fascinating but challenging group of clinical disorders. This is further complicated by the fact that a confident diagnosis often requires careful consideration of clinical presentation, imaging studies, and when available, histology, by a multidisciplinary team of experts.

Insights gained over the past two decades about idiopathic pulmonary fibrosis (IPF) and other ILDs have greatly advanced our understanding of these conditions and have helped facilitate earlier diagnosis and intervention and improvements to patient care. Recently, the concept of progressive fibrosing ILD has emerged, as many patients with fibrosing ILDs show rapid deterioration similar to IPF, thereby requiring close monitoring. This publication explores fibrosing ILDs, in recognition of the need for further education about these conditions.

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What are progressive fibrosing ILDs?

Kevin R. Flaherty, MD
Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, USA.

Interstitial lung diseases (ILDs) are a heterogeneous group of diseases characterized by inflammation and/or fibrosis (scarring) of the lung parenchyma.

Some ILDs have a known cause, such as those related to connective tissue diseases (CTDs) or to exposure to organic or inorganic material that leads to an exaggerated immune response. Other ILDs have no identifiable cause (idiopathic).

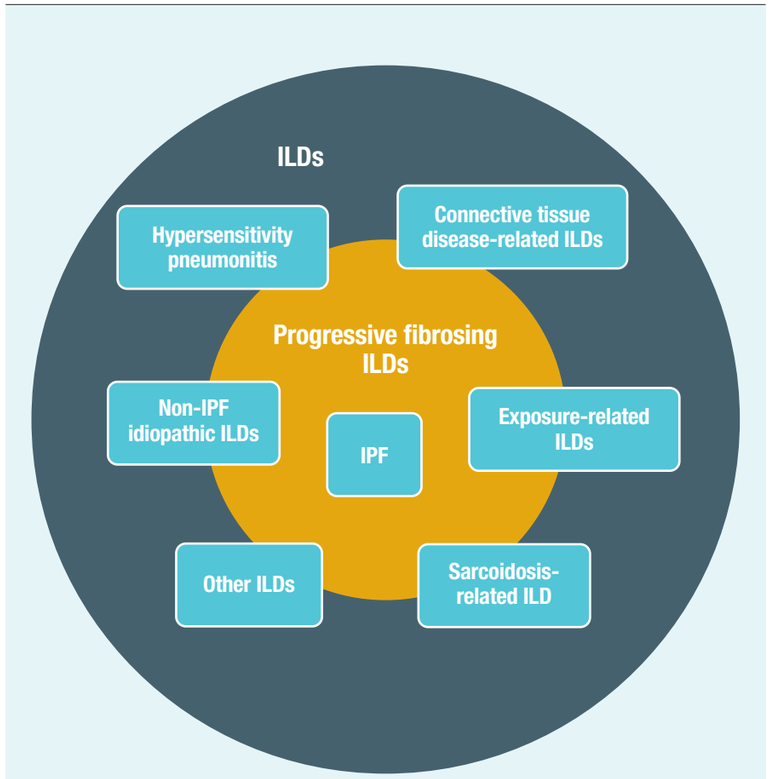
Some patients with ILD develop fibrosing disease. Pulmonary fibrosis may become self-sustaining and progressive. This results in the progressive loss of lung volume (forced vital capacity or FVC) and of the ability of the lungs to exchange oxygen with the blood (diffusion capacity or DLco). Patients with ILDs typically develop dyspnea, cough and fatigue. Ultimately progressive ILD is fatal.

Idiopathic pulmonary fibrosis (IPF) is, by definition, a progressive fibrosing ILD. In addition, a proportion of patients with other fibrosing ILDs develop a progressive phenotype. Although some studies have identified risk factors for worse outcomes in patients with ILDs, the course of disease for an individual patient remains difficult to predict.

Important!

Irrespective of the etiology for the ILD, once ILD has become fibrosing and progressive, it confers a poor prognosis.

ILDs that may develop a progressive fibrosing phenotype



Impact of progressive fibrosing ILDs

DLco, diffusion capacity of the lung for carbon monoxide.

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IPF: the prototypic progressive fibrosing ILD

Joao A. de Andrade, MD
Vanderbilt University School of Medicine, Nashville, TN, USA.

Idiopathic pulmonary fibrosis (IPF) may be described as the "prototypic" progressive fibrosing ILD because it is always fibrosing and always progressive.

IPF is the most well-studied of the ILDs and has provided important learnings about the pathogenesis, course and treatment of progressive fibrosing ILDs.

IPF is characterized by a pattern of fibrosis on HRCT or biopsy known as usual interstitial pneumonia (UIP). Patients with other fibrosing ILDs may also have a UIP pattern on HRCT or biopsy. In general, IPF has a worse prognosis than other fibrosing ILDs, but there are some patients with other progressive fibrosing ILDs whose lung function deteriorates as quickly as is seen in IPF.

Acute deteriorations in lung function, known as acute exacerbations, occur in a proportion of patients with IPF. These usually require hospitalization and are associated with very high mortality. Patients with other fibrosing ILDs may also experience acute exacerbations.

Two antifibrotic drugs have been approved by the FDA for the treatment of IPF: nintedanib and pirfenidone. These reduce the rate of decline in FVC by approximately 50% and there is increasing evidence that they improve life expectancy. Importantly, the INPULSIS trials of nintedanib showed that patients with well-preserved FVC (FVC > 90% predicted) at baseline had the same decline in FVC over the next year, and received the same benefit from treatment, as patients with more advanced disease at baseline, demonstrating that patients whose IPF appears stable are still at risk of progression in the short term.

Important!

Given the progressive nature of IPF and its poor prognosis, all patients with IPF should be considered for antifibrotic treatment at diagnosis.

FDA, Food and Drug Administration; HRCT, high-resolution computed tomography.

Decline in FVC in patients with IPF with baseline FVC >90% and ≤90% predicted in the placebo group of the INPULSIS trials

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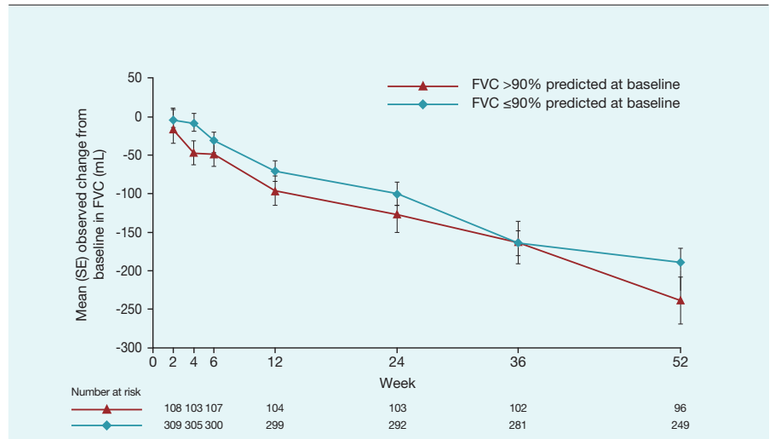
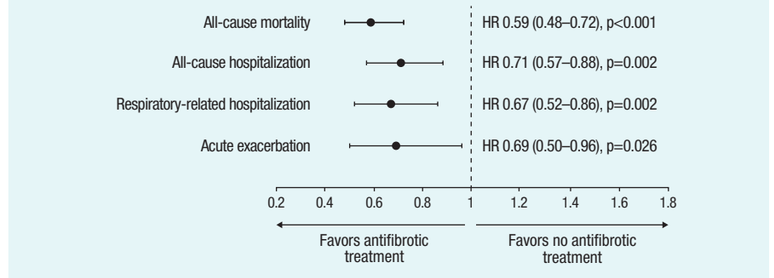


Risk of outcomes in patients who did and did not receive antifibrotic therapy in a propensity score-matched analysis of 1213 patients with IPF

Adapted with permission from: Kang J et al. Antifibrotic treatment improves clinical outcomes in patients with idiopathic pulmonary fibrosis: a propensity score matching analysis. Sci Rep 2020;10:15620.



Data shown are hazard ratio (95% confidence interval) calculated based on univariable Cox proportional hazard models.

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The IPF-PRO Registry: improving our understanding of IPF

Laurie D. Snyder, MD and Scott M. Palmer, MD
Duke Clinical Research Institute and Duke University Medical Center, Durham, NC, USA.

The IPF-PRO Registry (NCT01915511) is an observational registry that enrolled 1002 patients with IPF at 46 sites across the US between June 2014 and October 2018.

The registry is supported by Boehringer Ingelheim Pharmaceuticals, Inc, and co-ordinated by the Duke Clinical Research Institute. It was set up to improve understanding of the natural history of IPF, its diagnosis and treatment, and the burden that IPF places on patients and healthcare resources. In addition, the collection of biological samples has enabled important research into circulating molecules that may serve as biomarkers for the presence, severity, or progression of IPF.

Patients enrolled in the registry are followed prospectively while receiving usual care, with follow-up visits approximately every six months. Data collected include pulmonary function tests, patient-reported outcomes, and treatments. Regular follow-up from a call center helps to reduce missing data on patients' vital status and interactions with the healthcare system.

Some of the key learnings from the IPF-PRO Registry so far are depicted in this article. Future analyses will include investigations into trajectories of decline in lung function, hospitalizations and post-hospitalization mortality, associations between treatment practices and outcomes, and factors associated with lung transplant.

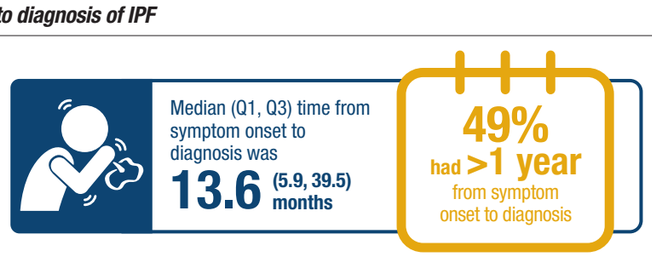
Important!

Real-world data such as those collected in the IPF-PRO Registry will help us improve our understanding of the impact of IPF on patients and healthcare resources and how we might improve the way we diagnose and treat this devastating disease.

IPF-PRO, Idiopathic Pulmonary Fibrosis-PRospective Outcomes; DLco, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity; CASA-Q, cough and sputum assessment questionnaire; SF-12, 12-item short form survey; SGRQ, St George's Respiratory Questionnaire.

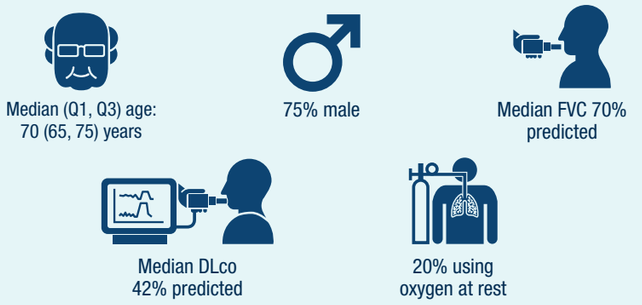
Enrolling centers

Time to diagnosis of IPF



Based on patients who received a new diagnosis of IPF at the enrolling center.

Patient characteristics at enrollment



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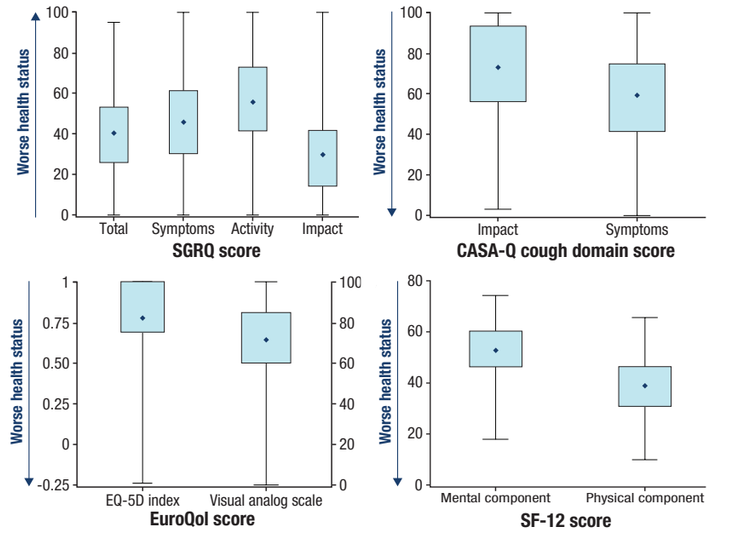
Snyder LD et al. Time to diagnosis of idiopathic pulmonary fibrosis in the IPF-PRO Registry. BMJ Open Respir Res 2020;7:e000567.
Podcast: https://www.usscicomms.com/respiratory/snyder/IPF-PROtimetodiagnosis

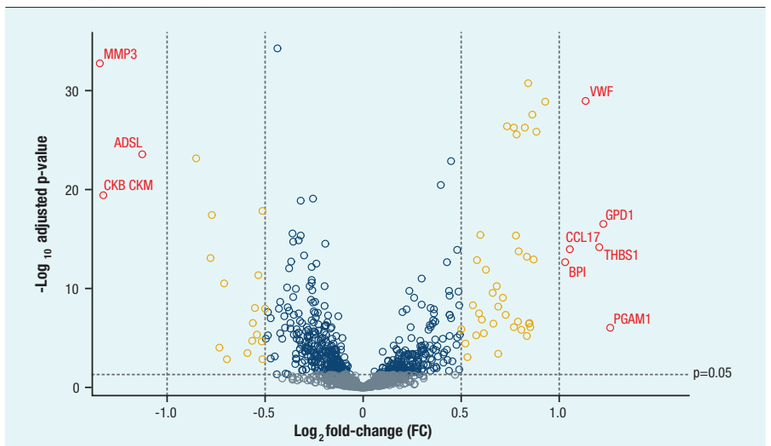
Patient-reported outcomes at enrollment

Reprinted from CHEST, 157, O'Brien EC et al., Disease severity and quality of life in patients with idiopathic pulmonary fibrosis: a cross-sectional analysis of the IPF-PRO Registry, 1188-1198, Copyright (2020), with permission from Elsevier.



The diamonds denote the mean values. The boundaries of each box show the interquartile range (Q1 to Q3) and the whiskers the minimum and maximum observed values.

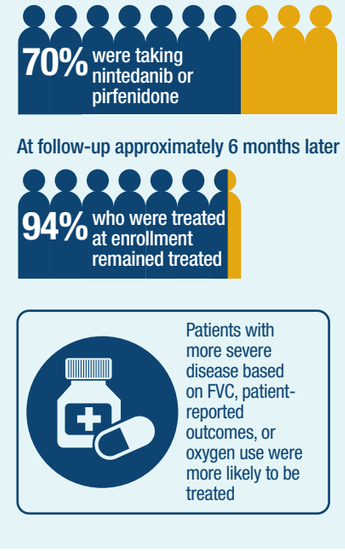
Circulating proteins in patients with IPF compared with controls



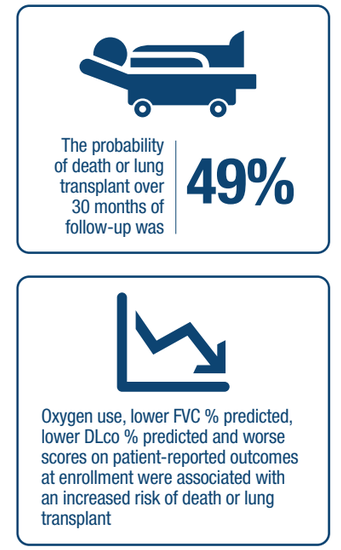
Univariate linear regression was used to compare circulating protein concentrations between patients in the IPF-PRO Registry and controls. For nine proteins, (shown in red), the p-value for the difference in mean concentration in patients with IPF versus controls was <0.05 and the $\log_2$ fold-change in concentration was >1 (i.e. the difference in concentrations was more than a doubling). P-values were corrected for multiplicity.

ADSL, adenylosuccinate lyase; BPI, bactericidal permeability-increasing protein; CCL-17, C-C motif chemokine 17; CKB CKM, creatine kinase B-type;creatine kinase M-type; GPD1, glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic; MMP3, stromelysin-1; PGAM1, phosphoglycerate mutase 1; THBS1, thrombospondin-1; VWF, von Willebrand factor.

Antifibrotic drug use



Predictors of mortality



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Breaking bad news to patients with IPF

Walter F. Baile, MD
University of Texas MD Anderson Cancer Center, Houston, TX, USA (retired).

Breaking bad news such as a diagnosis of IPF is a complex and challenging communication that is easily affected by emotions (both the patient's and the clinician's).

Clinicians may be tempted to try to reduce the patient's distress by downplaying the serious nature of the disease, deflecting difficult questions, or rushing through the conversation. This rarely works and may leave patients confused and dissatisfied.

Evidence-based models can help clinicians to improve their skills in having conversations with patients and their loved ones about topics that are difficult to talk about. The SPIKES (Setting, Perception, Invitation for information, Knowledge, Empathy, Strategy and Summary) protocol is a skills-based, patient-centered process developed to help clinicians in breaking bad news. Emphasis is given to preparing for the visit, understanding the patient's perceptions of their illness, providing accurate and understandable information, responding to the patient's emotions with empathy, and providing a plan for the future. In addition to helping clinicians to communicate a diagnosis of IPF or to discuss the prognosis of the disease, the SPIKES framework may be used to guide other discussions that require an empathetic approach, such as those around disease progression and planning for end of life. At every stage, provision of information should be individualized, taking account of how much information the patient wants to receive at that time.

The six steps of SPIKES for breaking bad news

SETTING up the interview
Consider what you want to say, arrange for privacy, involve significant others, sit down, connect with the patient, manage time constraints and avoid interruptions

Assessing the patient's PERCEPTION
Use open-ended questions to create a picture of how the patient perceives their situation, for example, "What have you been told about your medical situation so far?"

Obtaining the patient's INVITATION
Assess the patient's readiness to hear the information and determine how much information they want at this time

Giving KNOWLEDGE and information to the patient
Consider the patient's level of comprehension and vocabulary, use plain language, avoid being blunt or vague

Addressing the patient's EMOTIONS with empathic responses
If the patient becomes upset, respond with empathic, exploratory or validating statements

STRATEGY and SUMMARY
Summarize the information and check patient understanding; form a plan for the future and provide reassurance about continuity of care

Important!

Effective, empathetic communication is a skill that clinicians can learn and practice. Improving communication skills doesn't change a patient's diagnosis, but can help to lessen the impact that IPF has on the lives of patients and their loved ones.

A series of videos explaining the SPIKES protocol in detail is available at:
https://www.pulmonaryfibrosis360.com/resources

Examples of empathic, exploratory, and validating statements

Empathetic	Exploratory	Validating
"I'm sorry to have to tell you this."	"Tell me more about it."	"I can understand how you felt that way."
"I can see how upsetting this is to you."	"You said it frightened you?"	"It appears that you've thought things through very well."
"I can tell you weren't expecting to hear this."	"You said you were concerned about your family. Tell me more."	"Many other patients have had similar experiences."

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What questions do patients with IPF have?

Russell K. Amling and Bill Vick
PF Warriors

Most patients with IPF have never heard of IPF at the time they are diagnosed. Patients will have many questions about what having IPF means for their lives.

Many patients want to take a proactive approach to managing their IPF and to do this, they need to understand their disease.

Some of the questions that patients with IPF may have shortly after they are diagnosed are shown here. However, it's important that clinicians do not assume that they know the questions that a patient will have. The questions that a particular patient has may differ from those that the last patient you met had, and from those that their family has. The only way that a clinician can find out the questions that an individual patient has is to ask them.

Patients of older age may be more reluctant to ask questions of their doctor. Encourage them to bring their questions and make time to answer them. Asking patients to write their questions down can be helpful. Patients will have questions immediately on receiving a diagnosis of IPF, but many questions will come to their minds later. Clinicians need to make sure that patients know that the right time for them to ask questions is any time.

Russell: *As a patient, I was always concerned regarding my health. I have always asked my doctors questions pertaining to what, why, when and how. I am an 87-year-old veteran of the Korean War. In 1944, I acquired paralytic polio from the neck down to the bottom of my feet for five months. I needed many ear surgeries. In 2002, I had a quad bypass. In 2006-2007, I had two spinal fusions; in 2009, a knee replacement; three years ago, IPF; three months ago, Valley fever. At times, the answers that I received from my doctor were basic, but I have tried to ask more in-depth questions. I set up another 30-minute visit with the doctor about a week later just to ask these more important questions.*

- *Have I got IPF because I used to smoke or because I was exposed to asbestos or pesticides?*
- *How long do you think I've had this?*
- *How long will I live?*
- *What can I expect my life to be like now and later?*
- *Will IPF affect me mentally?*
- *What is the best treatment for IPF?*
- *How will I know if the treatment is working?*
- *What are the side effects of treatment?*
- *Is exercise good for me?*
- *Would a special diet help?*
- *Does cold weather make my condition worse?*
- *Should I have a flu shot? Or other jabs?*
- *Will I need oxygen?*
- *What about stem cell therapy?*
- *Are there any experimental programs I could try?*
- *Where can I find more information?*
- *I have other things going on with my health, does this change the timelines?*

References

Support patients with IPF by joining PF Warriors at https://pfwarriors.com or https://Facebook.com/pfwarrior.
A patient and caregiver information and resource guide "Living with PF-ILD" is provided on joining the group.

Detection, monitoring and management of ILD associated with systemic sclerosis

Anna Maria Hoffmann-Vold, MD
Department of Rheumatology, Oslo University Hospital, Oslo, Norway.

ILD is a common manifestation of systemic sclerosis (SSc) and is associated with significant morbidity and mortality. Although risk factors for the development of SSc-ILD have been identified, *all* patients with SSc should be regarded as at risk of ILD.

Expert groups have developed consensus algorithms for the detection, monitoring and management of SSc-ILD. These recommend that all patients diagnosed with SSc should receive an HRCT scan to screen for ILD and to ascertain its extent. In addition, patients should undergo PFTs (FVC and DLco) to establish baseline measurements. The severity of SSc-ILD at the time of diagnosis is prognostic of long-term outcome. Severity should be determined based on HRCT, PFTs and other parameters such as exercise-induced oxygen desaturation, symptoms, and HRQL.

Regular monitoring of patients with SSc-ILD is essential to assess progression. Progression of SSc-ILD is associated with poor outcome. Monitoring should include regular PFTs and assessment of symptoms, plus repeat HRCT as deemed appropriate by the clinician.

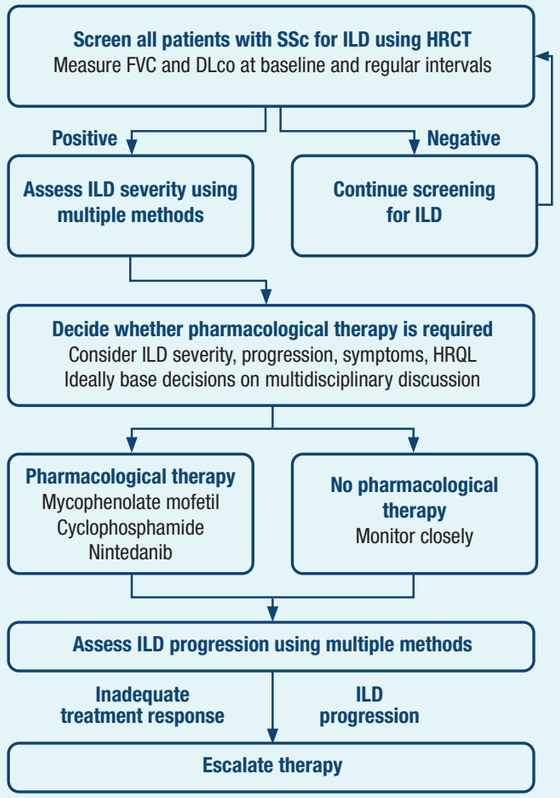
The decision on when to initiate or escalate pharmacological treatment for SSc-ILD should be made based on assessment of ILD severity and progression, ideally following multidisciplinary discussion, taking the views of the patient into account. There is no established treatment algorithm for SSc-ILD, but cyclophosphamide, mycophenolate and nintedanib have shown efficacy in slowing the progression of SSc-ILD in randomized clinical trials. Nintedanib has been approved by the FDA for reducing the rate of decline in lung function in patients with SSc-ILD. All the drugs used to treat SSc-ILD have side-effects, which should be proactively assessed and managed by the clinical care team.

Patients with SSc-ILD should be offered supportive care as needed. This may include symptom relief, pulmonary rehabilitation, or supplemental oxygen. Many patients find support groups such as those run by the Scleroderma Foundation (https://www.scleroderma.org) valuable for providing information, support and a sense of community.

DLco, diffusing capacity of the lungs for carbon monoxide; FDA, Food and Drug Administration; FVC, forced vital capacity; HRCT, high-resolution computed tomography; HRQL, health-related quality of life; PFTs, pulmonary function tests.

Algorithm for screening, monitoring and management of SSc-ILD proposed by European consensus group

Adapted with permission from Lancet Rheumatology, 2, Hoffmann-Vold AM et al., The identification and management of interstitial lung disease in systemic sclerosis: evidence-based European consensus statements, E71-E83, Copyright Elsevier (2020).



Important!

All patients diagnosed with SSc should be screened for ILD at baseline using an HRCT scan. PFTs alone are not sufficient to ascertain whether SSc-ILD is present.

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Understanding the results of the SENSCIS trial

Toby M. Maher, MD
Keck School of Medicine, University of Southern California, Los Angeles, CA, USA.

The SENSCIS trial was a randomized, double-blind, placebo-controlled trial of nintedanib in 576 subjects with systemic sclerosis-associated ILD (SSc-ILD).

Subjects had fibrotic SSc-ILD and were at risk of progression, but were not required to have shown recent progression of ILD. Patients who had taken stable therapy with mycophenolate or methotrexate for ≥6 months were allowed to participate. Subjects received nintedanib or placebo until the last subject enrolled had reached week 52 of treatment.

The primary endpoint was the rate of decline in FVC (mL/year) over 52 weeks. Nintedanib reduced the rate of decline in FVC over 52 weeks by 44% compared with placebo (-52.4 vs -93.3 mL/year; difference: 41.0 [95% 2.9, 79.0]; p=0.04). While the absolute effect of nintedanib versus placebo was lower in patients who were taking mycophenolate at baseline than in those who were not, its relative effect was similar between these subgroups (40% and 46%, respectively).

Nintedanib had no significant effect on skin fibrosis or on HRQL over 52 weeks. The adverse events reported were mainly gastrointestinal events, particularly diarrhea. Adverse events led to treatment discontinuation in 16.0% of subjects treated with nintedanib compared to 8.7% who received placebo.

Decline in FVC in patients with SSc-ILD is associated with mortality. The results of the SENSCIS trial show that nintedanib provides a clinically meaningful benefit in slowing the progression of SSc-ILD, both when used as monotherapy and as add-on to mycophenolate.

Important!

Nintedanib has been approved by the FDA for slowing the rate of decline in pulmonary function in patients with SSc-ILD.

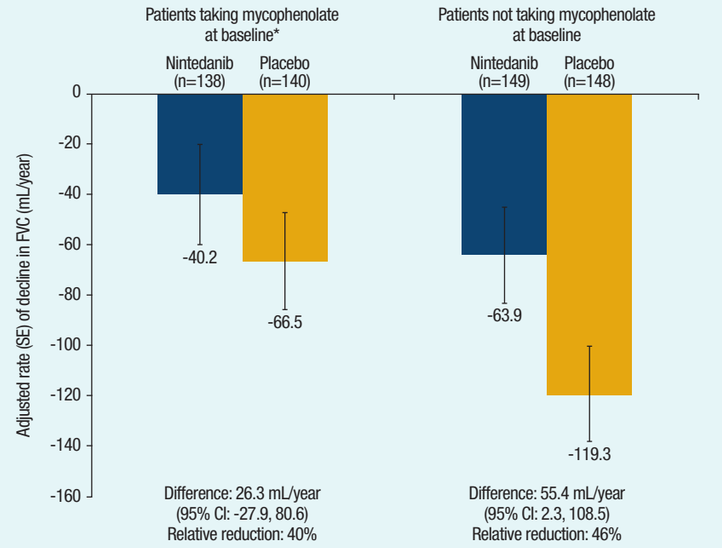
Take a quiz! Test your understanding of the results of the SENSCIS trial by taking a quiz at: **https://www.usscicomms.com/respiratory/SENSCISquiz**

CI, confidence interval; FDA, Food and Drug Administration; FVC, forced vital capacity; HRCT, high-resolution computed tomography; HRQL, health-related quality of life; SE, standard error.

Key inclusion criteria

Rate of decline in FVC (mL/year) over 52 weeks in patients randomized to nintedanib or placebo

Reproduced with permission from Lancet Respiratory Medicine, 9, Highland KB et al., Efficacy and safety of nintedanib in patients with systemic sclerosis-associated interstitial lung disease treated with mycophenolate: a subgroup analysis of the SENSCIS trial, 96-106, Copyright Elsevier (2021).



*Patients taking mycophenolate had been taking a stable dose for ≥6 months before randomization.

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Impact, monitoring and management of CTD-ILDs

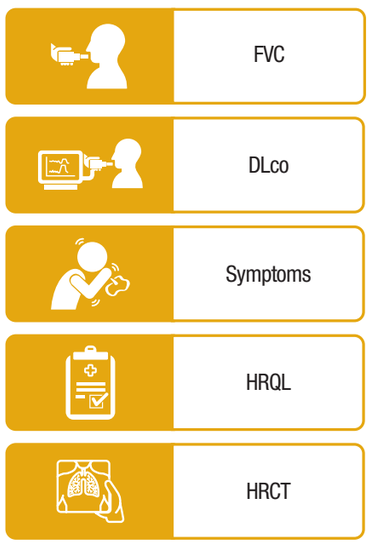
Teng Moua, MD
Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, USA.

ILD is a common manifestation of CTDs including rheumatoid arthritis (RA), systemic sclerosis (SSc), polymyositis/dermatomyositis, and Sjögren's syndrome.

Risk factors for the development of CTD-ILDs have been identified, but it remains impossible to predict with accuracy which patients with CTDs will develop ILD. ILD may be present on HRCT even in the absence of impaired lung function or symptoms.

A proportion of patients with CTD-ILDs develops a progressive fibrosing phenotype, characterized by increasing fibrosis on HRCT, decline in lung function, worsening symptoms, and high mortality. Although some risk factors for ILD progression and mortality in patients with CTD-ILDs have been identified, its course remains unpredictable. It is important that patients with CTD-ILDs are closely monitored so that patients whose ILD is progressing can be promptly identified and managed. Monitoring should include PFTs, assessment of symptoms and, where deemed appropriate, a repeat HRCT scan.

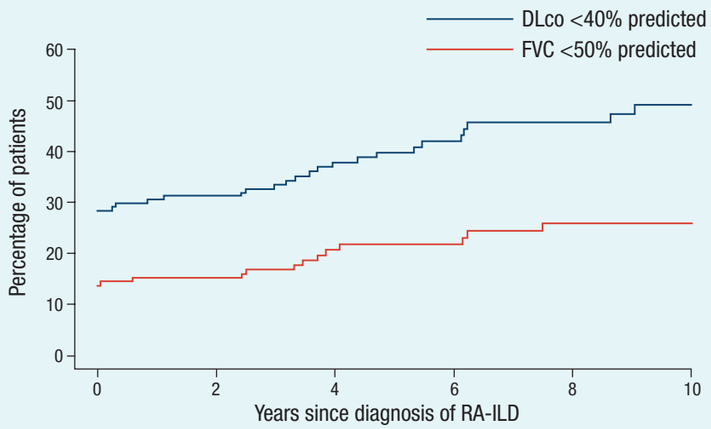
Monitoring progression of CTD-ILDs



CTD, connective tissue disease; DLco, diffusion capacity of the lung for carbon monoxide; FVC, forced vital capacity; FDA, Food and Drug Administration; HRCT, high-resolution computed tomography; HRQL, health-related quality of life; PFTs, pulmonary function tests; RA-ILD, rheumatid arthritis-associated ILD.

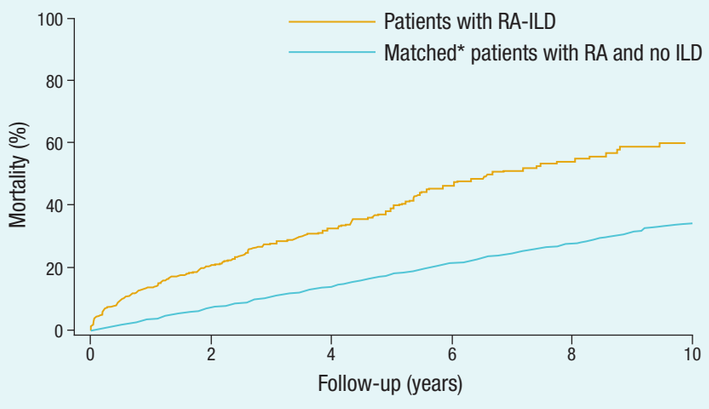
Development of severe lung function impairment following diagnosis of RA-ILD

Adapted with permission from: Zamora-Legoff JA, et al. Progressive decline of lung function in rheumatoid arthritis-associated interstitial lung disease. Arthritis Rheumatol 2017;69:542–9.



Kaplan–Meier estimates of mortality in patients with RA-ILD compared with matched patients with RA and no ILD

Adapted with permission from: Hyldgaard C et al. A population-based cohort study of rheumatoid arthritis-associated interstitial lung disease: comorbidity and mortality. Ann Rheum Dis 2017;76:1700-06.



*Matched by age, sex, and time since diagnosis of rheumatoid arthritis.

The management of patients with CTD-ILDs requires a multidisciplinary and individualized approach. The decision to initiate or escalate treatment should consider factors such as the severity of the ILD, evidence of progression, risk factors for progression, the patient's overall health status and the patient's preferences, and ideally be based on multidisciplinary discussion including at minimum a pulmonologist and rheumatologist, and perhaps also a radiologist.

There are no established algorithms for the treatment of CTD-ILDs. Immunomodulatory therapies are the mainstay of therapy for CTDs, but other than in patients with SSc-ILD, their efficacy in slowing the progression of ILD has not been established in randomised controlled trials. Nintedanib has been approved by the FDA for reducing decline in lung function in patients with SSc-ILD or chronic fibrosing ILDs with a progressive phenotype. In addition to pharmacological therapy, the care of patients with CTD-ILDs may include pulmonary rehabilitation, treatment of comorbidities, the use of supplemental oxygen, and supportive care. Supportive care should not only be provided as end-of-life care, but as needed by the patient throughout the course of their disease.

Important!

The course of CTD-ILD is unpredictable, so patients should be closely monitored for progression. Management of patients with CTD-ILDs requires a multidisciplinary and individualized approach, to enable effective management of both the ILD and other manifestations of the CTD.

Multidisciplinary and individualized approach to management of CTD-ILDs

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Key learnings from the INBUILD trial

Kevin R. Flaherty, MD
Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, USA.

The INBUILD trial was a randomized, placebo-controlled trial of nintedanib in 663 patients with fibrosing ILDs other than IPF who met criteria for progression of ILD within the two years before screening.

Patients with a wide range of ILD diagnoses participated in the trial. The most frequent diagnoses were hypersensitivity pneumonitis and autoimmune disease-related ILDs, particularly RA-ILD.

The primary endpoint was the rate of decline in FVC (mL/year) over 52 weeks. In the overall population, nintedanib reduced the rate of decline in FVC over 52 weeks by 57% compared with placebo (-80.8 vs -187.8 mL/year; difference: 107.0 [95% CI: 65.4, 148.5]; p<0.001). Findings in the co-primary analysis population of patients with a UIP-like fibrotic pattern on HRCT (n=412) and in patients with other fibrotic patterns on HRCT (n=251) were similar.

As in previous trials, the adverse events reported in patients treated with nintedanib were mainly gastrointestinal events, particularly diarrhea. Adverse events were managed using symptomatic therapies and dose adjustment. Over 52 weeks, adverse events led to permanent discontinuation of treatment in 19.6% of patients treated with nintedanib and 10.3% of patients who received placebo.

Important!

In the INBUILD trial, nintedanib slowed the rate at which fibrosing ILDs progressed irrespective of the underlying diagnosis. Based on the results of this trial, nintedanib has been approved by the FDA for the treatment of patients with chronic fibrosing ILDs and a progressive phenotype.

CI, confidence interval; FDA, Food and Drug Administration; FVC, forced vital capacity; IIP, idiopathic interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; HRCT, high-resolution computed tomography; NSIP, non-specific interstitial pneumonia; RA-ILD, rheumatoid arthritis-associated ILD; UIP, usual interstitial pneumonia.

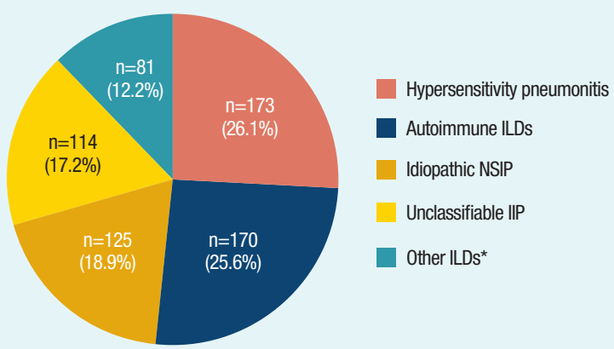
Key inclusion criteria

At least one of the following criteria for progression of ILD within the 24 months prior to screening:

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

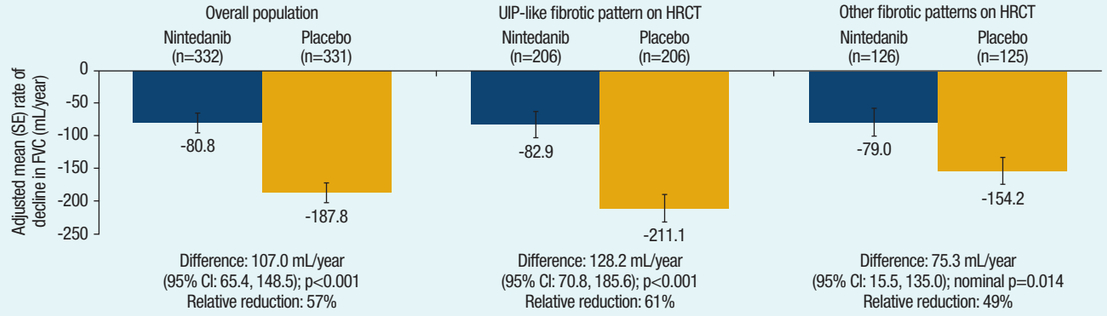
*Reticular abnormality with traction bronchiectasis, with or without honeycombing.

ILD diagnoses



*Sarcoidosis, exposure-related ILDs, and other terms in the "Other fibrosing ILDs" category of the case report form.

Rate of decline in FVC (mL/year) over 52 weeks by fibrotic pattern on HRCT



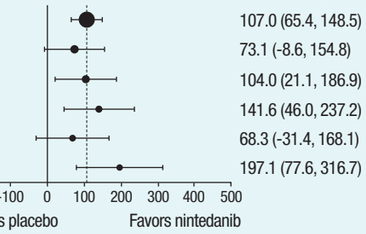
Although the INBUILD trial was not designed to study individual ILDs, subgroup analyses suggested that there was no difference across subgroups by diagnosis in the rate at which FVC declined in the placebo group or in the effect of nintedanib in reducing the rate of FVC decline. These findings support the hypothesis that once progressive fibrosis has developed, it continues to progress, irrespective of the original trigger.

Some patients continued in the INBUILD trial for more than 52 weeks. The median duration of follow-up over the whole trial was ~19 months. The trial was not powered to show a significant difference between nintedanib and placebo on mortality, but over the whole trial, the hazard ratio for the risk of death in patients treated with nintedanib versus placebo was 0.78 (95% CI: 0.50, 1.21). The hazard ratio for the risk of acute exacerbation of ILD or death in patients treated with nintedanib versus placebo was 0.67 (95% CI: 0.46, 0.98). Deaths and acute exacerbations of ILD were more common in patients with a UIP-like fibrotic pattern on HRCT, but patients with other fibrotic patterns on HRCT were also at high risk of these events over the follow-up period.

Rate of decline in FVC (mL/year) over 52 weeks with nintedanib vs placebo by ILD diagnosis

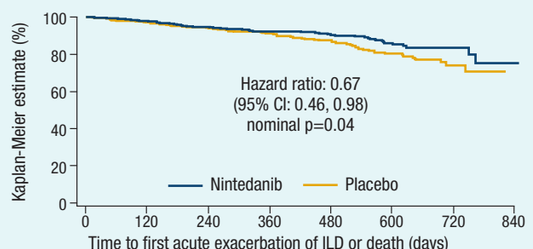
Reproduced with permission from Lancet Respiratory Medicine, 8, Wells AU et al, Nintedanib in patients with progressive fibrosing interstitial lung diseases-subgroup analyses by interstitial lung disease diagnosis in the INBUILD trial: a randomised, double-blind, placebo-controlled, parallel-group trial, 453-460, Copyright Elsevier (2020).

	N analysed Nintedanib	N analysed Placebo	Difference in rate of decline in FVC (95% CI)
All patients	332	331	107.0 (65.4, 148.5)
Hypersensitivity pneumonitis	84	89	73.1 (-8.6, 154.8)
Autoimmune ILDs	82	88	104.0 (21.1, 186.9)
Idiopathic NSIP	64	61	141.6 (46.0, 237.2)
Unclassifiable IIP	64	50	68.3 (-31.4, 168.1)
Other ILDs	38	43	197.1 (77.6, 316.7)



Treatment-by-subgroup-by-time interaction p=0.41.

Time to first acute exacerbation of ILD or death



No. of patients								
Nintedanib	332	325	314	305	268	127	35	1
Placebo	331	320	311	298	252	121	35	0

n (%) with event: Nintedanib: 46 (13.9%) Placebo: 65 (19.6%)

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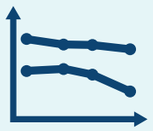
Information for patients with fibrosing CTD-ILDs

Lesley Davila, MD
Division of Rheumatic Diseases, University of Texas Southwestern Medical Center, Dallas, TX, USA.

Patients with fibrosing CTD-ILDs need information on the way that their ILD will be monitored, treatment options, and the various forms of support available to them.

Important information to communicate to patients with CTD-ILDs

1. Monitoring your CTD-ILD



The course of CTD-ILD varies between patients and may vary over time

Regular monitoring is important to check if your CTD-ILD is getting worse and if your treatment needs changing

Your care team will regularly assess:

Symptoms of pulmonary and non-pulmonary disease

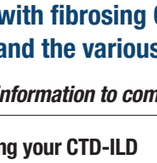
Lung function

Any side-effects of treatment

2. Treatment options for your CTD-ILD

Your care team will discuss treatment options with you. These may include:

Drugs that slow the progression of ILD or relieve symptoms



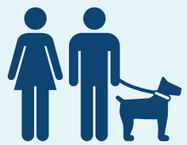
Supplemental oxygen if you have low levels of oxygen in your blood

Pulmonary rehabilitation to help alleviate your symptoms

3. Sources of support

Your care team can answer any questions you have

Patient support groups (on-line or face to face) can be a valuable source of information and support



Your family and friends: help them understand the support that you need

Beware that not all information you find on-line is accurate or relevant to you

Important!

The care team for patients with CTD-ILDs should include specialists in both pulmonary and rheumatology to care for all aspects of the CTD. Clinicians play a critical role in providing accurate information to patients with CTD-ILDs and answering their questions about their disease.

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Towards a better understanding of chronic fibrosing ILDs: the ILD-PRO Registry

Laurie D. Snyder, MD and Scott M. Palmer, MD
Duke Clinical Research Institute and Duke University Medical Center, Durham, NC, USA.

In 2018, the IPF-PRO Registry was expanded to become the IPF-PRO/ILD-PRO Registry (NCT01915511).

The ILD-PRO part of the registry is enrolling patients aged ≥30 years who have chronic fibrosing ILDs other than IPF, with reticular abnormality and traction bronchiectasis (with or without honeycombing) confirmed by HRCT scan and/or lung biopsy, and meet criteria for progression of ILD within the prior two years.

Patients with any chronic fibrosing ILD other than IPF are eligible to participate. To date, the registry has enrolled patients with autoimmune disease-related ILDs, hypersensitivity pneumonitis, and idiopathic non-specific interstitial pneumonia, among other diagnoses.

The ILD-PRO Registry will illuminate the natural history and impact of progressive fibrosing ILDs and current practices in their diagnosis and management. The registry also includes a biobank of biological samples that will be used in the investigation of biomarkers. The data generated will add to the information on non-IPF fibrosing ILDs being collected by other registries, such as the PFF registry in the US and the CARE-PF registry in Canada.

Inclusion criteria for ILD progression used in the ILD-PRO Registry

Relative decline in DLco ≥10% predicted

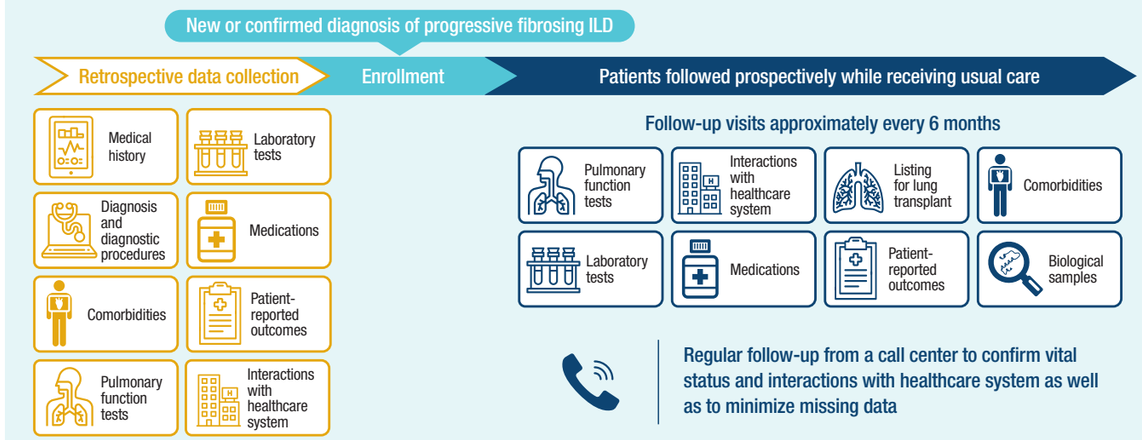
Relative decline in FVC ≥10% predicted

Relative decline in FVC ≥5–<10% predicted plus worsened respiratory symptoms

Relative decline in FVC ≥5–<10% predicted plus increased extent of fibrotic changes on HRCT

Worsened respiratory symptoms plus increased extent of fibrotic changes on HRCT

Design of the ILD-PRO Registry



IPF-PRO™ ILD-PRO™

Reference

Palmer SM et al. Improving our understanding of progressive fibrosing interstitial lung diseases (ILDs): design of the ILD-PRO Registry. Abstract and eposter at American Thoracic Society congress 2020. SMART poster available at: https://www.usscicomms.com/respiratory/ATS2020/palmer

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