Progressive Fibrotic Interstitial Lung Disease (PF-ILD)

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ILD Clinical Presentation Topics

1. ILD Definition and Patient Population
2. Clinical Information on the PF-ILD Concept
3. Rationale for New Code

ILD Definition and Patient Population

- **Encompasses a large group of pulmonary disorders**
  - Affects the interstitium (tissue and space around the alveoli)

- **General consensus is that some form of injury of the alveolar epithelial cells initiates an inflammatory response coupled with repair mechanisms**[1]
  - Reflected pathologically as inflammation, fibrosis, or a combination of both
  - Alteration of the interstitial space leads to clinical symptoms consistent with restrictive ventilatory deficit and poor gas exchange

- **Some patients with different types of ILD can develop a distinct, progressive fibrosing phenotype**
  - Similar to Idiopathic Pulmonary Fibrosis (IPF) with worsening of respiratory symptoms, lung function, quality of life, functional status, and early mortality[2, 3, 4]

- **High unmet need for further characterization and treatment options**[5]
  - Two interventional studies are evaluating treatment benefits of two anti-fibrotic therapies in non-IPF progressing fibrosing ILD[6, 7]

1. Marvin Schwartz & Talmadge E. King, *Interstitial Lung Disease* (PMPH USA, 5th ed. 2010).
2. EJ Kim, HR Collard, & TE King Jr, *Rheumatoid Arthritis-associated Interstitial Lung Disease: The Relevance of Histopathologic and Radiographic Patterns*, 136 CHEST 1397–1405 (2009).
3. CJ Ryerson, et al., *Prevalence and Prognosis of Unclassifiable Interstitial Lung Disease*, 42 EUR. RESPIR. J. 750–757 (2013).
4. JS Vourlekis, et al., *The Effect of Pulmonary Fibrosis on Survival in Patients with Hypersensitivity Pneumonitis*, 116 AM. J. MED. 662–668 (2004).
5. Athol Wells, et al., *What's in a name? That which we call IPF, by any other name would act the same*, 42 EUR. RESPIR. J. (2018) (Manuscript Review).
6. Hoffmann-La Roche. (2017). A Study of Pirfenidone in Patients with Unclassifiable Progressive Fibrosing Interstitial Lung Disease (Clinicaltrials.gov Identifier NCT03099187).
7. Boehringer Ingelheim. (2017). Efficacy and Safety of Nintedanib in Patients With Progressive Fibrosing Interstitial Lung Disease (PF_ILD) (Clinicaltrials.gov Identifier NCT02999178).

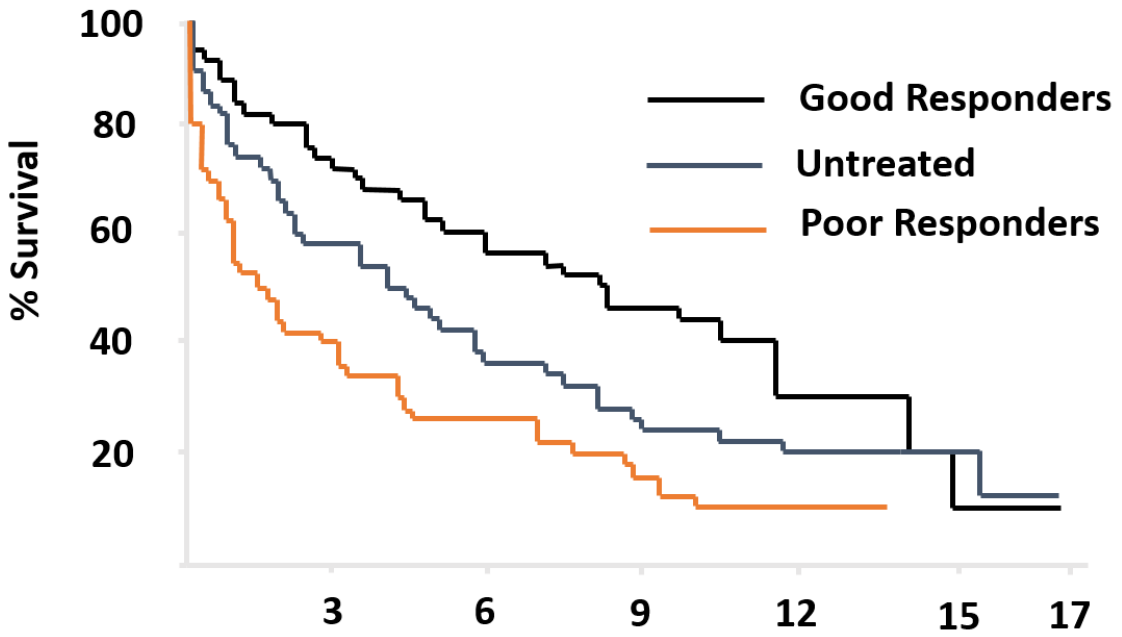
PF-ILD Concept

- **Historically: Likely grouped many of the ILDs into a general category of pulmonary fibrosis**
  - Lots of heterogeneity
  - Difficult to study

Steroids Improved Survival in Some Patients

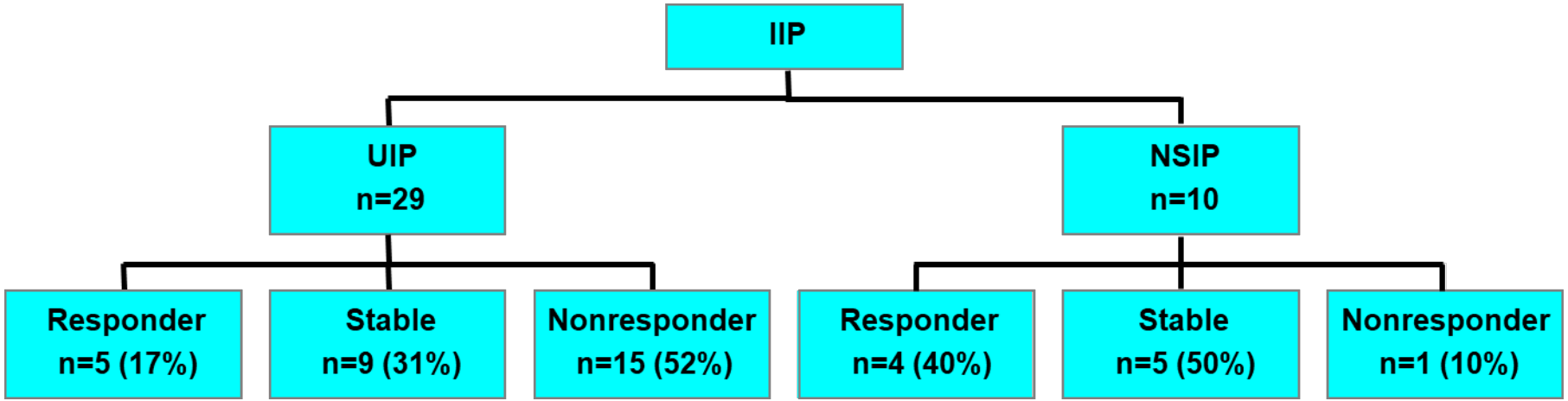
Improved survival

- Women, younger age, good steroid response



M Turner-Warwick et al., *Cryptogenic fibrosing avleolitis: response to corticosteroid treatment and its effect on survival*, 35 THORAX 593-9 (1980).

Response to Steroid Therapy in UIP and NSIP



P<0.05 for difference in distribution of responses between patients with UIP and NSIP.

K Flaherty et al., *Clinical significance of histological classification of idiopathic interstitial pneumonia*, 42 EUR. RESPIR. J. 275-83 (2002).

PF-ILD Concept

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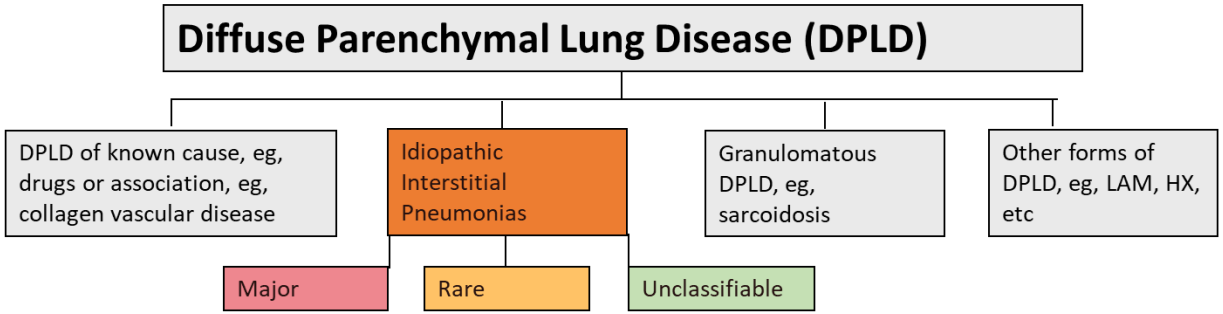
- **Currently:** **Emphasis on diagnosis**
  - Helps determine therapy and prognosis
  - Likely helped success in IPF clinical trials
  - Fails to account for subsequent disease behavior

Classification of Interstitial Lung Diseases



Idiopathic Pulmonary Fibrosis

Nonspecific Interstitial Pneumonia (idiopathic)

Acute Interstitial Pneumonia

Respiratory Bronchiolitis Interstitial Lung Disease

Desquamative Interstitial Pneumonia

Cryptogenic Organizing Pneumonia

Lymphoid Interstitial Pneumonia

Pleuroparenchymal Fibroelastosis

Category	CRP diagnosis	Major radiology-pathology Patterns
Chronic fibrosing IP	IPF iNSIP	UIP NSIP
Smoking-related IP	RB-ILD DIP	Respiratory Bronchiolitis Desquamative Interstitial Pneumonitis
Acute/subacute IP	COP AIP	Organizing pneumonia Diffuse alveolar damage

1. American Thoracic Society & European Respiratory Society, *Consensus Statement*, 165 AM. J. RESPIR. CRIT. CARE MED. 277-304 (2002).
2. WD Travis et al., *An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias*, 188 AM. J. RESPIR. CRIT. CARE MED. 733-48 (2013).

Initial Diagnosis No Longer Prognostic after Accounting for Change in Lung Function

Baseline DLco and change in FVC are associated with poor prognosis in patients with fibrotic interstitial pneumonia

Factors	Hazard Ratio	95% CI	P value
Male	2.724	1.277–5.813	0.010
Initial DLco % predicted	0.972	0.949–0.996	0.022
6-month change in FVC	0.925	0.893–0.958	<0.001
Age	1.027	0.992–1.064	0.134
NSIP	0.854	0.349–2.093	0.730
Resting PaO_2	0.995	0.961–1.031	0.798
Initial FVC % predicted	0.987	0.964–1.010	0.262

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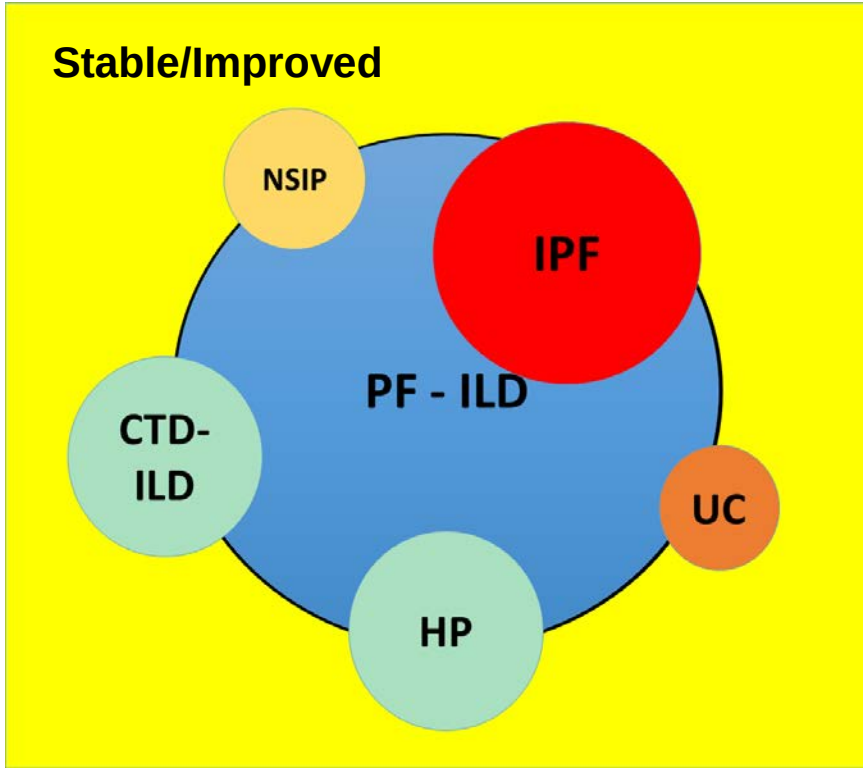
- **Future:** **Combine diagnosis and behavior (phenotype)**
  - Although no FDA-approved treatments exist for patients with fibrotic ILD other than IPF, several clinical trials are in progress[1, 2, 3]

1. Hoffmann-La Roche. (2017). A Study of Pirfenidone in Patients With Unclassifiable Progressive Fibrosing Interstitial Lung Disease (Clinicaltrials.gov Identifier NCT03099187).
2. Boehringer Ingelheim. (2017). Efficacy and Safety of Nintedanib in Patients With Progressive Fibrosing Interstitial Lung Disease (PF-ILD) (Clinicaltrials.gov Identifier NCT02999178).
3. Boehringer Ingelheim. (2015). A Trial to Compare Nintedanib With Placebo for Patients With Scleroderma Related Lung Fibrosis (Clinicaltrials.gov Identifier NCT02597933).

PF-ILD Concept



UC – unclassifiable
HP – hypersensitivity pneumonitis

Rationale for New Code

- **Enable more specific identification of patients with ILD with a progressive fibrotic phenotype**
- **Facilitate research and characterization of this patient population**
- **Enhance understanding of the diseases to aid in diagnosis, disease management, and treatment**
- **Facilitate more responsive monitoring and tracking of ILDs, while enhancing providers' ability to accurately respond to the type of ILD diagnosed**
- **Streamline claims processing and enable clearer diagnoses in patient records, particularly as new treatments become available**