# ERS 2016 Congress Highlights – Interstitial Lung Disease (ILD)

*London, UK*
*September 3rd – 7th 2016*

The 26th European Respiratory Society International Congress, (ERS) – the largest respiratory meeting in the world – was held over the 3rd - 7th of September in London, United Kingdom.
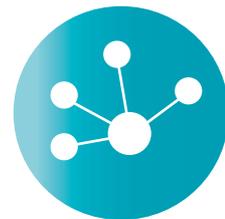
International experts discussed new data with regards to interstitial lung diseases (ILD) and idiopathic pulmonary fibrosis (IPF).

**Diagnosis and multidisciplinary discussion for ILD**

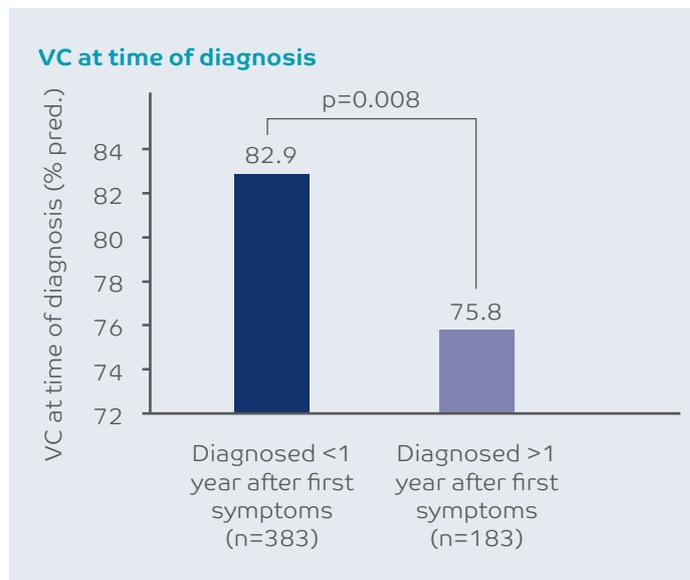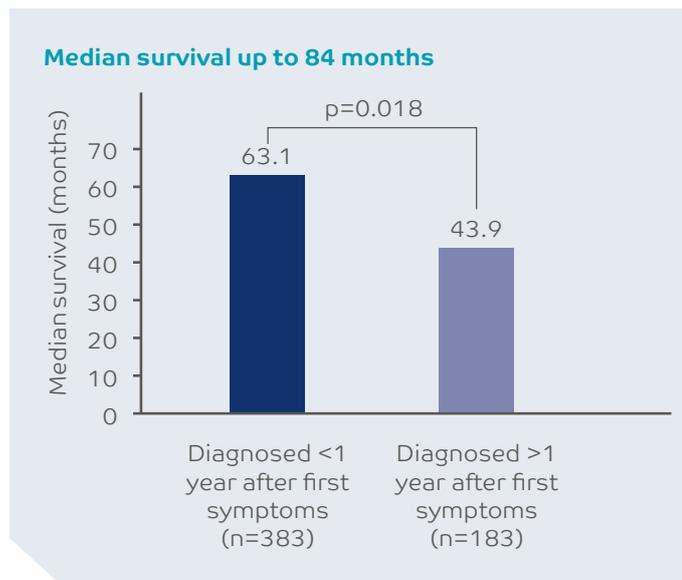**Clinical characteristics of patients with ILD and IPF in the real world**

**Predicting disease progression and mortality in IPF**

# Diagnosis and multidisciplinary discussion for ILD

## New findings around the diagnosis of ILD and IPF

### Early diagnosis and treatment of IPF

New data from the EMPIRE-IPF[1] registry show that early diagnosis and treatment of IPF matters in the prognosis of patients with IPF.[2] The 566 patients were categorized by time from first symptoms to diagnosis below or above 1 year. Compared to the later diagnosed group (n=183), the earlier diagnosed group (n=383) showed better median survival from the diagnosis up to 84 months (63.1 vs 43.9 months; p=0.018) and a higher VC at the time of diagnosis (82.9% of predicted vs 75.8% of predicted; p=0.008). There was no difference in rate of VC decline.



**Median survival up to 84 months**

Median survival (months): 63.1 (Diagnosed <1 year after first symptoms (n=383)) vs 43.9 (Diagnosed >1 year after first symptoms (n=183)); p=0.018

**VC at time of diagnosis**

VC at time of diagnosis (% pred.): 82.9 (Diagnosed <1 year after first symptoms (n=383)) vs 75.8 (Diagnosed >1 year after first symptoms (n=183)); p=0.008

Data from other registries which were presented at the congress also emphasized the need for improved, earlier diagnosis of ILD and IPF.

- Results from the British BTS IPF registry showed that 47% of the 767 patients with IPF had already had symptoms for more than 24 months before presentation[3]

### Diagnosis of UIP on HRCT- Impact of the 2011 IPF diagnostic guidelines

The investigators asked two Canadian general pulmonologists to review HRCTs of patients with ILD before and after applying current IPF diagnostic guidelines[4] to identify UIP pattern on HRCT.[5] Application of the guidelines led to improved agreement for possible UIP (from 66% to 72%) and inconsistent UIP (from 78% to 88%), but not for definite UIP (from 75% to 78%). This is of some concern, since according to the 2011 diagnostic guidelines, the only way to diagnose IPF without conducting a lung biopsy is a definite UIP pattern on HRCT.

## Surgical lung biopsy (SLB) for ILD and associated mortality rates

Analysis of Hospital Episodes Statistics data from 1997-2008 showed the associated mortality rates of SLB for the diagnosis of ILD in England (n= 2937).[6]

The researchers noted that the number of biopsies increased over time and identified the following risk factors for mortality:

- Male sex
- Increasing age
- Increasing co-morbidity
- Open surgery

The most common cause of death for all cases was interstitial lung disease.

**Mortality rates after SLB**
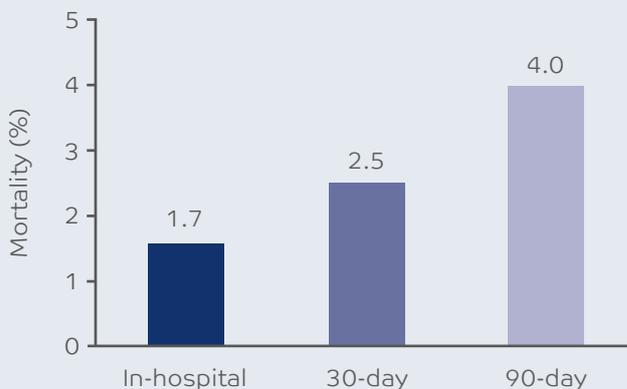


## Frequency of diagnostic procedures for patients with ILD in Germany

The German EXCITING-ILD registry (n=201) reported the following frequency of diagnostic procedures for patients with ILD[7]

*Frequency of diagnostic procedures for patients with ILD*



91% CT    49% HRCT    88% PFT    75% BAL    24% SLB    58% MDT

CT=Computed Tomography; HRCT=High-Resolution CT; PFT=Pulmonary Function Test; BAL=Bronchoalveolar lavage; SLB=Surgical Lung Biopsy; MDT= Multidisciplinary Team

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## MDT is a best practice for the diagnosis of ILD

### MDT as best practice for the diagnosis of ILD

The importance of a multi-disciplinary team (MDT) as best practice for the diagnosis of ILD was highlighted by a Spanish investigation. The study evaluated the diagnostic steps taken for all patients assessed in the Bellvitge University Hospital ILD Unit during 2014 (n=158).[8]

Diagnosis was obtained by the MDT, evaluating the following parameters stepwise, until a confident diagnosis was reached:

*1.* Detailed patient history (including antibodies and family history)

*2.* HRCT evaluation by two independent radiologists

*3.* Pathology

*4.* MDT committee discussion

Nearly all patients could be diagnosed and in 23 cases (14.6%), committee discussion determined the diagnosis. In addition, the initial diagnosis of 18 out of 91 cases (19.8 %) had to be modified after Multidisciplinary Team Discussion (MDD).

**ILD diagnosis**



**Modification of initial diagnosis**
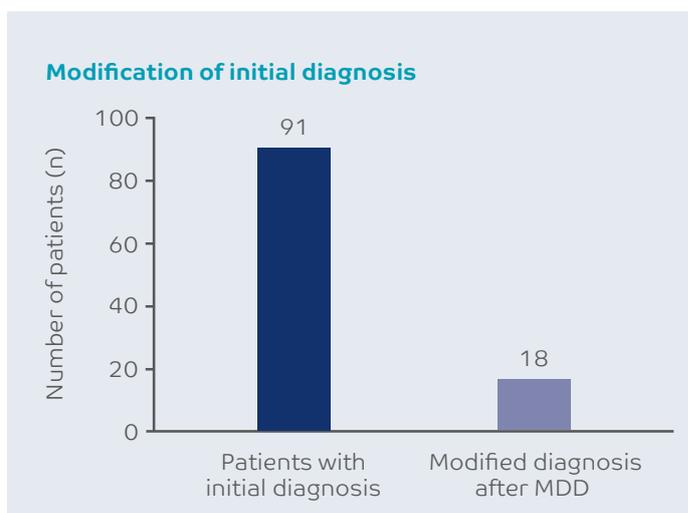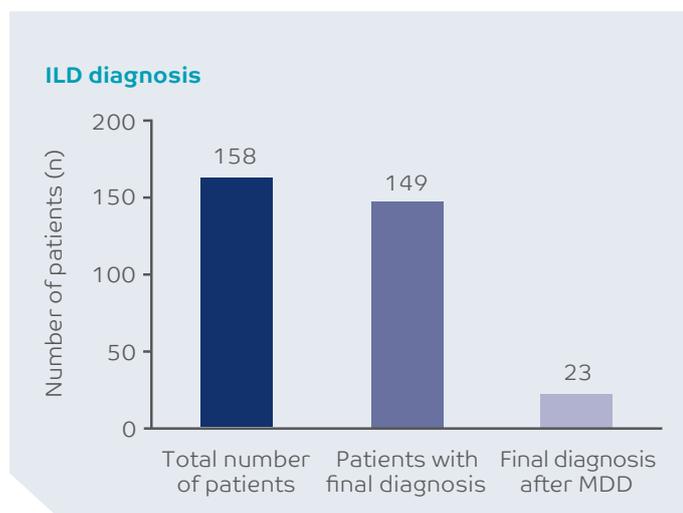


The importance of MDT for diagnosis was also demonstrated by results from the British BTS-IPF registry.[3] The investigators found that 90% of cases diagnosed with IPF (out of a total of 767 patients) were reviewed by MDT.

### Patients with IPF are often exposed to occupational and domestic hazards

Interim results from the PROOF registry (Belgium and Luxembourg) show that patients with IPF (n=175) might be exposed to occupational and/or domestic hazards more often than generally assumed.[9] The authors highlight that a history of exposure makes IPF diagnosis more difficult and that, therefore, MDT is more important.

**Occupational and domestic exposures (n=175)**
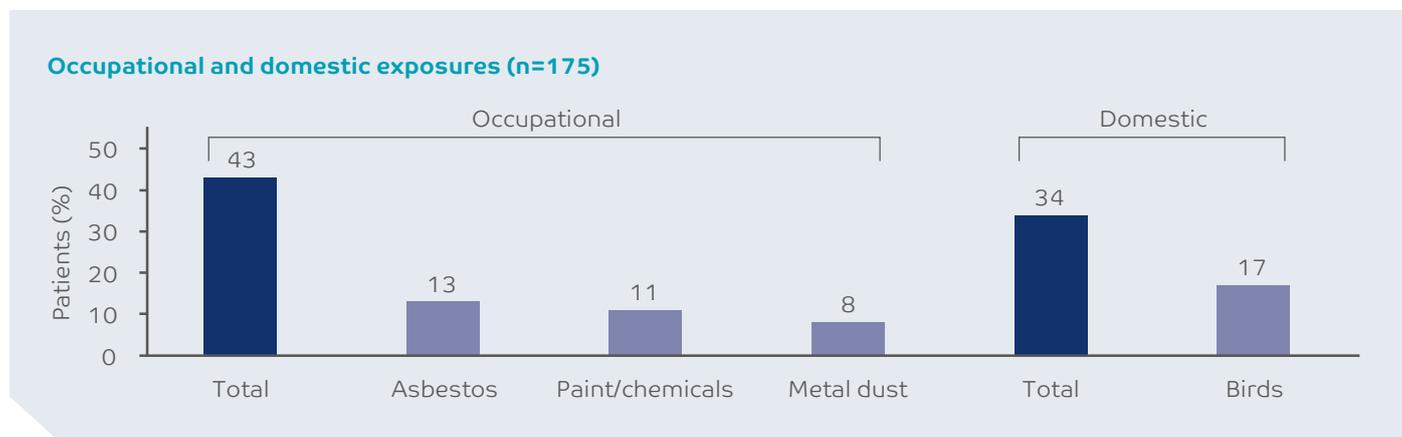
# Clinical characteristics of patients with ILD and IPF in the real world

## German registry reports many ILD patients with severe disease and with ILD-associated hospitalizations

The German EXCITING-ILD researchers presented several characteristics of the ILD patients enrolled in the registry (started in 10/2014; data cut-off 1/2016; n=201).[7] Notably, they found that many patients presented with severe disease (measured by GAP-ILD index) and that ILD associated hospitalizations occur often (47% of patients included in the registry had been hospitalized within the 6 months before enrolling in the registry and of these, 65% were hospitalized for ILD reasons).

**GAP-ILD index in patients enrolled in EXCITING-ILD (n=201)**
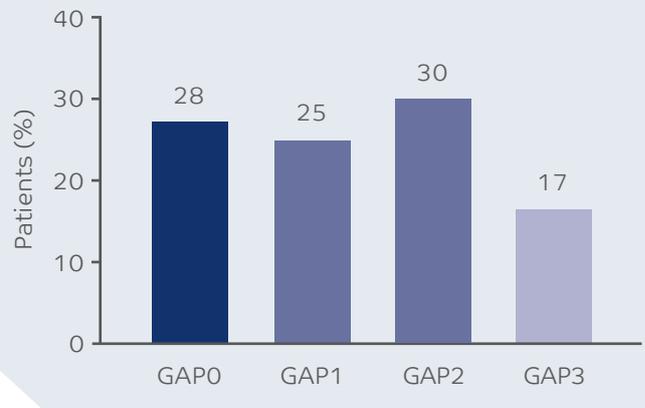


| | IPF | CTD-ILD |
|---|---|---|
| % of patients with ILD  (n=1084) | 14  (n=148) | 14  (n=151) |
| *Characteristics* | | |
| Age (years) | 65±8 | 51±14 |
| Female sex (%) | 26 | 74 |
| Current smokers (%) | 44 | 13 |
| Mean FVC (% pred.) | 58 | 58 |
| $DL_{CO}$ (%) | 64 | 67 |

## Incidence of IPF and CTD-ILD in India

For the first time, incidence of IPF and CTD-ILD in India was investigated in the ILD-India registry: 1084 Indian patients with newly onset ILD were evaluated by MDD among ILD experts and key characteristics for those patients newly diagnosed with IPF (per 2011 criteria[4]) and CTD-ILD were reported.[10]

## Quality of life of patients with IPF affected by lung function and comorbidities

A group of investigators around Dr. Kreuter found a close relationship between lung function, comorbidities and quality of life, measured by 3 scores (EQ-5D-VAS, EQ-5D index and SGRQ).[11]

- The quality of life of 572 patients with IPF from the INSIGHTS-IPF registry worsened significantly for all scores with increasing number of comorbidities (p<0.001)

- FVC declines >10% showed significant negative effects for all scores

- A change of over 6% of FVC predicted was associated with a change of SGRQ total score of over 4 points, which is deemed clinically relevant

## Smoking status in patients with ILD and IPF

A lot of patients with ILD in general, and with IPF in particular, have a history of smoking. At ERS, several groups reported on the smoking status of patients included in their registries:

- 57% of patients with ILD enrolled in the German EXCITING ILD registry (n=201) are current or ex-smokers.[7]

- 44% of newly diagnosed patients with IPF in India were smokers (ILD-INDIA, n=148)[10]

- 63% of British patients with IPF (BTS-IPF registry, n=767) were current or former smokers[3]

**Smoking status of patients with IPF from the BTS-IPF (n=767)**

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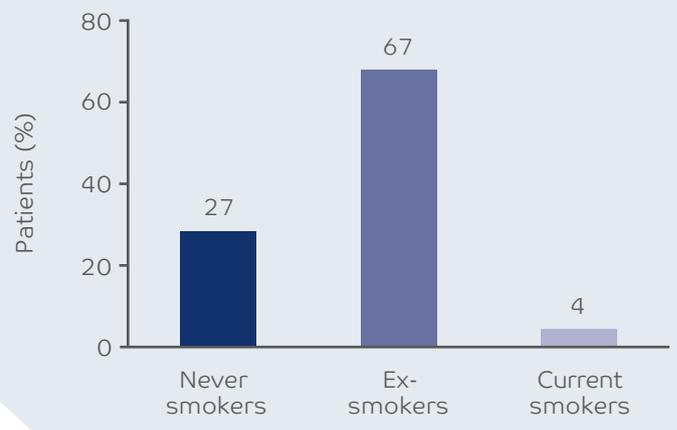
# Predicting disease progression and mortality in IPF

### Progression free survival in Australian patients with IPF below and above 80% FVC predicted

Patients with IPF from the Australian IPF registry (n=631) were analyzed with regards to progression free survival (PFS) above and below 80% FVC predicted.[12] PFS was defined as decline in FVC>10% or $DL_{CO}$>15% or death).

Factors associated with PFS:
- Male gender
- Impaired quality of life (SGRQ)
- Depression
- Cough severity
- Lower baseline FVC and $DL_{CO}$

Characteristics of patients with FVC>80% predicted (n=235)
- Older age (p=0.001)
- Female sex (p<0.001)
- Improved PFS (HR 1.61; 95% CI 1.3,2.0; p<0.001)

However, 18% (n=41) of those patients still progressed at 12 months.

### $DL_{CO}$ predicts mortality better than FVC

In order to find the best indicator of predicting mortality in IPF, investigators compared the accuracy of GAP and CPI scores as well as several univariate parameters in patients with IPF (n=209).[13]

While $DL_{CO}$ was the only significant parameter in all multivariate models (p=<0.001), all three lung function parameters ($DL_{CO}$, FVC and $FEV_1$) were found significant for predicting mortality alone, while age and gender were not. The analysis revealed that $DL_{CO}$ predicts mortality better than FVC or $FEV_1$.

| *Single Parameters* | *C Statistic* |
|---|---|
| $DL_{CO}$ | C=0.7518 |
| FVC | C=0.6765 |
| $FEV_1$ | C=0.6522 |

### Extent of emphysema in patients with IPF has an impact on FVC decline

In an analysis of 455 patients with IPF, patients with over 15% emphysema on HRCT showed less decline in FVC over 48 weeks than those without or with emphysema below 15%.[14]

**Distribution of emphysema in a patient population with IPF (n=455)**
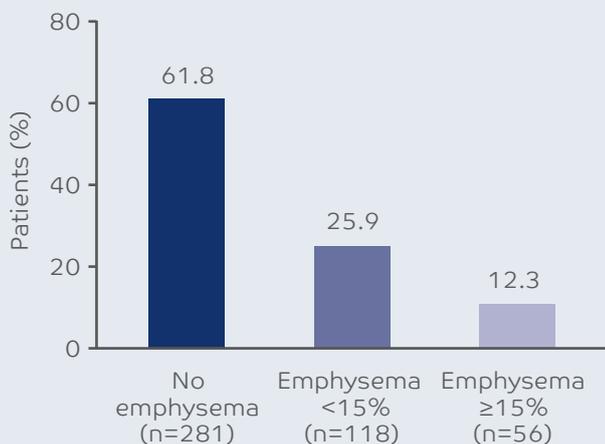


**Impact of emphysema ≥15% on FVC decline over 48 weeks (n=455; p=0.037)**
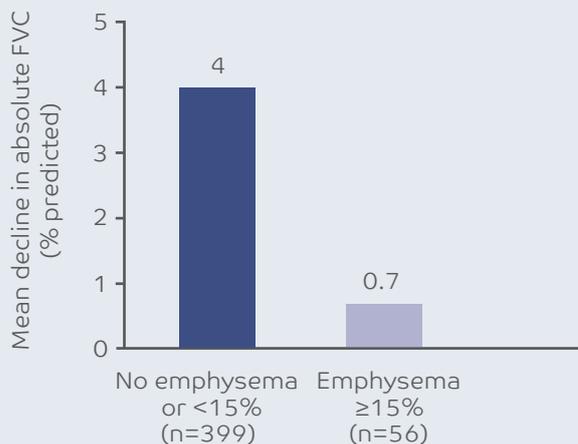


### Survival and lung function parameters not influenced by HRCT pattern

A subgroup analysis of patients from the Czech population of the EMPIRE[1] registry (n=513) showed that survival (from diagnosis up to 84 months) and lung function parameters are not influenced by the HRCT pattern of the patient at diagnosis.[15] The investigators compared patients previously diagnosed with IPF who, on HRCT, showed UIP pattern (n=423), possible UIP pattern (n=71) or a pattern inconsistent with UIP (n=19).

There were no significant differences in survival (Kaplan-Meier survival curves and median survival) or in lung function (FVC and $DL_{CO}$ values at the time of diagnosis or rate of decline) between the groups, indicating that patients with atypical HRCT patterns should be treated like patients with UIP pattern.

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## References

1. EMPIRE Registry: Homepage. Available at: http://empire.registry.cz/index-en.php. Accessed September 5, 2016.

2. Vasakova M., et al. Does early diagnosis of idiopathic pulmonary fibrosis matter? Real- world´s data from the EMPIRE registry. *ERJ* 2016;48: Suppl–60:PA794.

3. Spiteri M., et al. First insights from the BTS idiopathic pulmonary fibrosis (IPF) registry. *ERJ* 2016;48:Suppl–60:PA2099.

4. Raghu G., et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788–824.

5. Mendoza O., et al. Can current guidelines improve the diagnosis of a usual interstitial pneumonia among general radiologists? *ERJ* 2016;48: Suppl–60:PA796.

6. Hutchinson JP., et al. Surgical lung biopsy for the diagnosis of interstitial lung disease in England: 1997-2008. *ERJ* 2016;48:Suppl–60:PA802.

7. Kreuter M., et al. Interims analysis of the EXCITING-ILD registry (registry for exploring clinical and epidemiological characteristics of interstitial lung diseases). *ERJ* 2016;48:Suppl–60:PA3905.

8. Ortega P., et al. Relevance of the expert ILD clinical-radiological evaluation of referred cases to the MDT. *ERJ* 2016;48:Suppl–60:PA811.

9. Wuyts W., et al. PROOF: A prospective observational registry to describe the disease course and outcomes of idiopathic pulmonary fibrosis patients in a real-world clinical setting in Belgium and Luxembourg: Exposure in the interim report of 175 IPF patients. *ERJ* 2016;48:Suppl–60:OA4572.

10. Collins B., et al. ILD-India registry: Idiopathic pulmonary fibrosis (IPF) and connective tissue disease (CTD) associated interstitial lung disease (CTD-ILD) (Collins/ Raghu, 174- SUN) / ILD India registry: results from new ILD India Registry data base. *ERJ* 2016;48:Suppl–60:PA812.

11. Kreuter M., et al. Symptoms and quality of life in relation to lung function and comorbidities in patients with idiopathic pulmonary fibrosis: INSIGHTS-IPF registry. *ERJ* 2016;48:Suppl–60:OA4570.

12. Jo H., et al. Disease progression in early idiopathic pulmonary fibrosis: Insights from the Australian IPF registry. *ERJ* 2016;48:Suppl–60:PA2100.

13. Gonzalez A., et al. Predicting mortality in idiopathic pulmonary fibrosis. Which parameters should be used to determine eligibility for treatment? Analysis of a UK prospective cohort. *ERJ* 2016;48:Suppl–60:OA282.

14. Cottin V., et al. Analyses of the relationship between FVC, extent of fibrosis and extent of emphysema in patients with idiopathic pulmonary fibrosis (IPF). *ERJ* 2016;48:Suppl–60:OA4568.

15. Vasakova M., et al. Do typical and atypical HRCT patterns make difference in prognosis of patients with IPF? *ERJ* 2016;48:Suppl–60:PA795.

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## Glossary

6MWD = 6-minute walk distance

AAT = Antiacid therapy

ADR = Adverse drug reaction

AE = Adverse event

BSC = Best supportive care

BTS = British Thoracic Society

CI = Confidence interval

CPI = Composite physiologic index

CPU = Compassionate use program

CTD-ILD = Connective tissue disease associated ILD

$DL_{CO}$ = Diffuse capacity of the lung for carbon monoxide

EQ-5D = EuroQuol

EQ-5D-VAS = EuroQuol visual analogue scale

ERS = European Respiratory society

FVC = Forced vital capacity

GAP = Gender-Age-Physiology index

GERD = Gastroesophageal reflux disease

HR = Hazard ratio

HRCT = High resolution computed tomography

HRQoL = Health-related quality of life

ILD = Interstitial lung disease

IPF = Idiopathic pulmonary fibrosis

MDD = Multi-disciplinary discussion

MDT = Multi-disciplinary team

NAC = N-acetylcysteine

NPU = Named patient use

PFS = Progression free survival

SAE = Serious adverse event

SGRQ = St George's Respiratory Questionnaire

SLB = Surgical lung biopsy

TEAE = Treatment emergent AE

UIP = Usual Interstitial Pneumonia

VC = Vital Capacity

**If you would like to view the full report which includes real world experience with and new data on antifibrotics in IPF, please visit the product website.**

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