Poster

Effect of antifibrotic therapy on survival in patients with idiopathic pulmonary fibrosis: data from the IPF-PRO Registry

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Effect of antifibrotic therapy on survival in patients with idiopathic pulmonary fibrosis: data from the IPF-PRO Registry

IPF-PRO™ ILD-PRO™

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INTRODUCTION

- Idiopathic pulmonary fibrosis (IPF) is a progressive fibrosing interstitial lung disease associated with high mortality.[1]
- No single clinical trial has been powered to show an effect of antifibrotic therapy on mortality in patients with IPF, but pooled trial data suggest that these therapies may improve survival.[2,3] Real-world studies provide additional evidence on the effect of antifibrotic therapies on survival.[4]
- The Idiopathic Pulmonary Fibrosis Prospective Outcomes (IPF-PRO) Registry is a prospective observational US registry of patients with IPF.[5]

AIM

- To investigate the effect of antifibrotic therapy on mortality and other outcomes in patients with IPF.

METHODS

IPF-PRO Registry

- Patients with IPF that was **diagnosed or confirmed at the enrolling center in the previous 6 months** were enrolled at 46 sites between June 2014 and October 2018.
- Patients were **followed prospectively**, with follow-up data collected as part of routine clinical care until death, lung transplant, or withdrawal.

Outcomes

- The effect of antifibrotic therapy (nintedanib or pirfenidone) on the following outcomes was assessed:
  - **Death (primary outcome)**
  - Death or lung transplant
  - Respiratory-related hospitalization
  - Acute worsening of IPF (defined as any healthcare encounter deemed due to acute worsening of IPF)
  - Composite of death, lung transplant, acute worsening of IPF, and absolute decline in FVC ≥10% predicted.

Analyses

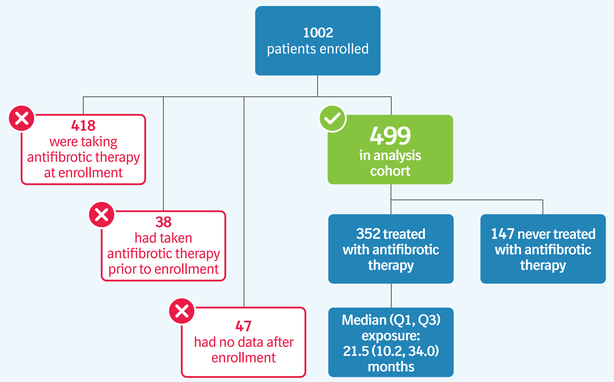
- To obtain the most accurate assessment of the effect of antifibrotic therapy on outcomes, a **new-user design** was implemented, i.e., the analysis cohort was limited to patients who started antifibrotic therapy on or after the day of enrollment or had never taken antifibrotic therapy.
- The effect of antifibrotic therapy on each outcome was assessed using **causal inference method for longitudinal treatment initiation**.[6] This accounts for patient characteristics that could confound the relationship between therapy and outcomes and for treatment initiations and discontinuations during follow-up.
- **Multiple "mini" randomized trials** were constructed, where each trial started when a patient or patients initiated antifibrotic therapy. "Treated" patients were those who started therapy on that day while "control" patients were those who had not started therapy as of that day and were still at risk of the outcome.

CONCLUSIONS

- Analyses of data from the IPF-PRO Registry based on causal inference methodology suggest that patients with IPF who were treated with antifibrotic therapy had improved survival. The low hazard ratio (0.53) suggests that the lack of statistical significance (p=0.06) may be due to insufficient power.
- The reasons behind the observation of numerical increases in the risks of respiratory-related hospitalization and healthcare encounters deemed due to acute worsening of IPF in patients treated with antifibrotic therapy are unclear.

RESULTS

Analysis cohort



Patient characteristics at enrollment

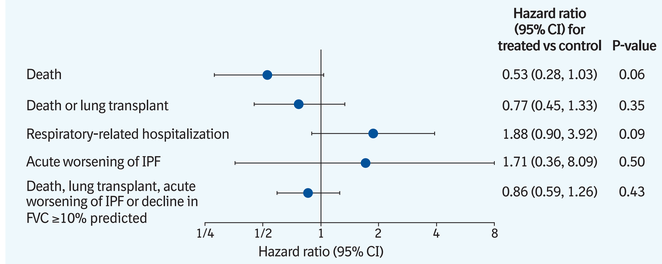
	Treated (n=352)	Never treated (n=147)
Male	260 (74)	102 (69)
Age, years	70 (65, 75)	73 (66, 78)
Body mass index, kg/m²	29.4 (26.7, 32.5)	28.0 (25.1, 31.7)
Definite IPF[7]	232 (66)	83 (56)
Family history of ILD	69 (20)	18 (13)
FVC % predicted	70.6 (60.0, 80.8)	71.3 (58.8, 84.4)
DLco % predicted	44.3 (34.9, 52.9)	44.4 (33.2, 56.8)
Oxygen use at rest	49 (14)	26 (19)
Oxygen use with activity	93 (27)	41 (29)

Data are median (Q1, Q3) or n (%) of patients.

Estimated event rates

	1-year event rate (95% CI)		2-year event rate (95% CI)	
	Treated	Control	Treated	Control
Death	6.6 (6.1, 7.1)	10.2 (9.5, 10.9)	15.0 (14.1, 15.9)	21.6 (20.1, 23.1)
Death or lung transplant	10.1 (9.5, 10.7)	12.2 (11.5, 12.9)	20.7 (19.5, 21.8)	24.2 (23.2, 25.1)
Respiratory-related hospitalization	14.0 (12.8, 15.2)	8.6 (8.0, 9.2)	20.4 (18.5, 22.3)	13.1 (12.0, 14.2)
Acute worsening of IPF	7.0 (5.5, 8.5)	3.6 (3.1, 4.1)	12.3 (10.7, 13.9)	6.8 (6.0, 7.6)
Death, lung transplant, acute worsening of IPF or decline in FVC ≥10% predicted	18.7 (17.6, 19.9)	21.1 (20.3, 21.8)	36.6 (34.5, 38.6)	40.1 (39.4, 40.8)

Associations between antifibrotic therapy and outcomes



Model adjusted for age, sex, race/ethnicity, region, insurance type, distance from enrolling center, time from symptom onset to new/confirmed diagnosis of IPF at enrolling center, diagnosis of IPF prior to referral to enrolling center, definite IPF,[7] referral to enrolling center by pulmonologist, family history of ILD, body mass index, FVC % predicted, DLco % predicted, oxygen use at rest, oxygen use with activity, hospitalization in prior 12 months, respiratory-related hospitalization in prior 12 months, coronary artery disease, congestive heart failure, pulmonary hypertension, gastroesophageal reflux disease, chronic obstructive pulmonary disease, obstructive sleep apnea, ex or current smoker, statin use, Inspiratory crackles, clubbing, St George's Respiratory Questionnaire total score, Cough and Sputum Assessment Questionnaire cough symptoms domain, 12-item short-form survey mental component score, EuroQoL-5D index, EuroQoL visual analog scale.

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IPF-PRO™ Registry enrolling centers: Albany Medical Center, Albany, NY; Baylor College of Medicine, Houston, TX; Baylor University Medical Center at Dallas, Dallas, TX; Cleveland Clinic, Cleveland, OH; Columbia University Medical Center/New York Presbyterian Hospital, New York, NY; Duke University Medical Center, Durham, NC; Froedtert & The Medical College of Wisconsin Community Physicians, Milwaukee, WI; Houston Methodist Lung Center, Houston, TX; Lahey Clinic, Burlington, MA; Loyola University Health System, Maywood, IL; Lynchburg Pulmonary Associates, Lynchburg, VA; Medical University of South Carolina, Charleston, SC; National Jewish Health, Denver, CO; NYU Medical Center, New York, NY; Piedmont Healthcare, Austell, GA; Pulmonary Associates of Stamford, Stamford, CT; PulmonIx LLC, Greensboro, NC; Renovatio Clinical, The Woodlands, TX; Salem Chest and Southeastern Clinical Research Center, Winston Salem, NC; South Miami Hospital, South Miami, FL; St. Joseph's Hospital, Phoenix, AZ; Stanford University, Stanford, CA; Temple University, Philadelphia, PA; The Oregon Clinic, Portland, OR; Tulane University, New Orleans, LA; UNC Chapel Hill, Chapel Hill, NC; University of Alabama at Birmingham, Birmingham, AL; University of California, Davis, Sacramento, CA; University of California Los Angeles, Los Angeles, CA; University of Chicago, Chicago, IL; University of Cincinnati Medical Center, Cincinnati, OH; University of Louisville, Louisville, KY; University of Miami, Miami, FL; University of Michigan, Ann Arbor, MI; University of Minnesota, Minneapolis, MN; University of Pennsylvania, Philadelphia, PA; University of Pittsburgh, Pittsburgh, PA; University of Virginia, Charlottesville, VA; UT Southwestern Medical Center, Dallas, TX; Vanderbilt University Medical Center, Nashville, TN; Vermont Lung Center, Colchester, VT; Wake Forest University, Winston Salem, NC; Washington University, St. Louis, MO; Weill Cornell Medical College, New York, NY; Wilmington Health and PMG Research, Wilmington, NC; Yale School of Medicine, New Haven, CT.

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