PA2201

Functional Decline Over Time in Patients With Idiopathic Pulmonary Fibrosis Treated With Pirfenidone: The PROOF Registry

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BACKGROUND

- Idiopathic pulmonary fibrosis (IPF) is a progressive, fatal, fibrosing lung disease associated with a median survival time from diagnosis of 2–5 years[1–3]
- Progressive and debilitating symptoms, including cough and exercise limitation, cause restrictions to daily activities and growing dependence on family members and caregivers[4]
- Two antifibrotics, pirfenidone and nintedanib, are currently available for the treatment of patients with IPF[5,6]
  - Both pirfenidone and nintedanib have been shown to reduce disease progression compared with placebo over a minimum of 1 year in Phase III clinical trials[7–9]
- Although clinical trials provide essential data regarding the efficacy and safety of treatments, the restrictive inclusion and exclusion criteria can generate uncertainty when applying results to real-world populations of patients
  - Currently, there is a lack of data available on longitudinal treatment outcomes in real-world populations of patients with IPF
- The PROOF registry is an ongoing, observational study, initiated in 2013 to monitor disease progression in a real-world population of patients with IPF[10]
  - Patients in the PROOF registry have been shown to have a range of comorbidities and comedications[10]

AIMS

- Here, we present data on longitudinal changes in lung function over 24 months in patients with IPF who received pirfenidone for any duration of treatment in the PROOF registry

METHODS

- The PROOF registry enrolled patients from eight centres in Belgium and Luxembourg between October 2013 and January 2016
- Eligible patients were over 18 years of age, with a multidisciplinary team diagnosis of definite or probable IPF[3]
  - Patients were treated at the discretion of their clinician and were eligible for inclusion irrespective of any treatments received
  - Patients were excluded if they were enrolled in a clinical trial at the time of registry inclusion or if they were unable to give informed consent
- Here we present data from patients treated with pirfenidone at any time during follow-up in the PROOF registry, for any duration of treatment
- Demographic and disease characteristics were collected upon inclusion in the registry
- Lung function was assessed at the time of inclusion (Month 0) and at Months 3, 6, 12 and 24 post-inclusion using:
  - Percent predicted forced vital capacity (FVC)
  - Percent predicted diffusing capacity for carbon monoxide (DLco)
- The percentage of patients experiencing categorical lung function decline compared with Month 0 was assessed at Months 3, 6, 12 and 24 using the following definitions:
  - ⩾ 10% decline in percent predicted FVC
  - ⩾ 15% decline in percent predicted DLco
  - Absolute (e.g. an absolute decline of 10% could be from 60% to 50%) and relative (e.g. a relative decline of 10% could be from 60% to 54%) declines were considered
- Kaplan–Meier curves were used to graphically display time-to-event analyses for ⩾ 10% absolute decline in percent predicted FVC and ⩾ 15% absolute decline in percent predicted DLco

RESULTS

Patient Population

- Between October 2013 and January 2016, 277 patients with IPF were enrolled in the PROOF registry
- In total, 233 (84.1%) patients were treated with pirfenidone at any time during follow-up in the PROOF registry, for any duration of treatment (ever-treated)
  - Mean (standard deviation [SD]) duration of follow-up in the PROOF registry was 20.1 (10.4) months for patients ever-treated with pirfenidone
  - Mean (SD) duration of treatment was 634.9 (465.3) days
- In total, 223 (95.7%) patients ever-treated with pirfenidone had a definite diagnosis of IPF, while 10 (4.3%) had a probable diagnosis
- Patient demographics at registry inclusion are presented in **Table 1**

Table 1. Patient Demographics at Registry Inclusion

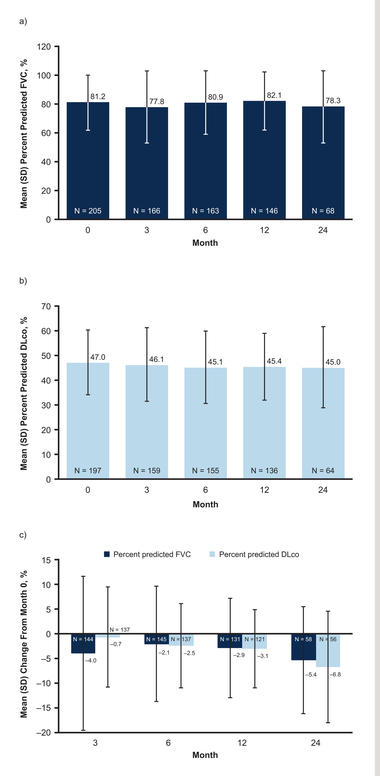
Parameter*	Ever-treated† with pirfenidone (N = 233)
Male	181 (77.7)
White	219 (94.0)
Mean (SD) age, years	69.4 (8.5)
Supplemental oxygen use at or after registry inclusion	25 (10.7)
Smoking status	
Never	65 (27.9)
Current	15 (6.4)
Former	153 (65.7)

SD, standard deviation.
* Data presented as n (%) unless otherwise specified.
† Ever-treated patients received pirfenidone at any time during follow-up for any duration of treatment.

Longitudinal Lung Function in Patients Ever-Treated With Pirfenidone

- At Month 0, mean (SD) percent predicted FVC was 81.2% (19.0) and mean (SD) percent predicted DLco was 47.0% (13.2)
- Mean (SD) percent predicted FVC and DLco at Months 0, 3, 6, 12 and 24 are shown in **Figure 1a** and **1b**, respectively
  - Mean (SD) absolute changes from Month 0 in percent predicted FVC and DLco at Months 3, 6, 12 and 24 are shown in **Figure 1c**

Figure 1. Mean (SD) Percent Predicted FVC (a) or DLco (b) at Months 0, 3, 6, 12 and 24 in Patients Ever-Treated With Pirfenidone in the PROOF Registry.* Mean (SD) Absolute Changes From Month 0 in FVC and DLco at Months 3, 6, 12 and 24 in Patients Ever-Treated With Pirfenidone in the PROOF Registry (c)

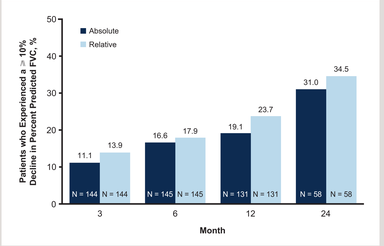


DLco, diffusing capacity for carbon monoxide; FVC, forced vital capacity; SD, standard deviation.
* Patients were included in the calculation for a time point if they had a lung function measurement available for that time point, regardless of whether they had a baseline measurement.

Categorical Lung Function Decline in Patients Ever-Treated With Pirfenidone

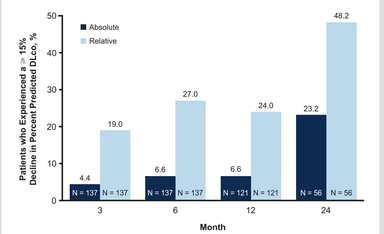
- The percentage of patients that experienced a ⩾ 10% absolute or relative decline in percent predicted FVC or a ⩾ 15% absolute or relative decline in percent predicted DLco from Month 0 is presented in **Figures 2** and **3**, respectively
  - The mean (SD) time to ⩾ 10% absolute decline in percent predicted FVC was 20.1 (0.6) months (**Figure 4**)
  - The mean (SD) time to ⩾ 15% absolute decline in percent predicted DLco was 23.4 (0.5) months (**Figure 5**)

Figure 2. Percentage of Patients Ever-Treated With Pirfenidone* who Experienced a ⩾ 10% Absolute or Relative Decline in Percent Predicted FVC from Month 0



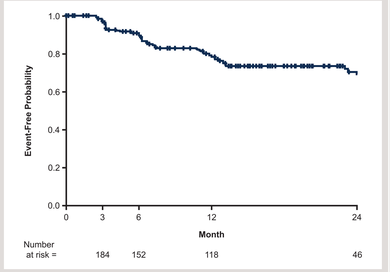
FVC, forced vital capacity.
* Patients were included in the calculation for a time point if they had an FVC measurement available for that time point and an FVC measurement collected at baseline.

Figure 3. Percentage of Patients Ever-Treated With Pirfenidone* who Experienced a ⩾ 15% Absolute or Relative Decline in Percent Predicted DLco From Month 0



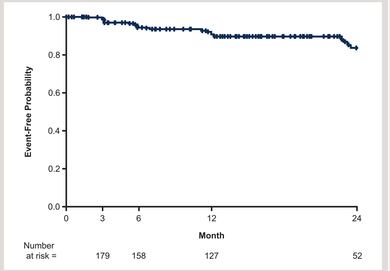
DLco, diffusing capacity for carbon monoxide.
* Patients were included in the calculation for a time point if they had a DLco measurement available for that time point and a DLco measurement collected at baseline.

Figure 4. Time to First ⩾ 10% Absolute Decline From Month 0 in Percent Predicted FVC in Patients Ever-Treated With Pirfenidone



FVC, forced vital capacity.
The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

Figure 5. Time to First ⩾ 15% Absolute Decline From Month 0 in Percent Predicted DLco in Patients Ever-Treated With Pirfenidone



DLco, diffusing capacity for carbon monoxide.
The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time.

Limitations

- One potential limitation of this registry is the enrolment of a relatively small population of patients located across a limited geographic area. In addition, missing data due to patients being lost to follow-up over time or data not being collected at all time points for all patients means that some outcomes were summarised using small sample sizes

CONCLUSIONS

- The PROOF registry provides valuable, real-world data on disease progression in patients with IPF
- Over 12 months of follow-up in the PROOF registry, pulmonary function remained largely stable in patients with IPF who received pirfenidone for any duration of treatment
  - Pulmonary function remained similar at 24 months of follow-up, although patient numbers were lower
- Overall, the rates of disease progression seen in the PROOF registry are largely comparable with the progression reported in Phase III clinical trials over 12 months[7,8]

DISCLOSURES

Data within the poster are directly derived from research sponsored by F. Hoffmann-La Roche, Ltd./Genentech, Inc.

Wim A. Wuyts is on the speakers' bureau for F. Hoffmann-La Roche, Ltd. and Boehringer Ingelheim. His institution has received funding from both companies.

Benjamin Bondue has received consulting and/or lecture fees from F. Hoffmann-La Roche, Ltd. and Boehringer Ingelheim.

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http://bit.ly/2opWYYt

Presented at the European Respiratory Society International Congress; 15–19 September 2018; Paris, France.

This poster was sponsored by F. Hoffmann-La Roche, Ltd.
Third-party writing assistance was furnished by CMC AFFINITY, a division of Complete Medical Communications, Ltd.