Incidence of Multiple Progression Events in Patients With Idiopathic Pulmonary Fibrosis (IPF) in the Pooled CAPACITY and ASCEND Trials

OA3401

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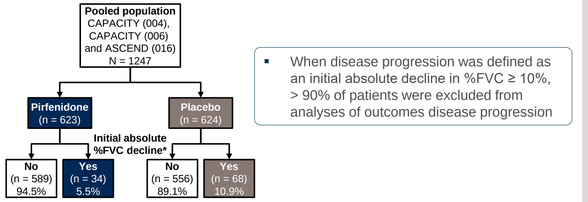
BACKGROUND

- The clinical course of IPF is variable and complex; disease progression events include declines in %FVC, declines in 6MWD and respiratory-related hospitalisations[1-5]
- When assessing disease progression by the occurrence of a single event in a specified period of time, other relevant progression events may be excluded **(Figure 1)**
- The impact of pirfenidone on the incidence of multiple disease progression events in patients with IPF is unknown

6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity; IPF, idiopathic pulmonary fibrosis.

Figure 1. Should disease progression be defined solely by the occurrence of a single disease progression event?[1]



- When disease progression was defined as an initial absolute decline in %FVC ≥ 10%, > 90% of patients were excluded from analyses of outcomes disease progression

%FVC, percent predicted forced vital capacity.
* Initial absolute decline in %FVC ≥ 10% occurring during the first 3 months or 6 months of study treatment.
1. Nathan SD, et al. *Thorax*. 2016;71:429–435.

OBJECTIVE

- The goal of this study was to determine the incidence of multiple disease progression events in the first 12 months of pirfenidone treatment vs. placebo
- Multiple-event analyses, which use a greater proportion of the data, may provide a more complete characterisation of treatment efficacy

METHODS

Source Data and Study Population

- All patients randomised to pirfenidone 2403 mg/day (n = 623) or placebo (n = 624) in the CAPACITY (004), CAPACITY (006) and ASCEND (016) studies (N = 1247)*

Analysis

- Patients were analysed for the incidence of the following progression events:
  - Relative decline in %FVC ≥ 10%
  - Absolute decline in 6MWD ≥ 50 m
  - Respiratory-related hospitalisation
  - All-cause mortality
- The proportions of patients with an event were compared using the χ^2 test
- Time-to-event comparisons were performed using the log-rank test and proportional hazards regression to estimate the hazard ratio (95% CI)
- Missing data for %FVC and 6MWD were not imputed

6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity.
* CAPACITY (004), NCT00287716; CAPACITY (006), NCT00287729; ASCEND (016), NCT01366209.

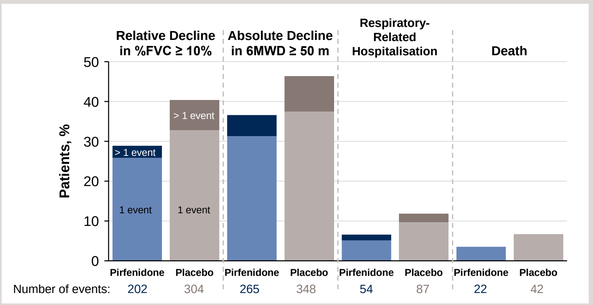
RESULTS

Table 1. Demographics and baseline characteristics

Characteristic*	Pirfenidone (n = 623)	Placebo (n = 624)
Age, years	68.0 (45–80)	68.0 (40–80)
Male, %	74.3	74.5
White, %	95.0	94.6
%FVC	71.1 (48–124)	70.3 (48–136)
%DLco	44.0 (27–81)	44.1 (27–170)
6MWD, m	400.0 (112–731)	413.5 (163–716)
UCSD SOBQ score	31.0 (0–100)	31.5 (0–105)
FEV_1/FVC ratio	0.84 (0.69–0.99)	0.84 (0.69–0.97)
Supplemental O_2, %	24.9	24.0
HRCT ("definite IPF"), %	92.3	93.6
Time since diagnosis, years	1.1 (> 0–5)	1.1 (> 0–4)

6MWD, 6-minute walk distance; %DLco, percent predicted diffusing capacity of carbon monoxide; %FVC, percent predicted forced vital capacity; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HRCT, high-resolution computed tomography; UCSD SOBQ, University of California–San Diego Shortness of Breath Questionnaire.
* Values expressed as the median (range) unless otherwise indicated.

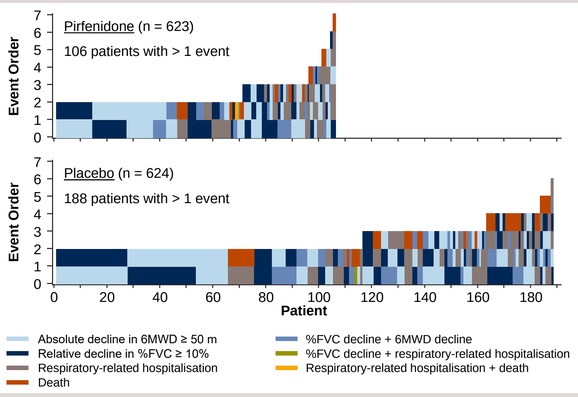
Figure 2. Disease progression events at 12 months in patients treated with pirfenidone vs. placebo*



6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity.
* Pirfenidone, n = 623. Placebo, n = 624

- Declines in %FVC and 6MWD comprised the majority of progression events **(Figure 2)**
- The recurrence of the same event type within 12 months was infrequent

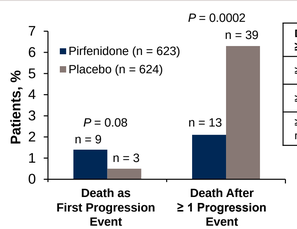
Figure 3. Incidence and sequence of multiple events at 12 months in patients treated with pirfenidone vs. placebo



6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity.

- A lower proportion of patients who received pirfenidone had > 1 event compared with those who received placebo (17.0% vs. 30.1%; P < 0.0001; **Figure 3**)

Figure 4. Incidence of death as a progression event up to 12 months in patients treated with pirfenidone vs. placebo

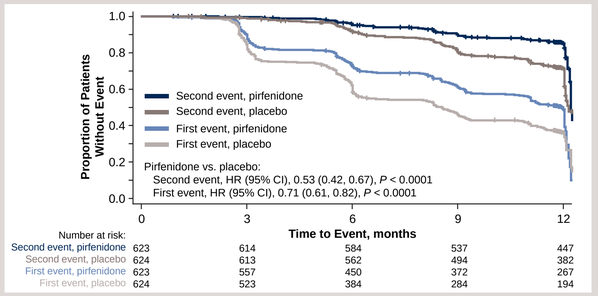


Death After ≥ 1 Progression Event	Pirfenidone (n = 13)	Placebo (n = 39)
≥ 1 prior %FVC decline	7	25
≥ 1 prior 6MWD decline	7	18
≥ 1 prior respiratory-related hospitalisation	10	34

6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity.

- Death following ≥ 1 progression event occurred significantly less frequently in patients treated with pirfenidone compared with placebo (2.1% vs. 6.3%, P = 0.0002; **Figure 4**)

Figure 3. Incidence and sequence of multiple events at 12 months in patients treated with pirfenidone vs. placebo



6MWD, 6-minute walk distance; %FVC, percent predicted forced vital capacity.

- Patients who received pirfenidone were at lower risk of experiencing a single progression event and at lower risk of experiencing a second progression event compared with placebo **(Figure 5)**

CONCLUSIONS

- Pirfenidone treatment significantly reduced the incidence of multiple progression events compared with placebo
- This analysis suggests that continued treatment with pirfenidone confers a benefit despite the occurrence of any single disease progression event
- A multiple events-driven approach may allow for shortening the duration and reducing the number of patients in clinical trials

DISCLOSURES

Steven D. Nathan, MD

- Personal financial relationships with commercial interests relevant to this presentation during the past 12 months
  - **Consultant:** Actelion, Bayer, Boehringer Ingelheim, Geno, Genentech/Roche, Gilead, United Therapeutics
  - **Speakers bureau:** Bayer, Boehringer Ingelheim, Gilead, Genentech/Roche, United Therapeutics
- Relevant institutional financial interests
  - **Research funding:** Actelion, Bayer, Boehringer Ingelheim, Gilead, Genentech/Roche, United Therapeutics

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For more information, go to:
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