# Characteristics and management of patients with idiopathic pulmonary fibrosis treated with pirfenidone capsule or tablet formulation

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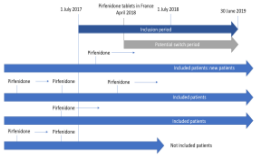
## INTRODUCTION

- Idiopathic pulmonary fibrosis (IPF) disease is a chronic inflammatory progressive lung disorder characterized by scare tissue within the lung and involving activated macrophages and alveolar epithelial cells. [1] [2]
- Pirfenidone (Esbriet®) is indicated in the treatment of the IPF and is now available in tablets instead of capsules.
- This study aims to describe management of patients treated with pirfenidone and the course of change of treatment between the 2 dosage formulations.

## METHODS

- This retrospective, secondary data use study collected data from an existing, broader cohort, the RaDiCo-PID cohort of patients who received at least one dose of pirfenidone during the study period.

**Figure 1: Study Design**




- The RaDiCo-PID cohort is a longitudinal, national, non-randomized, retrospective and prospective multicentre study assessing any patients diagnosed with IPF based on current guidelines. [3] Recruiting centres and patients were sought by relying on the support of the Rare Disease Network for rare pulmonary diseases (RespiFIL: Filière Maladies Rares des Maladies Respiratoires Rares) and the involvement of French patient associations.
- **Main inclusion criteria:** The target study population included all IPF patients recruited in the RaDiCo-PID cohort treated at least once with pirfenidone between 1 July 2017 and 30 June 2019.
- **Exclusion criterias:** Participation in a trial involving an anti-fibrotic drug or an investigational drug in the IPF indication; patients aged < 18 years.

**Objectives**

**Primary objective:** to describe patients treatment with pirfenidone and the change of treatment between the two dosage formulations (capsule or tablet).

**Secondary objectives:** to assess treatment persistency and describe IPF patients (socio-demographic and medical characteristics and quality of life).

## RESULTS

- A total of 826 patients were recruited between 1 July 2017 and 30 June 2019.
- Three populations were defined (Pop1, Pop2 and Pop3) (Figure 2).

**Figure 2 : Patient Flow chart of the study**


- A total of 288 patients were treated with pirfenidone (83% started with pirfenidone capsule). Among them 162 patients (56.3%) newly initiated pirfenidone (69.8% starting with pirfenidone capsule).
- There were no meaningful differences between the baseline characteristics (gender, age at inclusion/at diagnosis) by formulation of the 256 pts treated with pirfenidone during the potential switch.

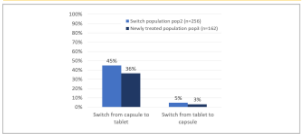
**Table 1: Demography at inclusion - Included population, pop1 (N=288)**

| | Tablet (N=48) | Capsule (N=118) | Switch (N=122) | Total (N=288) |
|---|---|---|---|---|
| **Mean age at inclusion, year (SD)** | 71.2 (8.7) | 72.8 (8.0) | 72.7 (8.1) | 72.5 (8.2) |
| **Men, n (%)** | 45 (93.8%) | 88 (74.6%) | 110 (90.2%) | 243 (84.4%) |
| **Mean FEV FVC fraction (SD)** | 0.7 (0.5) | 0.7 (0.1) | 0.7 (0.1) | 0.7 (0.1) |
| **Tobacco status, n (%)** | | | | |
| No | 8 (16.7%) | 36 (30.8%) | 28 (23.0%) | 72 (25.1%) |
| Active | - | 5 (4.3%) | 5 (4.1%) | 10 (3.5%) |
| Passive | - | 5 (4.3%) | 2 (1.64%) | 7 (2.4%) |
| Deprived | 40 (83.3%) | 71 (60.7%) | 87 (71.31%) | 198 (69.0%) |
| **Mean duration between diagnosis and treatment, month (SD)** | 12.2 (33.1) | 10.1 (17.8) | 25.8 (23.2) | 17.1 (24.1) |
| **Concomitant treatments, n (%)** | | | | |
| Oxygen | 16 (34.8%) | 40 (48.2%) | 44 (38.3%) | 100 (41.0%) |
| Steroids | 15 (33.3%) | 44 (53.7%) | 40 (35.1%) | 99 (40.7%) |
| **Comorbidities and Risk factors, n (%)** | | | | |
| Cardiovascular disease | 33 (70.2%) | 86 (75.4%) | 100 (83.3%) | 219 (77.9%) |
| Gastrointestinal disease | 16 (33.3%) | 53 (46.9%) | 59 (50.4%) | 128 (46.0%) |
| Endocrine disease | 16 (34.8%) | 33 (29.7%) | 35 (30.2%) | 84 (30.8%) |
| **Symptoms, n (%)** | | | | |
| Dyspnea | 40 (90.9%) | 95 (88.0%) | 106 (93.8%) | 241 (90.9%) |
| Cough | 33 (76.7%) | 80 (74.8%) | 75 (66.4%) | 188 (71.5%) |
| Fatigue | 5 (10.6%) | 12 (10.7%) | 18 (15.1%) | 35 (12.6%) |

**Formulation switch**

- Within the switch population (patients treated with pirfenidone, at least until April 2018), the switch rate from capsule to tablets was 45% with a 95%CI= [38.83; 51.02]. Within the newly treated population (first pirfenidone prescription after 1 July 2017), the switch rate from capsule to tablet formulation was 36%.
- The reverse switch (change from tablet to capsule formulation) was low within the two populations with 3% or 5% of the population respectively (Figure 3).

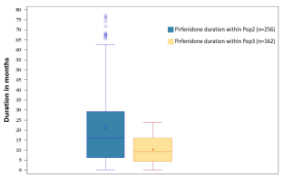
**Figure 3: Formulation switch of pirfenidone within switch population pop2 (N=256) and newly treated pop3 (N=162)**




**Treatment duration**

- The duration of pirfenidone treatment was assessed within switch population and newly treated population.
- Overall, mean treatment duration was 21.5 months (±18.7) and median (Q1;Q3) was 16.2 [6.3; 29.3] with a mean dose of 2106.7 (±460.7) mg/day.
- In newly treated patients at inclusion (Pop3), the mean treatment duration was 10.3 ±7.01 months.

**Figure 4: Duration of pirfenidone treatment in months – switch population pop2 (N=256) and newly treated pop3 (N=162)**



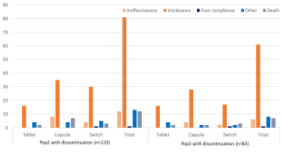

**Treatment discontinuation and causes**

- Overall, 119/256 patients (46.5%) discontinued treatment, 81/119 (68.1%) for intolerance and 21/119 (10.1%) for ineffectiveness.
- There were globally less discontinuations in the tablets and switch groups compared to the capsules only group.

**Table 2: Treatment discontinuation within patients treated up to 1st April 2018 - pop2 and newly treated - pop3**

| | Tablet | Capsule | Switch | Total |
|---|---|---|---|---|
| **Switch population: pop2** | 48 | 89 | 119 | 256 |
| **Treatment discontinuation** | 22 (45.8%) | 54 (60.7%) | 43 (36.1%) | 119 (46.5%) |
| **95%CI** | [36.68; 54.79] | [51.90; 69.45] | [27.50; 44.77] | [37.52; 55.45] |
| **Newly treated population: pop3** | 48 | 53 | 61 | 162 |
| **Treatment discontinuation** | 22 (45.8%) | 36 (67.9%) | 25 (41.0%) | 83 (51.2%) |
| **95%CI** | [33.33; 58.34] | [56.21; 79.64] | [28.64; 53.33] | [38.69; 63.78] |

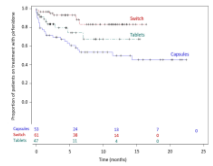
**Figure 5: Causes of treatment discontinuation within patients with discontinuation in switch population pop2 (N=256) and newly treated pop3 (N=162)**




**Time to pirfenidone discontinuation**

- As shown in Figure 6, there were globally less discontinuation in the tablets and switch groups compared with the capsules only group.

**Figure 6: Kaplan-Meier analysis of time to pirfenidone discontinuation (N=162)**




**Safety**

- Adverse events were reported in 112 (38.9%) patients and serious adverse events were reported in 5 (4.9%) patients.
- The most frequent adverse events are shown in Table 3. All are well known adverse events of pirfenidone described in the Summary of the Product Characteristics.

**Table 3: Most frequents adverse events – Patients with events (N=112)**

| N (%) | Patients with events |
|---|---|
| Skin rash | 33 (29.5%) |
| Fatigue | 23 (20.5%) |
| Weight loss | 22 (19.6%) |
| Anorexia | 20 (17.9%) |
| Diarrhea | 13 (11.6%) |
| Nausea | 11 (9.8%) |

- Liver function tests showed AST levels ≥ 3N in 41 (25.3%) and ALT levels ≥ 3N in 42 (26%) patients, bilirubin levels were normal in 153 (94%) patients.

## CONCLUSION

- This study shows real-life data in patients with IPF treated with or switching between the two dosage forms of pirfenidone (capsule or tablet).
- Among newly diagnosed patients 30% started pirfenidone treatment with the tablet formulation.
- The switch rate from capsule to tablet population was 45%.
- Half of the patients who switched formulation did it within the first 10 months of the new formulation dispensation becoming available.
- The rate of reverse switch from tablet to capsule was very low.
- These observations suggest a good acceptability of the tablet formulation by patients and physicians.

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**DISCLOSURES**

V. Cottin: Roche, Boehringer Ingelheim, Galapagos, Galectin, Fibrogen and Shionogi

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