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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 scar 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 RadCo-PiD cohort of patients who received at least one dose of pirfenidone during the study period.

Figure 1: Study Design



- The RadCo-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 (ResPiR): 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 RadCo-PiD cohort treated at least once with pirfenidone between 1 July 2017 and 30 June 2019.
- Exclusion criteria:** 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.

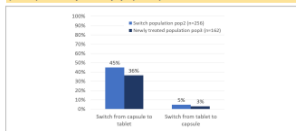
Table 1: Demography at inclusion - included population, pop1 (N=288)

	Tablet (N=81)	Capsule (N=138)	Switch (N=109)	Total (N=288)
Mean age at inclusion, year (SD)	71.2 (8.7)	71.2 (8.7)	71.2 (8.7)	71.2 (8.7)
Sex, n (%)	41 (50.6%)	69 (50.0%)	52 (47.7%)	162 (56.3%)
Mean FVC % Predicted (SD)	67.1 (10.5)	67.1 (10.5)	67.1 (10.5)	67.1 (10.5)
Smoking status, n (%)				
N/A	8 (9.9%)	34 (24.6%)	38 (34.9%)	72 (25.0%)
Active	1 (1.2%)	1 (0.7%)	1 (0.9%)	3 (1.0%)
Passive	1 (1.2%)	2 (1.4%)	2 (1.8%)	5 (1.7%)
Unknown	40 (49.4%)	71 (51.3%)	67 (61.5%)	178 (61.5%)
Mean duration between diagnosis and treatment, month (SD)	12.2 (18.1)	10.1 (17.4)	25.8 (24.3)	17.3 (24.4)
Concomitant treatments, n (%)				
Corticosteroids	15 (18.5%)	40 (29.0%)	44 (40.4%)	99 (34.4%)
Immunosuppressants and Risk factors, n (%)				
Cardiovascular disease	33 (40.9%)	86 (61.6%)	100 (91.7%)	219 (76.0%)
Auto-immune disease	34 (42.0%)	59 (42.8%)	39 (35.8%)	132 (46.0%)
Endocrine disease	35 (43.2%)	33 (23.9%)	35 (32.1%)	103 (35.8%)
Symptoms, n (%)				
Dyspnea	46 (56.9%)	95 (68.8%)	106 (97.2%)	247 (85.7%)
Cough	33 (40.9%)	82 (59.4%)	75 (68.8%)	188 (65.3%)
Weight loss	1 (1.2%)	2 (1.4%)	38 (34.9%)	41 (14.2%)

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 [38.8; 51.0]. 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).

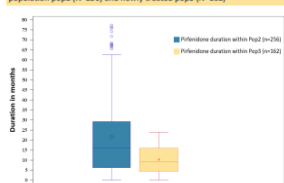
Figure 3: Formulation switch of pirfenidone within switch population pop2 (N=256) and newly treated pop3 (N=162)



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 (IQR) 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)



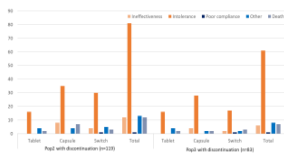
Treatment discontinuation and causes

- Overall, 119/256 patients (46.5%) discontinued treatment, 81/119 (68.1%) for intolerance and 21/119 (10.1%) for inefficacy.
- 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	123	256
Treatment discontinuation	22 (45.8%)	54 (60.7%)	43 (35.0%)	119 (46.5%)
IPFCD	10 (20.8%)	31 (34.8%)	27 (22.0%)	68 (26.5%)
Newly treated population: pop3	46	55	65	162
Treatment discontinuation	22 (47.8%)	30 (54.5%)	25 (38.5%)	77 (47.5%)
IPFCD	10 (21.7%)	24 (43.6%)	18 (27.7%)	52 (31.5%)

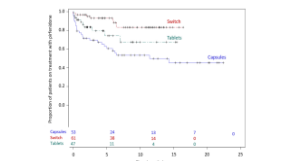
Figure 5: Causes of treatment discontinuation within patients with discontinuation in switch population pop2 (N=256) and newly treated pop3 (N=162)



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 frequent 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%)
Acid reflux	20 (17.9%)
Dyspnea	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, Sanofi, Galvani, Fibrogen and Shionogi