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

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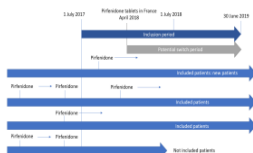
INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) disease is a chronic inflammatory progressive lung disorder characterized by scarce tissue within the lung and involving activated macrophages and alveolar epithelial cells.^[1,2]
 Pirfenidone (Ebsriet[®]) 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 (ResPIL: 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.

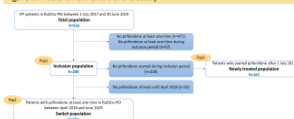
Objectives

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)

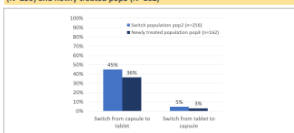
	Tablet (N=88)	Capsule (N=192)	Switch (N=88)	Total (N=288)
Mean age at inclusion, year (SD)	71.2 (8.7)	71.2 (8.5)	71.7 (8.3)	71.3 (8.2)
Mean, n (%)	41 (50.0%)	83 (42.7%)	110 (125.2%)	244 (84.4%)
Mean FVC fraction (SD)	0.7 (0.2)	0.7 (0.2)	0.7 (0.3)	0.7 (0.3)
Gender, n (%)				
Male	8 (9.1%)	36 (18.8%)	38 (43.2%)	72 (25.1%)
Female	-	54 (28%)	54 (61.6%)	102 (35.3%)
Previous, n (%)	5 (5.7%)	21 (10.9%)	7 (7.9%)	23 (7.9%)
Diagnosed, n (%)	40 (45.5%)	73 (38.0%)	81 (92.1%)	188 (65.3%)
Mean duration between diagnosis and treatment, month (SD)	12 (10.1)	10 (11.4)	25.4 (24.3)	17.3 (24.4)
Concomitant treatments, n (%)				
Corticosteroids	15 (17.0%)	40 (20.8%)	44 (50.0%)	100 (34.6%)
Immunosuppressants	11 (12.5%)	44 (22.9%)	40 (45.5%)	99 (34.3%)
Cardiovascular disease, n (%)	33 (37.5%)	86 (44.8%)	100 (113.6%)	219 (76.1%)
Respiratory disease, n (%)	33 (37.5%)	86 (44.8%)	86 (97.7%)	205 (71.2%)
Endocrine disease, n (%)	33 (37.5%)	33 (17.2%)	33 (37.5%)	100 (34.7%)
Symptoms, n (%)				
Dyspnea	40 (45.5%)	55 (28.6%)	100 (113.6%)	244 (84.7%)
Cough	33 (37.5%)	82 (42.7%)	75 (85.2%)	188 (65.3%)
Hoarse	5 (5.7%)	22 (11.5%)	18 (20.5%)	45 (15.6%)

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 [38.8; 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).

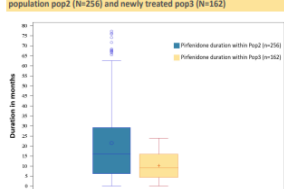
Figure 3: Formulation switch of pirfenidone within switch population pop2 (N=256) and newly treated pop3 (N=162)



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 2166.7 (1460.7) 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)



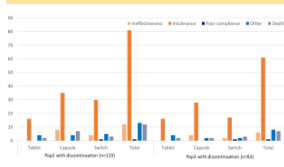
Treatment discontinuation and causes

Overall, 119/256 patients (46.5%) discontinued treatment, 81/119 (68.1%) for intolerance and 11/119 (10.1%) for effectiveness.
 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	110	248
Treatment discontinuation	22 (45.8%)	54 (60.7%)	43 (38.2%)	119 (47.9%)
Effect	18 (37.5%)	31 (34.8%)	17 (15.3%)	66 (26.6%)
Newly treated population - pop3	48	82	82	212
Treatment discontinuation	22 (45.8%)	38 (46.3%)	21 (25.6%)	81 (38.2%)
Effect	18 (37.5%)	24 (29.3%)	14 (17.1%)	56 (26.4%)

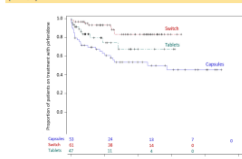
Figure 5: Causes of treatment discontinuation within patients with discontinuation in switch population pop2 (N=256) and newly treated pop3 (N=162)



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
33 (29.5%)	Skin rash
22 (19.6%)	Fatigue
22 (19.6%)	Weight loss
20 (17.9%)	Abdominal pain
13 (11.6%)	Dyspnea
11 (9.8%)	Nausea

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