A real-world retrospective study on the utilization of anti-fibrotic drugs in Greece during the period 2019-2023

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INTRODUCTION

- Interstitial lung diseases (ILDs) constitutes of a heterogeneous group of chronic, progressive, and fatal diseases affecting the interstitium and/or the alveoli leading to irreversible loss of lung function[1,2].
- During the last decade specialized drugs have been introduced, namely pirfenidone and nintedanib, with anti-fibrotic properties[3,4].
- Pirfenidone is indicated for the treatment of idiopathic pulmonary fibrosis (IPF) while nintedanib for the treatment of IPF, chronic progressive ILDs and systemic sclerosis associated ILD (SSc-ILD).
- Clinical efficacy and safety of both drugs have been demonstrated in IPF patients[5,6] while the recently updated clinical guidelines by the European Respiratory Society recommend their utilization[7].
- However, there is lack of real-world data concerning the adoption of anti-fibrotic agents for the Greek market, given that both drugs are associated with adverse events that may require dose adjustments or even treatment discontinuation particularly for elderly population[8,9].
- Therefore, studies generating real-world evidence are deemed necessary to define the number of patients as well as the population demographics.

OBJECTIVES

We aimed to evaluate the utilization patterns of available anti-fibrotic medications in the Greek market over the period 2019–2023.

METHODS

Study design: Observational, retrospective, longitudinal cohort study

Patients: Patients receiving anti-fibrotic therapy - pirfenidone (any brand) and nintedanib (Ofev®)- between January 1, 2019, and December 31, 2023, were included. Data was extracted from the Greek National Electronic Prescription Database (IDIKA). Patients were categorized into two subgroups based on ICD-10 codes: (a) IPF (ICD-10 code J84.1), and (b) progressive pulmonary fibrosis (PPF), defined as any ICD-10 code other than IPF suggesting fibrosing lung disease.

Data extraction: all prescriptions issued through IDIKA from Jan 1, 2019, to Dec 31, 2023, under the ATC codes L04AX05, L01XE31 (**Figure 1**).

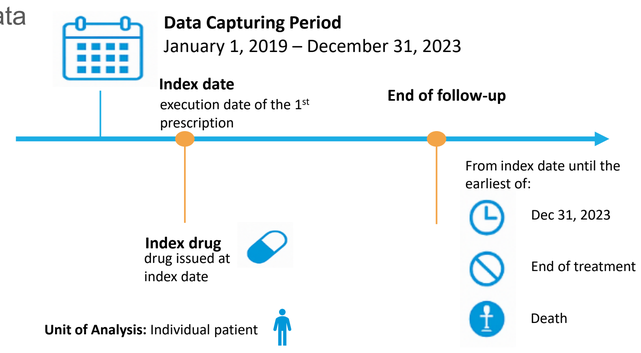
Pharmacoutilization-based epidemiology

- To estimate the annual incidence and prevalence of patients with IPF and PPF in Greece, the numerator was defined as the number of patients diagnosed with IPF or PPF with at least one executed prescription in the corresponding year of the study period (2019 – 2023) for which the prevalence or incidence was estimated.
- The denominator was the total adult population as obtained from the 2021 Greek Census.
- Both incidence and prevalence were expressed as cases per 100,000 population.

Data analysis:

All analyses were descriptive and were performed using the statistical program STATA 17.0.

Figure 1: Data capturing period & patients' follow-up.



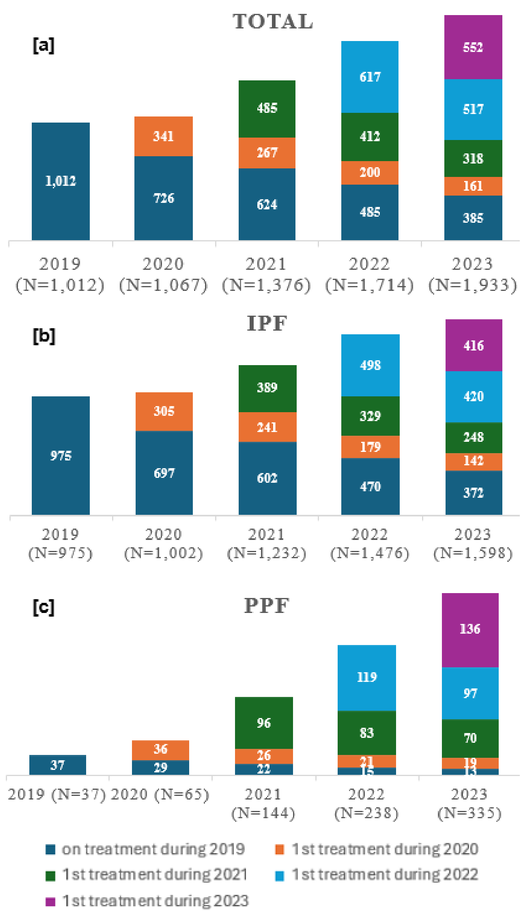
RESULTS

Table 1: Demographic characteristics of patients on anti-fibrotic treatment during the 2019-2023 period.

Characteristics	Patients on anti-fibrotic treatment	IPF	PPF	SSc-ILD	RA-ILD
	N=3,007	N=2,583	N=424	N=197	N=52
Sex, n (%)					
Male	2073 (69%)	1917 (74%)	156 (37%)	35 (18%)	23 (44%)
Female	934 (31%)	666 (26%)	268 (63%)	162 (82%)	29 (56%)
Mean (SD) age at index date, years	71.6 (9.3)	72.6 (8.4)	65.3 (11.9)	59.1 (12.0)	69.3 (8.6)
Age at index date (years), n (%)					
< 50	83 (3%)	38 (2%)	45 (11%)	41 (21%)	
50 – 65	572 (19%)	420 (16%)	152 (36%)	98 (50%)	14 (27%)
66 – 75	1238 (41%)	1101 (43%)	137 (32%)	46 (23%)	25 (48%)
76+	1114 (37%)	1024 (40%)	90 (21%)	12 (6%)	13 (25%)

Note: SSc-ILD and RA-ILD are subgroups of the PPF group. **Abbreviations**: ILD; interstitial lung disease, IPF; idiopathic pulmonary fibrosis, PPF; progressive pulmonary fibrosis, RA; rheumatoid arthritis, SD; standard deviation, SSc; systemic sclerosis.

Figure 2: Number of patients on anti-fibrotic treatment each year, stratified by the year of first treatment initiation overall [a], and by diagnosis subgroup: [b] IPF, [c] PPF.



Patient characteristics

- Among 3,007 patients identified as receiving anti-fibrotic treatment, 85.9% were diagnosed with IPF and 14.1% with PPF. The majority of patients were male (68.9%), with a mean (SD) age of 71.6 (9.3) years(**Table 1**).

Patients on anti-fibrotic treatment

- An increasing number of patients on anti-fibrotic medication was introduced each year reaching a peak at 2022 (n=617) (**Figure 2a**).

IPF vs PPF

- The number of newly treated (naïve) IPF patients increased annually, ranging from 305 to 498 in 2020 and 2022, respectively. In the initial year (2019) 975 IPF patients were recorded. The corresponding number of newly treated PPF patients increased also annually ranging from 36 (2020) to 136 (2023) patients. The initial number of PPF patients recorded (2019) was 37 patients (**Figure 2b, 2c**).
- Among IPF naïve patients, 79%, 85%, and 84% remained on treatment one year after initiation in 2020, 2021, and 2022, respectively. The corresponding figures for PPF patients were 72%, 86%, and 82% (**Figure 2b, 2c**).
- The number of naïve patients initiating anti-fibrotics for PPF increased by 167% in 2021, 231% in 2022, 278% in 2023, compared with 2020, reflecting its growing clinical adoption and the European Medicines Agency approval for PPF in 2023. Uptake likely began slightly before approval, driven by early access and increasing physician awareness (**Figure 2c**).

Adoption of anti-fibrotic agents in naïve IPF patients

- Since 2020, the number of naïve patients initiating nintedanib for IPF increased by 28% in 2021, 79% in 2022 and 52% in 2023 (**Table 2**).
- The number of naïve patients initiating pirfenidone for IPF increased by 27% in 2021 and 28% in 2022, remaining stable thereafter (+2% in 2023) compared with 2020 (**Table 2**).

Table 2: Number of naïve patients (N=1,995) for each year stratified by initial drug and by year of treatment.

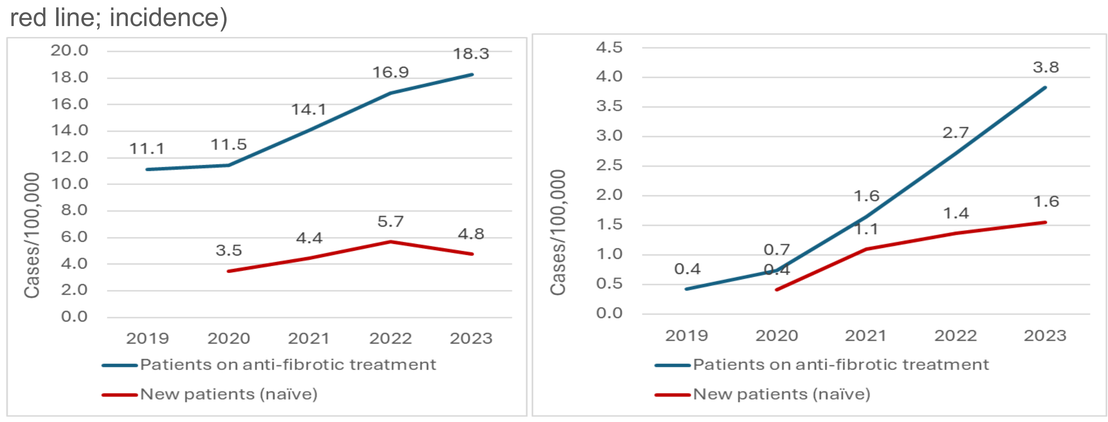
No of naive patients initiating treatment each year	IPF	
	Nintedanib N=1,169	Pirfenidone N=439
2020	209	96
2021	267	122
2022	375	123
2023	318	98

Notes: Only patients with their first prescription after January 1, 2020, were classified as new cases (naïve). Ofev® (nintedanib) was approved in 2023 for the treatment of progressive pulmonary fibrosis.

Epidemiology

- Pharmacoutilization-based prevalence peaked in 2023 at 18.3 and 3.8 cases per 100,000 population for IPF and PPF, respectively. Incidence rates ranged between 3.5–5.7/100,000 population for IPF and 0.4–1.6/100,000 population for PPF throughout the study period (**Figure 3**).

Figure 3: Pharmacoutilization-based epidemiology (left, IPF; right, PPF) (blue line; prevalence, red line; incidence)



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CONCLUSIONS

- This is the biggest cohort reported concerning the utilization of anti-fibrotic therapies in Greece.
- The findings suggest increasing adoption of anti-fibrotic therapies in Greece, over the past five years.
- We demonstrate consistent patient retention on treatment and a growing recognition of fibrosing ILDs beyond IPF.
- Although our approach contains inherent limitations considering a potential underestimation of disease burden by excluding untreated or mildly affected individuals, the pharmacoutilization rates demonstrate an increasing prevalence of IPF and ILDs in general in the Greek population.
- We expect that these findings will inform future healthcare planning and support the need for broader clinical access and awareness regarding anti-fibrotic therapy in IPF and PPF.

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