Pirfenidone effectiveness in idiopathic pulmonary fibrosis with different radiologic patterns

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Introduction

The registration trials of pirfenidone in idiopathic pulmonary fibrosis (IPF) included mosty patients with definite usual interstitial pneumonia (UIP) pattern and the evidence for effect of this drug in the patients with probable/possible UIP patterns is missing. Aim of the study was to assess the effectiveness of pirfenidone in patients with different degrees of IPF diagnostic certainty of radiologic patterns.

Patients and methods

The study included patients treated with pirfenidone with admission visit for the EMPIRE registry in the period from 1 January 2015 to 31 December 2018, with follow-up cut-off as of 29 October 2019. IPF was diagnosed according to the 2011 ATS/ERS/JRS/ALAT criteria. Central radiological readings were not carried out; the patients are enrolled by experienced interstitial lung diseases centres in various European countries.

Overall survival (OS) and progression-free survival (PFS) rates, and time trends of lung functions from the pirfenidone therapy initiation were analysed and compared in patients with different radiologic patterns (UIP, Possible UIP, Inconsistent with UIP). The statistical models were adjusted for age, height, sex, dyspnoea, and forced vital capacity (FVC) at baseline.

Results

808 patients treated with pirfenidone were included in the analysis: 582 with UIP pattern, 191 with possible UIP pattern, and 35 with inconsistent with UIP pattern. The groups did not differ in number of associated disorders and GAP index.

No consistent trends and differences between the radiological groups were observed in terms of the lung functions (Table 1). FVC and diffusing capacity for carbon monoxide (DLCO) remained stable in the UIP and Possible UIP group, and declined below or close to the level of statistical significance in the Inconsistent with UIP group. On the other hand, the UIP group was the only one with a statistically significant decline of the 6-minute walking distance (6MWD) test.

Overall survival and progression-free survival rates during 3-year follow-up were similar across all diagnostic groups (Figure 1 and 2). The OS rates ranged from 45.9% to 62.3%, the PFS rates ranged from 3.6% to 18.3%. Median time of OS was not reached in the UIP and Possible UIP group. Median time of PFS was 15.3, 14.7, and 20.3 months in the UIP, Possible UIP and Inconsistent with UIP group (Table 2).

Conclusions

Our study shows on a large cohort of IPF patients that pirfenidone effect is similar and consistent in all patients with IPF, regardless radiologic patterns.

UIP and Possible UIP groups profit from pirfenidone treatment in a similar way both with regard to lung functions and survival rates. The limitation of the study is low number of the patients with inconsistent with UIP pattern, however it is logical, since most of the patients with UIP have either UIP or possible UIP pattern. Also the lack of central reading of high resolution computed tomography (HRCT) images may influence the results, on the other hand the centres have radiologists experienced in interstitial lung disease and, moreover, the EMPIRE registry is a real-world registry.

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The study was approved by Ethics Committee of Thomayer Hospital and Institute for Clinical and Experimental Medicine, Prague, Czech Republic, and local ethics committees in individual countries and sites involved in the registry.

Disclosures

MV received fees from Boehringer Ingelheim and Roche for consultancy, advisory boards and presentations, and an independent grant from Roche; MSte received fees for advisory boards from Boehringer Ingelheim, Roche and Teva; NM received fees for advisory boards and presentations from Boehringer Ingelheim and Roche; KL received payments for lectures, advisory boards, research and congress participation from Boehringer Ingelheim and Roche; JTT was an advisory board member and received fees for lectures from Boehringer Ingelheim and Roche; MStu received research grants from Boehringer Ingelheim and Roche; DJ was an advisory board member and received fees from Boehringer Ingelheim and Roche; NS was an advisory board member for Boehringer Ingelheim; VM, MH, SL, and LD declare no conflicts of interest.

Table 1. Annual rates of lung functions and physical activity decline in patients with pirfenidone in HRCT diagnostic groups

Parameter	UIP	Possible UIP	Inconsistent with UIP
FVC (% pred.)	-0.10 (-0.26; 0.06), p=0.229 (N=372)	-0.11 (-0.38; 0.17), p=0.441 (N=139)	-0.80 (-1.43; -0.16), p=0.014 (N=18)
DLCO (%)	-0.14 (-0.30; 0.02), p=0.083 (N=349)	-0.18 (-0.43; 0.08), p=0.179 (N=135)	-0.59 (-1.19; 0.01), p=0.052 (N=15)
6MWD (m)	-1.95 (-3.47; -0.42), p=0.012 (N=216)	1.48 (-0.77; 3.72), p=0.198 (N=81)	-4.98 (-10.91; 0.95), p=0.100 (N=15)

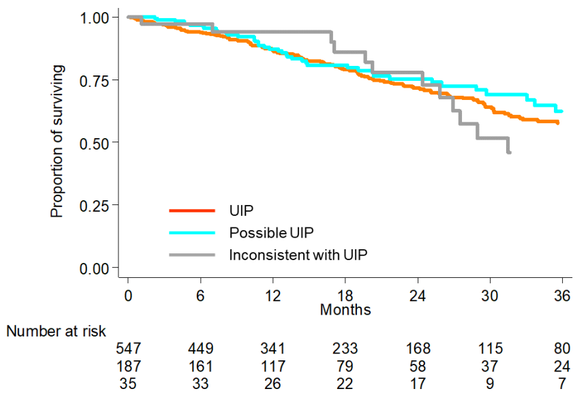

Figure 1. Overall survival of patients with pirfenidone in HRCT diagnostic groups

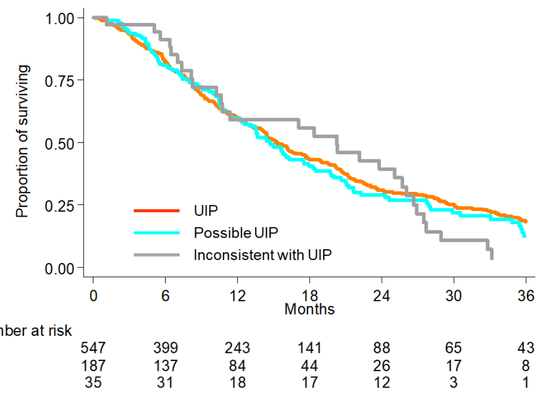

Figure 2. Progression-free survival of patients with pirfenidone in HRCT diagnostic groups

Table 2. Characteristics of overall survival and progression-free survival of patients with pirfenidone in HRCT diagnostic groups

	Median OS (months)	3-year OS (%, 95% CI)	p	Median PFS (months)	3-year PFS (%, 95% CI)	p
UIP	--	0.576 (0.512; 0.636)		15.3	0.183 (0.141; 0.229)	
Possible UIP	--	0.623 (0.503; 0.722)	0.640	14.7	0.125 (0.066; 0.203)	0.452
Inconsistent with UIP	31.5	0.459 (0.237; 0.656)		20.3	0.036 (0.003; 0.154)	
Possible UIP – Adjusted HR (95% CI)	0.971 (0.767; 1.229), p=0.805			0.971 (0.767; 1.229), p=0.805		
Inconsistent with UIP – Adjusted HR (95% CI)	1.033 (0.635; 1.680), p=0.897			1.033 (0.635; 1.680), p=0.897		