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Clinical Study Synopsis for Public Disclosure

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1. ABSTRACT

Name of company: Boehringer Ingelheim (BI)			
Name of finished medicinal product: Ofev (BI)			
Name of active ingredient: Nintedanib			
Report date: 10 Sep 2020	**Study number:** 1199-0375	**Version/Revision:** 1.0	**Version/Revision date:** N/A
Title of study:	Characteristics of IPF patients initiating nintedanib, pirfenidone or no antifibrotic treatment in the US		
Keywords:	Idiopathic pulmonary fibrosis, nintedanib, pirfenidone, patient characteristics, EMR		
Rationale and background:	Idiopathic Pulmonary Fibrosis (IPF) is a debilitating, life-limiting condition with a median survival range of 2.5 to 3.5 years from the time of diagnosis and an estimated incidence of 6.8-16.3 per 100,000 persons. Despite its rarity, the economic burden of IPF is significant, with the annual medical cost to the US healthcare system estimated at close to $2 billion in 2012. The goals of treatment for IPF are to slow disease progression, reduce symptoms, prevent acute exacerbations, and prolong survival. The treatment options for IPF were limited until the FDA approved two products in October 2014, Ofev (nintedanib, BI) and Esbriet (pirfenidone, Genentech), that slowed disease progression.		
Research question and objectives:	To understand characteristics of patients treated with nintedanib and pirfenidone, as well as patients who did not receive a prescription for an antifibrotic treatment. The primary objective was to describe and compare demographic, clinical, and other characteristics of IPF patients initiating nintedanib, pirfenidone, or not receiving prescription antifibrotic treatment. The secondary objective was to compare and contrast the probability of receiving nintedanib vs. pirfenidone and nintedanib or pirfenidone vs. being untreated in IPF patients using baseline patient characteristics.		
Study design:	A retrospective cohort database study		
Setting:	US population receiving healthcare in the ambulatory setting		
Subjects and study size, including dropouts:	This study included 347 IPF patients initiating nintedanib, 423 patients initiating pirfenidone, and 12,494 patients not receiving antifibrotic treatment.		
Variables and data sources:	The following demographic and clinical characteristics as well as medical interventions for IPF during the 12-month baseline period (pre-treatment) were evaluated and compared between overall cohorts and subgroups		

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	stratified on gender and index year: • Demographic characteristics (e.g., age, gender, race/ethnicity, geographic region, insurance type) • Clinical characteristics (e.g., selected comorbidities, weight and body mass index [BMI], blood pressure, smoking status, laboratory measures, pulmonary function tests) • Pharmacological interventions (e.g., index medication dose, time from the earliest diagnosis of IPF to index medication, other IPF treatments, bronchodilators, corticosteroids) • Non-pharmacological interventions (e.g., surgical procedures, supportive therapies, diagnostic procedures) The data source for this study was IQVIA's GE Centricity EMR database from October 2013 to October 2018.		
Results:	347 nintedanib-treated and 423 pirfenidone-treated patients were included in the study, as well as 12,494 untreated IPF patients. The mean age (standard deviation (SD)) at index was similar among the cohorts but slightly lower among untreated patients, ranging from 70.9 (8.9) for untreated to 72.1 (6.8) for pirfenidone patients. Among the two treated cohorts, about 88% of patients were White, while the untreated cohort had a slightly higher proportion of other and unknown race and consisted of 80% White patients (both $p<0.05$ vs. untreated). More than two-thirds of treated cohorts were male, while the untreated cohort consisted of equal proportions of each gender ($p<0.0001$ nintedanib vs. untreated and pirfenidone vs. untreated). Payer type was similar between the cohorts. In terms of clinical characteristics, untreated patients had a lower mean (SD) BMI (28.6 (6.5) kg/m^2 compared to nintedanib (29.5 (6.4) kg/m^2) and pirfenidone (30.1 (5.8) kg/m^2) patients (both $p<0.05$ vs. untreated), and categorical BMI showed similar trends. Untreated patients had a higher average CCI (1.1 (1.4)) compared with nintedanib (0.7 (1.0)) and pirfenidone (0.8 (1.1)) (both $p<0.0001$ vs. untreated). Untreated patients had more comorbidities, especially among male patients, including COPD, cardiovascular disorders (including heart failure, stroke, hypertension, and peripheral arterial diseases), mental disorders (depression and dementia), dyslipidaemia, and renal and hepatic impairment than treated patients.		

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	Pirfenidone patients had more obstructive sleep apnea and GERD than untreated patients. Comparing nintedanib to pirfenidone patients, a higher proportion of nintedanib patients had COPD (19.0% vs. 13.7%, p=0.0461); other comorbidities were similar between the treatment groups. In terms of diagnostic procedures and treatment history, a higher proportion of treated patients had below normal oxygen saturation (36.9% and 32.2% for nintedanib and pirfenidone, respectively, vs. 22.6% for untreated; both p<0.05), especially among those indexed in 2014-2016. A higher proportion of treated patients also had evidence of spirometry during the pre-index period (22.8% and 27.4% for nintedanib and pirfenidone, respectively vs. 16.0% for untreated; both p<0.05). For pharmacological interventions, more treated patients received prednisone, inhaled corticosteroids, long-acting beta agonists (LABA) and proton pump inhibitors. Nintedanib was more often prescribed than pirfenidone to patients who received inhaled corticosteroids or LABA in 2017 and 2018. Diagnostic procedures and treatment history were similar for nintedanib vs. pirfenidone patients. In general, stratified analyses on gender and index year (2014-2016 vs. 2017-2018) showed similar results as the overall cohorts. Multivariable logistic regression results were consistent with the above findings, suggesting that older age increases the odds of treatment, as does being overweight (vs. underweight or normal weight), having pre-index spirometry, below normal oxygen saturation, prednisone use, and GERD. Females were less likely to be treated vs. males, as were patients with COPD, cardiovascular diseases (heart failure, stroke, hypertension, peripheral arterial diseases) and severe diseases (dementia, renal or hepatic impairment, cancer). In the multivariable logistic regression model of the odds of receiving nintedanib vs. pirfenidone treatment, overweight patients (vs. underweight or normal weight) and patients with obstructive sleep apnea were less likely to be treated with nintedanib, while patients with COPD and those indexed in 2018 (vs. earlier) were more likely to be treated with nintedanib. Other characteristics were not significant predictors of receiving one treatment over another.		
Discussion:	IPF patients who were female were less likely to be treated than male IPF		

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	patients, as were younger patients compared to those of older age. Although untreated patients were, on average younger, they had more comorbidities such as COPD and cardiovascular disease which may suggest they were sicker and/ or receiving treatments perceived as cautions for IPF treatment. Overweight patients were more likely to be treated compared to underweight or normal weight patients, and when they were treated, were more likely to receive pirfenidone. Having a diagnosis of GERD, low oxygen saturation, treatment with prednisone, or spirometry increased the odds of receiving antifibrotic treatment. Overall, nintedanib patients were very similar to pirfenidone patients, with initiating treatment in 2018 or having COPD increasing the odds of receiving nintedanib over pirfenidone, and being overweight or having obstructive sleep apnea decreasing the odds of receiving nintedanib.		
Marketing Authorisation Holder(s):	N/A		
Names and affiliations of principal investigators:	[redacted]		