Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Nintedanib (Ofev)			
Name of active ingredient: Nintedanib (Ofev)			
Report date: 06 March 2023	**Study number:** 1199-0520	**Version/Revision:** 2.0	**Version/Revision date:** 04 May 2023
Title of study:	Economic burden associated with nintedanib non-adherence among Medicare beneficiaries with IPF		
Keywords:	Nintedanib, adherence, hospitalization, medical costs		
Rationale and background:	Recent systematic reviews found links between medication non-adherence and higher costs (Cutler et al., 2018) and elevated risks of inpatient hospitalization and mortality (Walsh et al., 2019). To our knowledge, however, there have been no studies examining the association between non-adherence and economic burden specific to nintedanib, antifibrotics, or idiopathic pulmonary fibrosis (IPF). A prior study by this study team quantified nintedanib adherence trajectories using group-based trajectory modelling (GBTM) and identified characteristics of patients associated with membership in each trajectory group. A handful of existing studies examined associations between medication non-adherence as measured from GBTM and subsequent health care resource use, although none were specific to the setting of interest here. This study seeks to build on our prior study and fill that gap in knowledge.		
Research question and objectives:	1) Quantify the association between nintedanib adherence trajectory group (as measured from a GBTM) and health care resource use, with a focus on inpatient hospitalization, among patients with IPF. 2) Quantify the association between a patient's nintedanib adherence trajectory group (as measured from a GBTM) and their medical costs among patients with IPF.		
Study design:	This is a non-interventional, retrospective cohort study.		
Setting:	The study sample consists of community-dwelling Medicare beneficiaries with IPF who initiate treatment with nintedanib.		
Subjects and study size, including dropouts:	In the 100% Medicare Part D claims data covering Jan 1, 2014, through Dec 31, 2018, there were 18,733 beneficiaries with at least one claim for nintedanib. The final analytic sample comprised 1,798 beneficiaries.		

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	Inclusion criteria: • Newly initiated nintedanib during 10/01/2014 to 12/31/2018 • Were at least 66 years old as of the date of their first nintedanib prescription claim (index date) • Qualified for Medicare based on age • Had at least 12 months of continuous enrollment in Medicare Parts A, B and D before (baseline period) and 12 months after the index date (follow-up period) • Had at least one inpatient or two outpatient claims (>14 days apart) with a diagnosis code for IPF (ICD-10-CM: J84.112; ICD-9-CM: 516.31) during the baseline period		
Variables and data sources:	This study uses administrative enrollment and claims data from the U.S. federal Medicare program for beneficiaries aged 65 years and older who were continuously enrolled in Original Medicare insurance coverage, including Parts A, B and D. The study uses Medicare data covering the period from October 1, 2013, through December 31, 2020. The main exposure was a five-category measure of adherence trajectory to nintedanib in the year following initiation: highly adherent, moderate adherent, high-then-poor, delayed-poor, and early-poor. The primary outcome was total all cause medical costs, which was calculated as the sum of total amounts paid (by payers and patients) for all medical services. Secondary outcomes were total IPF-related medical costs, which was calculated as the sum of total amounts paid (by payers and patients) for all medical services for an IPF-related reason (at least one IPF diagnosis code), all-cause inpatient hospitalization, and IPF-related inpatient hospitalization. A range of covariates included patient demographic characteristics (e.g., age, sex, race/ethnicity), residential location, clinical characteristics (e.g., comorbidity index, IPF-related health care costs and use), and all-cause health care costs and use. Summary statistics for baseline covariates and follow-up outcomes were computed for the analytic sample overall and stratified by nintedanib adherence trajectory group. Means were compared for joint equality across adherence groups with ANOVA tests; medians with Kruskal Wallis test; and proportions with $\chi 2$ tests.		

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Results:

The mean (standard deviation) age of the nintedanib initiators in the study cohort was 75 (5) years old. The study cohort was predominantly male (61%) and non-Hispanic white (91%).

Primary outcome: In the first follow-up year, the total medical costs for all causes were significantly higher for the high-poor, delayed-poor, and early-poor groups compared to the high adherers group.

Outcome name	Mean (SD)	Difference vs. High	Lower 95% CL	Upper 95% CL	p-value
Total all-cause medical costs ($) in Yr 1					
Early-Poor	18110 (26,365)	5462.41	2520.93	8403.90	0.000
Delayed-Poor	15375.10 (16,998)	2727.38	323.48	5131.27	0.026
High-Poor	17549.74 (27,854)	4902.02	767.60	9036.43	0.020
Moderate	13580.61 (18,479)	932.88	1880.17	3745.94	0.516
High	12647.73 (16,996)	-	-	-	-

Secondary outcomes:

Relative to beneficiaries in the high adherence trajectory group, beneficiaries in the high-poor, delayed-poor, and early-poor groups had higher use of all-cause inpatient hospitalization services.

Outcome name	Percentage	Difference vs. High	Lower 95% CL	Upper 95% CL	p-value
Any all-cause inpatient hospitalization in Yr 1					
Early-Poor	26.8%	6.4%	1.1%	11.7%	0.019
Delayed-Poor	29.4%	9.1%	2.8%	15.3%	0.005
High-Poor	30.0%	9.6%	2.5%	16.8%	0.008
Moderate	22.8%	2.4%	-4.0%	8.9%	0.463
High	20.4%	-	-	-	-

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Relative to beneficiaries in the high adherence trajectory group, beneficiaries in the high-poor group had higher use of IPF-related inpatient hospitalization services and IPF-related total costs on medical services.

Outcome name	Percentage	Difference vs. High	Lower 95% CL	Upper 95% CL	p-value
Any IPF-related inpatient hospitalization in Yr 1					
Early-Poor	12.2%	1.4%	-2.6%	5.4%	0.489
Delayed-Poor	14.1%	3.4%	-1.4%	8.2%	0.170
High-Poor	19.5%	8.7%	2.7%	14.8%	0.005
Moderate	11.4%	0.6%	-4.3%	5.5%	0.801
High	10.8%	-	-	-	-

Outcome name	Mean (SD)	Difference vs. High	Lower 95% CL	Upper 95% CL	p-value
Total IPF-related medical costs ($) in Yr 1					
Early-Poor	3860.62 (12,947)	620.87	-771.77	2013.51	0.382
Delayed-Poor	3696.54 (6,525)	456.79	-458.64	1372.21	0.328
High-Poor	6011.81 (16,239)	2772.06	422.10	5122.02	0.021
Moderate	2935.82 (4,574)	-303.94	-1074.77	466.90	0.439
High	3239.75 (6,313)	-	-	-	-

Discussion:	Adherence to nintedanib was associated with all-cause and, to a lesser extent, IPF-related hospitalizations and medical costs during the year adherence was measured. In the year after adherence was measured, patients in the delayed-poor adherence group had higher all-cause hospitalizations and medical costs. Further research is needed to unpack the mechanisms underlying these associations.
Marketing Authorisation Holder(s):	
Names and affiliations of principal investigators:	[redacted]