Impact of timing of nintedanib initiation among patients newly diagnosed with idiopathic pulmonary fibrosis

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BACKGROUND AND OBJECTIVE

- Idiopathic pulmonary fibrosis (IPF) is a chronic, incurable lung disease characterized by progressive lung function decline and early mortality[1]
- Nintedanib consistently reduced lung function decline among patients with preserved or reduced lung function in post hoc analyses of placebo-controlled trials,[2,3] but the effect of treatment timing on real-world outcomes is unknown
- This study examined medical costs and risk of hospitalization among patients with IPF by timing of nintedanib initiation within 12 months after diagnosis

METHODS

- **Study design:** Retrospective observational study using administrative claims data from the Optum Research Database
- **Study population:** Insured patients aged ≥40 years with ≥2 medical claims with an IPF diagnosis (ICD-9-CM 516.31 and/or ICD-10-CM J84.112) on separate dates from 01 Oct 2014 – 30 Jun 2019; continuous enrollment required for 6 months before IPF diagnosis (baseline) and up to 13 months after for cost analysis or 12 months after for hospitalization analysis (follow-up)
  - Exclusions: Baseline IPF diagnosis or antifibrotic prescription claims, connective tissue disease, unknown demographics
  - Study cohorts: Based on the time from IPF diagnosis to nintedanib initiation (1, 2-3, 4-6, or 7-12 months)
- **Analysis:** All-cause 12-month medical costs and all-cause follow-up hospitalization were assessed using marginal structural models to adjust for baseline variables and time-varying confounders (factors that could affect both treatment decisions and study outcomes, including spirometry testing, high-resolution computed tomography [HRCT], oxygen therapy, pulmonary rehabilitation)
  - Marginal structural models included weights to account for censoring and variations in treatment initiation timing[4]

STUDY LIMITATIONS

- Findings are most applicable to insured US patients who initiate nintedanib treatment within a year of IPF diagnosis
- Because information such as forced vital capacity value and HRCT results are not readily available in claims data, proxies (eg, oxygen use) were utilized as markers for disease severity

CONCLUSIONS

- Patients who initiate nintedanib soon after IPF diagnosis may have reduced hospitalization risk and lower medical costs
- Earlier intervention to preserve lung function in IPF may translate into measurable real-world benefit

RESULTS

Study Sample (Table 1)

- Among 449 patients, mean (SD) age was 72 (8) years, 68% were male, and 78% were enrolled in Medicare Advantage
- Baseline all-cause medical utilization and associated costs were not significantly different between cohorts (utilization data not shown)

Table 1. Baseline Patient Characteristics

Characteristic	Total (N=449)	Timing of nintedanib initiation after IPF diagnosis: Month 1 (n=168)	Months 2-3 (n=149)	Months 4-6 (n=71)	Months 7-12 (n=61)	Overall p-value
Age, years, mean (SD)	72 (8)	73 (7)	72 (7)	73 (9)	70 (8)	0.146
Male sex, n (%)	306 (68)	109 (65)	105 (71)	45 (63)	47 (77)	0.248
Insurance, n (%)						
Commercial	101 (23)	37 (22)	34 (23)	12 (17)	18 (30)	0.388
MAPD	348 (78)	131 (78)	115 (77)	59 (83)	43 (71)	0.395
Comorbidities, n (%)						
Chronic obstructive pulmonary disease	171 (38)	68 (41)	63 (42)	21 (30)	19 (31)	0.182
Obstructive sleep apnea	81 (18)	41 (24)	21 (14)	9 (13)	10 (16)	0.065
Heart failure	81 (18)	32 (19)	28 (19)	12 (17)	9 (15)	0.901
Pulmonary hypertension	45 (10)	17 (10)	12 (8)	9 (13)	7 (12)	0.672
Hospitalization, n (%)	117 (26)	45 (27)	41 (28)	18 (25)	13 (21)	0.835
All-cause PPPM (SD) medical costs, 2019 US$	1,927 (5,662)	1,694 (2,107)	1,716 (2,769)	1,705 (3,084)	3,340 (13,951)	0.222

IPF, idiopathic pulmonary fibrosis; MAPD, Medicare Advantage with Part D; PPPM, per patient per month; SD, standard deviation

Study Outcomes (Tables 2 and 3)

- Adjusted 12-month all-cause medical costs and adjusted all-cause hospitalization risk differed by the timing of nintedanib initiation (p=0.020 and p<0.001, respectively)
- 12-month all-cause medical costs were 69% higher for patients who initiated in months 2–3 vs month 1; costs were higher but not statistically different for patients initiating in months 4–6 and 7–12 vs month 1
- All-cause hospitalization risk was significantly higher among patients who were not yet treated vs patients treated before the end of months 2–3, 4–6, and 7–12: hazard ratios 1.97, p=0.026; 2.62, p=0.014; and 5.57, p<0.001, respectively

Table 2. Adjusted 12-Month All-Cause Medical Costs

Independent variable[a]	Cost ratio (95% CI)[b,c]	P-value	Predicted cost, 2019 US$
Nintedanib initiation month		0.020	
Month 1	Ref.	-	$17,428
Months 2–3	1.69 (1.20-2.38)	0.003	$29,423
Months 4–6	1.21 (0.81-1.81)	0.359	$21,045
Months 7–12	1.35 (0.91-2.00)	0.140	$23,459

[a]Model adjusted for demographics, month, baseline comorbidity score category, baseline healthcare resource utilization, and IPF-related treatments and assessments (spirometry testing, HRCT, oxygen therapy, pulmonary rehabilitation)
[b]Costs estimated using a weighted generalized estimating equation with gamma distribution and robust variance estimator
[c]Model was run among the subset of patients with 12 months of follow-up continuous enrollment and includes weights to represent the entire study sample

Table 3. Adjusted Follow-up All-Cause Hospitalization Risk

Independent variable[a]	Hazard ratio (95% CI)[b,c]	P-value
Categorical untreated vs treated variable		<0.001
Untreated vs treated in month 1	1.66 (0.74-3.73)	0.223
Untreated vs treated in months 2–3	1.97 (1.09-3.56)	0.026
Untreated vs treated in months 4–6	2.62 (1.22-5.63)	0.014
Untreated vs treated in months 7–12	5.57 (2.31-13.45)	<0.001

[a]Model adjusted for demographics, month, baseline comorbidity score category, baseline healthcare resource utilization, and IPF-related treatments and assessments (spirometry testing, HRCT, oxygen therapy)
[b]Hospitalization risk estimated using a weighted repeated-measures generalized estimating equation with robust variance estimator
[c]Results presented for the 12-month follow-up period among the 454 patients who initiated treatment within 13 months of the index date, totaling 3,329 patient-months

References: [1]Hiwatari N et al. *Respiration.*1993; 60(6):354-358. [2]Costabel U et al. *Am J Respir Crit Care Med.* 2016; 193(2):178-185. [3]Kolb M et al. *Thorax.* 2017; 72(4):340-346. [4]Robins, JM et al. *Epidemiology.* 2000; 11(5):550-560.

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