Low Utilization of Prostacyclin Therapy Prior to Death Among Medicare Patients With Pulmonary Arterial Hypertension

Mathai SC[1]; Morland K[2]; Classi P[2]; Chen H[3]; Forys A[3]; Nelsen A[2]

[1]John Hopkins School of Medicine, Baltimore, MD; [2]United Therapeutics Corporation, Durham, NC; [3]Xcenda LLC, Tampa, FL

BACKGROUND

- Treatment guidelines recommend prostacyclin therapies for the treatment of pulmonary arterial hypertension (PAH) as initial or add-on therapy based upon a patients' disease severity and risk status.[1,2]
- Despite this, previous studies have reported prostacyclin underutilization prior to death, even among those patients at a more severe PAH functional status.[3-5]
- Current estimates of prostacyclin underutilization are from patients receiving treatment at large PAH referral centers; this may not reflect the care patients receive in community-based settings.
- To our knowledge, there have been no claims-based studies evaluating PAH therapies utilized prior to death in a large, geographically diverse population such as Medicare patients.

OBJECTIVES

- To describe the characteristics of and treatments received by Medicare patients with PAH and within the subset of those who died.

METHODS

- A cross sectional retrospective analysis of PAH patients was completed using a 100% sample of Medicare administrative data from January 1, 2012 through December 31, 2017. Claims for Parts A and B medical services and Part D prescription drugs were accessed through the Centers for Medicare and Medicaid Services' (CMS) Virtual Research Data Center (VRDC).
- Patients were included in the study sample if they had claims for at least two PAH medications at least 30 days apart and at least two diagnosis codes in the primary position for primary pulmonary hypertension (ICD-9-CM 416.0, or ICD-10-CM 127.0) at least 30 days apart.
- Means, medians, interquartile ranges, and standard deviations (for continuous variables) and frequency distributions (for categorical variables) were used to characterize patient characteristics and prior treatments received.
- Analyses were performed for the overall sample and stratified by those who had a recorded all-cause death event.
- Additionally, a subgroup analysis was performed on those patients without comorbidities indicating WHO Groups 2-5 in an effort to more closely approximate a true WHO Group 1 PAH population.

RESULTS

- 29,372 patients met inclusion criteria. Patients were primarily female (74%), white (73%), averaged 69.5 years of age, and had a mean [SD] length of time in the dataset of 4.6 [1.7] years.
- 40.8% (n=11,993) of the study sample had a recorded death event. Patients who died had a mean [SD] length of follow-up time in the dataset of 3.4 [1.5] years prior to death.

Table 1. Patient Demographics and Clinical Characteristics

	All PAH Patients (N=29,372)	Died (N=11,993)
Age (as of last year in data), mean (SD)	69.5 (13.2)	71.3 (12.7)
Female, n (%)	21,627 (73.6%)	8,429 (70.3%)
Length of time (in years) in the dataset from first claim to death event or end of data, mean (SD)	4.6 (1.7)	3.4 (1.5)
Length of time (in years) in the dataset from first claim for a PAH drug or PH diagnosis code to death event or end of data, mean (SD)	3.5 (1.8)	2.6 (1.5)
Original reason for entitlement, n (%)		
Old age and survivor's insurance (OASI)	16,113 (54.9%)	7,156 (59.7%)
Disability insurance benefits (DIB)	12,155 (41.4%)	4,305 (35.9%)
Other*	1,104 (3.8%)	532 (4.4%)
Race, n (%)		
White	21,428 (73.0%)	8,998 (75.0%)
Black	5,852 (19.9%)	2,273 (19.0%)
Asian	514 (1.7%)	181 (1.5%)
Hispanic	849 (2.9%)	298 (2.5%)
Other†	729 (2.5%)	243 (2.0%)
Comorbidities‡, n (%)		
Hypertension	19,961 (68.0%)	7,703 (64.2%)
Diabetes	11,711 (39.9%)	4,957 (41.3%)
Coronary Artery Disease	9,400 (32.0%)	4,126 (34.4%)
Hyperlipidemia	6,482 (22.1%)	2,107 (17.6%)
Procedures performed from first claim to death event or end of data, n (%)		
Right heart catheterization	19,408 (66.1%)	7,436 (62.0%)
Echocardiography	28,508 (97.1%)	11,560 (96.4%)
CT imaging	1,663 (5.7%)	829 (6.9%)
Lung ventilation-perfusion	58 (0.2%)	17 (0.1%)
Year patient enters the sample§		
2012	14,994 (51.0%)	7,393 (61.6%)
2013	4,264 (14.5%)	1,842 (15.4%)
2014	3,585 (12.2%)	1,338 (11.2%)
2015	3,317 (11.3%)	949 (7.9%)
2016	2,318 (7.9%)	390 (3.3%)
2017	894 (3.0%)	81 (0.7%)

*Includes ESRD with or without DIB. †Includes North American Native, other, and unknown. ‡Defined as ≥2 diagnosis codes in the primary diagnosis code position on the claim. §Corresponds to the year the first PAH diagnosis or PAH drug was recorded.

Table 2. Breakdown of Other PH Group Comorbidities

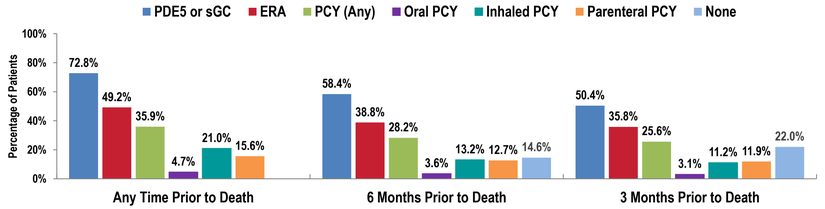
Condition	All PAH Patients (N=29,372)	Died (N=11,993)
WHO Group 2 (PH with left heart disease)*	14,143 (48.2%)	6,320 (52.7%)
WHO Group 3 (PH w/ lung disease)		
COPD	14,932 (50.8%)	6,932 (57.8%)
ILD	8,750 (29.8%)	3,986 (33.2%)
Alveolar hyperventilation disorder	159 (0.5%)	38 (0.3%)
Chronic exposure high altitude	<11 (0.0%)	<11 (0.0%)
Developmental lung diseases	3,760 (12.8%)	1,725 (14.4%)
WHO Group 4 (CTEPH)	3,627 (12.4%)	1,306 (10.9%)
WHO Group 5 (PH w/ unclear multifactorial mechanisms)†	16,856 (57.4%)	6,845 (57.1%)
≥1 of the above comorbidities (ie, WHO Group 2-5 conditions)	26,517 (90.3%)	11,138 (92.9%)

*Includes left ventricular systolic dysfunction, left ventricular diastolic dysfunction, valvular disease, congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies. †Includes hematologic disorders (chronic hemolytic anemia, myeloproliferative disorders, splenectomy), systemic disorders (sarcoidosis, pulmonary histiocytosis, lymphagioleiomyomatosis), metabolic disorders (glycogen storage disease, Gaucher disease, thyroid disorders), others (tumoral obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH).

Treatment Patterns Among PAH Patients Who Died

- Of those who died, only 35.9% (n=4,303) had received a prostacyclin therapy prior to death (4.7% [n=558] oral, 21.0% [n=2,521] inhaled, 15.6% [n=1,868] parenteral). 72.8% (n=8,736) and 49.2% (n=5,904) had a pharmacy claim for a phosphodiesterase-5 inhibitor (PDE5)/soluble guanylate cyclase (sGC) stimulator or any endothelin receptor antagonist (ERA) prior to death, respectively.
- In the 6 months prior to death, 28.2% (n=3,378) had received a prostacyclin therapy (3.6% [n=437] oral, 13.2% [1,588] inhaled, 12.7% [1,519] parenteral), 58.4% (n=7,008) a PDE5/SGC, 38.8% (n=4,655) an ERA, and 14.6% (n=1,746) no therapies.

Figure 1. PAH Therapies Utilized by Time Period Prior to Death (N=11,993)



PDE5- phosphodiesterase-5 inhibitor; SGC- soluble guanylate cyclase stimulator; ERA- endothelin receptor antagonist; PCY- prostacyclin.

Subgroup Analysis

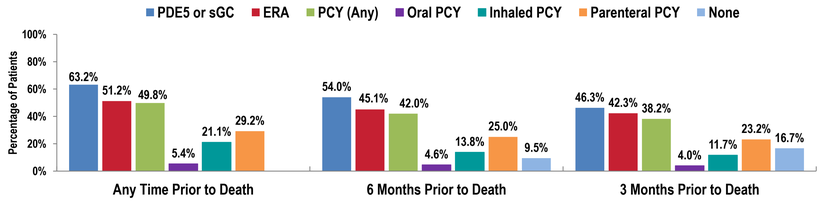
- After excluding comorbidities indicating WHO Groups 2-5, 2,855 patients met inclusion criteria for the subgroup analysis. 29.9% (n=855) of the subgroup sample had a recorded death event.

Table 3. Patient Demographics and Clinical Characteristics: Subgroup Analysis Population

	All PAH Patients (Excluding WHO Group 2-5 conditions) (N=2,855)	Died (Excluding WHO Group 2-5 conditions) (N=855)
Age (as of last year in data), mean (SD)	63.1 (15.1)	67.7 (14.5)
Female, n (%)	2,059 (72.1%)	605 (70.8%)
Length of time (in years) in the dataset from first claim to death event or end of data, mean (SD)	4.1 (2.0)	2.6 (1.6)
Length of time (in years) in the dataset from first claim for a PAH drug or PH diagnosis code to death event or end of data, mean (SD)	3.4 (2.0)	2.1 (1.5)
Original reason for entitlement, n (%)		
Old age and survivor's insurance (OASI)	1,163 (40.7%)	446 (52.2%)
Disability insurance benefits (DIB)	1,686 (59.1%)	405 (47.4%)
End stage renal disease (ESRD)	<11 (<1.0%)	<11 (<1.5%)
Both ESRD and DIB	<11 (<1.0%)	<11 (<1.5%)
Race, n (%)		
White	2,118 (74.2%)	661 (77.3%)
Black	431 (15.1%)	123 (14.4%)
Asian	55 (1.9%)	11 (1.3%)
Hispanic	146 (5.1%)	35 (4.1%)
Other*	105 (3.7%)	25 (2.9%)
Comorbidities†, n (%)		
Hypertension	1,103 (38.6%)	264 (30.9%)
Diabetes	693 (24.3%)	224 (26.2%)
Coronary Artery Disease	350 (12.3%)	93 (10.9%)
Hyperlipidemia	319 (11.2%)	60 (7.0%)
Procedures performed from first claim to death event or end of data, n (%)		
Right heart catheterization	1,377 (48.2%)	349 (40.8%)
Echocardiography	2,448 (85.7%)	676 (79.1%)
CT imaging	54 (1.9%)	22 (2.6%)
Lung ventilation-perfusion	<11 (<1.0%)	0 (0.0%)
Year patient enters the sample‡		
2012	1,537 (53.8%)	628 (73.5%)
2013	289 (10.1%)	82 (9.6%)
2014	249 (8.7%)	66 (7.7%)
2015	321 (11.2%)	45 (5.3%)
2016	296 (10.4%)	<30 (<3.5%)
2017	163 (5.7%)	<11 (<1.5%)

*Includes North American Native, other, and unknown. †Defined as ≥2 diagnosis codes in the primary diagnosis code position on the claim. ‡Corresponds to the year the first PAH diagnosis or PAH drug was recorded.

Figure 2. PAH Therapies Utilized by Time Period Prior to Death: Subgroup Analysis Population (N=855)



LIMITATIONS

- Patients were identified using a combination of drug therapies and PH diagnostic codes, but it is possible some patients were misclassified as PAH patients.
- The appropriateness of prostacyclin therapy based upon disease severity cannot be ascertained from claims data.
- The cause of death, the reasons for not receiving treatment, and prior history of treatments before the patient was enrolled in Medicare are not known.

CONCLUSIONS

- Real-world claims data shows approximately one-third of Medicare patients with PAH receive prostacyclins prior to death.
- Only 16% of patients received a parenteral prostacyclin prior to death.
- Even when applying stricter criteria in an attempt to approximate a true WHO Group 1 population, parenteral prostacyclin use is still only 29%.
- This is concerning given that parenteral prostacyclins are the gold standard treatment for high risk patients.
- Reasons for these treatment gaps are unclear and require further investigation.

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