Real-World Analysis of Treatment Patterns Among Hospitalized Pulmonary Arterial Hypertension Patients

Adesuwa Ogbomo[1], Yuen Tsang[2], Furaha Kariburyo[1], Mamta Jaiswal[1], Wan-Lun Tsai[1], Robert Dufour[2], Sumeet Panjabi[2]
[1]STATinMED Research, Plano, TX; [2]Janssen Scientific Affairs, South San Francisco, CA

BACKGROUND

- Pulmonary arterial hypertension (PAH) is a progressive, life-threatening disease characterized by sustained elevated pulmonary vascular resistance which leads to right heart failure and premature death.[1]
- PAH related hospitalizations are associated with negative health outcomes and high financial costs.
- In the GRIPHON trial, hospitalization for worsening of PAH was strongly associated with greater mortality risk.[2]
- A retrospective cohort study using administrative claim data found that the annual average total PH-related hospitalization costs, including initial and readmission, were $134,830 for commercially-insured and $53,039 for Medicare Advantage populations.[3]
- The above studies highlight the importance of hospitalization as a risk factor for worsening of PAH, mortality, and financial burden.
- European Society of Cardiology (ESC)/European Respiratory Society (ERS) pulmonary hypertension guidelines recommend escalation of therapy in patients with intermediate- or high-risk status for expected 1- year mortality.
- Although hospitalization is incorporated as a parameter in the REVEAL 2.0 risk score calculator for survival and in selecting the most appropriate treatment strategy,[4] there is limited data on post-hospitalization therapy management in PAH.

OBJECTIVE

This study examined PAH treatment patterns for 30 days prior to and 90 days post-hospitalization and treatment modification during the 90-day post-all-cause hospitalization discharge period.

METHODS

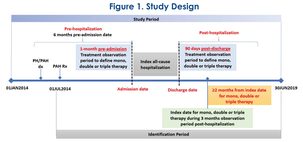
This is a retrospective database study using the Optum's deidentified Clinformatics® Data Mart Database from 01JAN2014-30JUN2019.

- The study period ranged from 01JAN2014-30JUN2019 and the identification period ranged from 01JUL2014-30JUN2019 for the Optum database (Figure 1).

Patients were included in the study if they met the following criteria:

- ≥1 PH/PAH diagnosis claim (ICD-9-CM: 416.0, 416.8 or ICD-10-CM: I27.0, I27.2, I27.89) in the inpatient setting OR ≥2 PH/PAH diagnoses claims ≥30 days apart in the outpatient setting during the study period.
- ≥1 claim for PAH medication on or after the initial diagnosis date during the study period (Table 1).
- ≥1 all-cause hospitalization on or after the initial drug date during the identification period
- ≥18 years of age at the time of admission date of index hospitalization
- Continuous health plan enrollment was required for ≥6 months prior to the first all-cause hospitalization and for ≥3 months post-discharge.
- No evidence of claims for pregnancy, labor, or erectile dysfunction during the study period.

Figure 1. Study Design



PAH: pulmonary arterial hypertension

Table 1. List of PAH Medications

Category	Medications
Phosphodiesterase (Type 5) enzyme inhibitors (PDE-5i)	Sildenafil
	Tadalafil
Endothelin receptor antagonists (ERAs)	Macitentan
	Ambrisentan
	Bosentan
Prostacyclin/ Prostacyclin analogues	Iloprost
	Beraprost
	Treprostinil
	Selexipag
	Epoprostenol
	Epoprostenol sodium
	Treprostinil
Soluble Guanylate Cyclase Stimulators	Riociguat

PAH: pulmonary arterial hypertension

METHODS - cont'd

Study Variables

- Patient demographics, including age, sex, and geographic region were captured during the 6-month pre-hospitalization period.
- Charlson Comorbidity Index (CCI) score, individual comorbidities, baseline PAH treatment, and all-cause health care utilization during the 6-month pre-hospitalization period were captured.

Study Outcomes

- Patient treatment status during the 30 days pre- and 90 days post-hospitalization period were captured as:
  - **Triple Therapy:** Patients prescribed 3 different classes of PAH medications with overlapping days of supply.
  - **Double Therapy:** Patients prescribed 2 different classes of PAH medications with overlapping days of supply.
  - **Monotherapy:** Patients prescribed 1 PAH medication class
  - **No PAH therapy:** Patients without evidence for PAH medication treatment.
- Treatment pattern modification was defined as change in PAH treatment during the 30 days pre-hospitalization to 90 days post hospitalization (Figure 2).

Statistical Analysis

- All study variables were analyzed descriptively, mean, standard deviation, median, and range were provided for continuous variables. Counts and percentages were reported for categorical variables.

Figure 2. PAH Treatment Pattern Modification

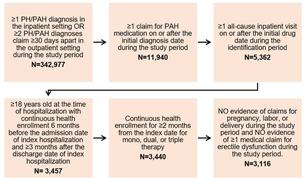
PAH: pulmonary arterial hypertension

RESULTS

After applying the study selection criteria, 3,116 PAH patients with ≥1 all-cause hospitalization were identified (Figure 3).

- The mean age was 68.1 years, and most patients were female (68%) with an average CCI score of 5.1 (Table 2).

Figure 3. Patient Flow Diagram



PAH: pulmonary arterial hypertension

Table 2. Descriptive Baseline Characteristics of Hospitalized PAH Patients

N=3116	N/Mean (%/SD)
Age (years)	68.1 (12.7)
Age Group (years)	
18-54	438 (14.1%)
55-64	639 (20.5%)
65+	2039 (65.4%)
Gender:	
Male	994 (31.9%)
Female	2122 (68.1%)
US Geographic Region	
Northeast	328 (10.5%)
North Central	751 (24.1%)
South	1428 (45.8%)
West and Other	609 (19.5%)
Charlson Comorbidity Index (CCI)	
Mean CCI	5.1 (3.0)
Comorbidities*	
Chronic obstructive pulmonary disease	1461 (46.9%)
Sleep disorders	1211 (1.9%)
Dyspnea	1961 (62.9%)
Diabetes	1050 (43.3%)
Hypertension	2540 (81.5%)
Coronary artery disease/ischemic heart disease	1271 (40.8%)
Lower respiratory infection	1221 (39.2%)
Apnea	580 (18.6%)
Obesity	810 (26.0%)
Renal insufficiency	1183 (37.9%)
Pneumonia	498 (16.0%)
Congenital heart disease	211 (6.8%)
Depression	547 (17.6%)
Liver disease	306 (9.8%)
Interstitial lung disease	479 (15.4%)
Venous thromboembolism	186 (10.8%)
Baseline PAH Medications	
Phosphodiesterase-5 (Type 5) enzyme inhibitors (PDE-5i)	1801 (57.8%)
Endothelin receptor antagonists (ERAs)	920 (29.5%)
Prostacyclin/prostacyclin analogues	337 (10.8%)
Soluble guanylate cyclase stimulators	191 (6.1%)
All-cause index hospitalization	
Length of stay (days)	6.6 (8.2)

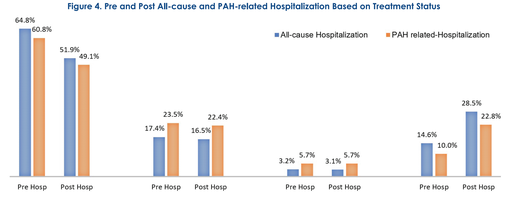
*only comorbidities ≥5% were reported
PAH: pulmonary arterial hypertension; SD: standard deviation

- Approximately 58% of the hospitalized PAH patients were on phosphodiesterase (Type 5) enzyme inhibitors (PDE-5i) medications and 30% had endothelin receptor antagonist (ERA) medication use during the 30-day pre-hospitalization period.
- The average length of stay for all-cause hospitalization was 7 days.
- A majority (65%) of the PAH patients had monotherapy during the 30-day pre-hospitalization period and 15% without evidence of PAH treatment within 30-day pre-admission (Table 2).

RESULTS - cont'd

- During the 30 days pre-all-cause hospitalization, 2,020 (64.8%) of PAH patients had monotherapy, 541(17.4%) had double therapy, 98 (3.2%) had triple therapy, and 456 (14.6%) had no evidence of PAH therapy (Figure 4).
- During the 90 days post-all-cause hospitalization period 1618 (51.9%) of the PAH patients were on monotherapy, 513 (16.5%) had double therapy, 96 (3.1%) were on triple therapy, and 889 (28.5%) had no evidence of PAH therapy (Figure 4).
- Among patients with PAH-related hospitalization (N=1,062), a majority of the patients were on monotherapy during the 30 days pre- and 90 days post-PAH-related hospitalization period (60.8% and 49.1%, respectively) followed by double therapy during the pre- and post-PAH-related hospitalization period (23.5% and 22.4%, respectively) (Figure 4).

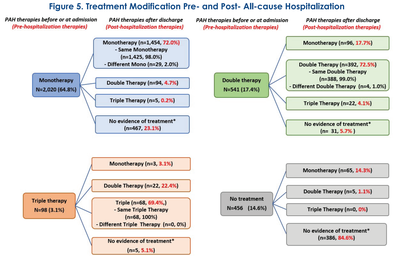
Figure 4. Pre and Post All-cause and PAH-related Hospitalization Based on Treatment Status



PAH: pulmonary arterial hypertension; pre hosp: pre-hospitalization; post hosp: post-hospitalization

- Overall, 73.8% (n=2,300) of hospitalized PAH patients did not have a change in PAH therapy from the pre- to post- all-cause hospitalization period, respectively.
- Compared to those on mono (n=2020), double (n=541), and triple therapy (n=98) during the pre- all-cause hospitalization period,
  - 72.0% (n=1,454) remained on mono, and 23.1% (n=467) had no evidence of therapy post-all cause hospitalization.
  - 72.5% (n=392) remained on double, 17.7% (n=96) had a reduction in treatment intensity to mono, and 5.7% (n=31) had no evidence of treatment post all-cause hospitalization.
  - 69.4% (n=68) remained on triple therapy, 22.4% (n=22) were observed to have a reduction in treatment intensity to double therapy, 3.1% (n=3) to monotherapy, and 5.1% (n=5) to no therapy post-all-cause hospitalization (Figure 5).
- Of the patients without evidence of PAH therapy during pre- all-cause hospitalization period, 84.6% (n=386) remained without treatment post-all-cause hospitalization (Figure 5).

Figure 5. Treatment Modification Pre- and Post- All-cause Hospitalization



*No evidence of treatment = patients without refill of the index therapy or with the refill date more than 30 days after the index therapy during the 3 months post-discharge
PAH: pulmonary arterial hypertension

LIMITATIONS

- As with all observational retrospective analyses, there are several important limitations associated with claims databases. The presence of a claim for a filled prescription does not indicate that the medication was consumed or taken as prescribed.
- PAH medication or other medications that were administered in the inpatient settings are not captured in the database and therefore could not be measured and included in the analyses. However, since the pre-hospitalization patterns are maintained post-hospitalization, the inpatient setting is likely not drastically different.

CONCLUSIONS

- **In this real-world study, hospitalization did not result in treatment modification in the 90 days post-hospitalization regardless of an all-cause or PAH-related hospitalization.**
- **A majority of the hospitalized patients (all cause and PAH-related) were on monotherapy pre- all-cause hospitalization and post- all-cause hospitalization.**
- **The pre- and post-hospitalization treatment patterns were consistent between PAH-related and all-cause hospitalized patients.**
- **All-cause and PAH-related hospitalization did not appear to have a major impact on PAH related therapy management.**
- **One possible explanation in part, for the observed treatment pattern is that providers relying on guidelines and non-REVEAL risk profiles for treatment decision making may not be considering hospitalization as a trigger for disease progression and therapy management (modification or intensification with combination therapy).**
- **Future studies should investigate the reasons for the limited modification of PAH therapy after a hospitalization event.**
- **Investigation of the effect of escalating and de-escalating PAH therapy following a hospitalization event on patient outcomes, re-admission, and costs is also warranted.**

References

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Disclosures

Adesuwa Ogbomo and Wan-Lun Tsai are employees of STATinMED Research, which is a paid consultant to Janssen Scientific Affairs. Furaha Kariburyo and Mamta Jaiswal were employees of STATinMED Research at the time of the study. Yuen Tsang and Sumeet Panjabi are employees of Janssen Scientific Affairs. Robert Dufour was an employee of Janssen Scientific Affairs at the time of the study.

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