3536

Presented at phoenix CHEST 2026 October 18-21, 2026 Phoenix, AZ

Determinants of monotherapy use and treatment patterns in pulmonary arterial hypertension: A contemporary real-world United States study

Ioana R. Preston[1], Kelly M. Chin[2], H. James Ford[3], John W. McConnell[4], Marc A. Simon[5], Jean M. Elwing[6], Katharine R. Clapham[7], John J. Ryan[8,*], Gina Nelson[9], Kathleen Frezza[10,†], Megan Flynn[9], Sherry Danese[11], Julie Ulloa[11], Mark Danese[11], Charles D. Burger[12], Martha Kingman[13]

[1]Lahey Hospital & Medical Center, Burlington, MA, USA; [2]UT Southwestern Medical Center, Dallas, TX, USA; [3]University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, USA; [4]Norton Healthcare, Louisville, KY, USA; [5]UCSF Medical Center, San Francisco, CA, USA; [6]College of Medicine, University of Cincinnati, Cincinnati, OH, USA; [7]University of Utah Hospital, Salt Lake City, UT, USA; [8]University of Utah Health, Salt Lake City, UT, USA; [9]Gossamer Bio, Inc., San Diego, CA, USA; [10]Chiesi USA, Cary, NC, USA; [11]OutcomesInsights, Calabasas, CA, USA; [12]Mayo Clinic, Jacksonville, FL, USA; [†]Consultant, Retired 2024 from UT Southwestern Medical Center, Dallas, TX, USA; [*]Current address: CommonSpirit Cardiology, Salt Lake City, UT, USA; [†]Current address: Affinia Therapeutics, Waltham, MA, USA

BACKGROUND

- Despite therapeutic advances, pulmonary arterial hypertension (PAH) remains a progressive disease with substantial morbidity and mortality[1]
- Although current guidelines recommend combination therapy and treatment intensification to achieve low-risk status,[2] monotherapy use persists across risk strata[3,4]
- Factors influencing monotherapy use in routine clinical practice remain poorly defined
- **We aimed to characterize contemporary PAH treatment patterns and factors associated with monotherapy use in large, experienced PH centers**

METHODS

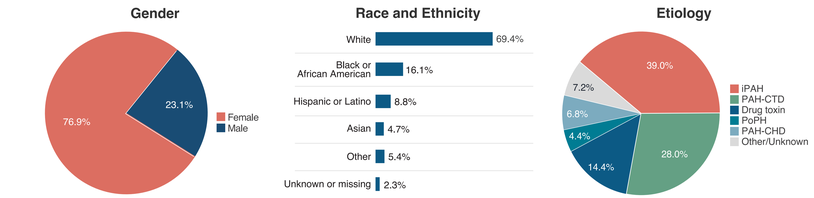
- This was a multicenter, retrospective, cross-sectional chart review from 7 geographically diverse US Pulmonary Hypertension Association (PHA)-accredited centers
- Demographic, clinical, hemodynamic, and treatment data were collected for consecutive adult patients with a right heart catheterization-confirmed PAH diagnosis made ≥ 6 months prior to study enrollment
- Mild PAH was defined as mean pulmonary arterial pressure 21–24 mmHg and pulmonary vascular resistance 2.1–2.9 Wood units[2,5]
- Data were collected from the first qualifying in-person office visit ("index visit") between January 1 and December 31, 2025
- Population and treatment patterns were reported descriptively; regression analyses identified patient- and disease-level predictors of monotherapy use
- The study protocol was reviewed and either exempted or approved by each institution's Institutional Review Board or Independent Ethics Committee

RESULTS

Demographics (N = 1,214)

- Most patients were female and White, with a mean (SD) age of 59.7 (14.9) years, and with either idiopathic or connective tissue disease-associated PAH

Figure 1. Demographics at the index visit



For race and ethnicity, users were allowed to select "all that apply"; therefore, responses sum to > 100%. CHD, congenital heart disease; CTD, connective tissue disease; (i)PAH, (idiopathic) pulmonary arterial hypertension; PoPH, portopulmonary hypertension.

Clinical Characteristics (N = 1,214)

- Most patients (90.8%) were WHO Functional Class II or III at the index visit (**Figure 2a**)
- Using centrally calculated REVEAL Lite 2 risk scores, just over half of the cohort was low risk, with the remainder relatively evenly split between intermediate and high risk (**Figure 2b**)
- In the overall study population, 9 patients (< 1%) met hemodynamic criteria for mild PAH

Figure 2a. WHO Functional Class (FC)

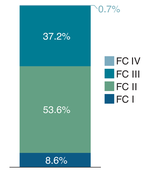
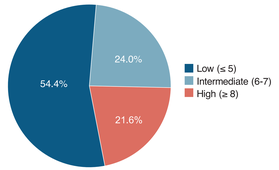


Figure 2b. REVEAL Lite 2 risk score[6]



Treatment Patterns

- In the overall population, 85.0% of patients were receiving dual-, triple-, or quadruple-agent combination therapy, whereas 13.1% were receiving monotherapy (**Figure 3a**)
- Treatment patterns varied only modestly across REVEAL Lite 2 risk categories, with dual and triple therapy most frequently used regardless of risk status (**Figure 3b**)
- Fewer than half of intermediate-risk (48.8%) and high-risk patients (41.4%) received triple- or quadruple+-agent regimens

Figure 3a. Overall treatment patterns

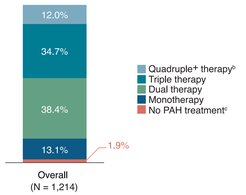
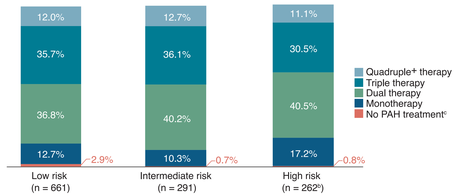


Figure 3b. Treatment patterns by REVEAL Lite 2 risk status[a]



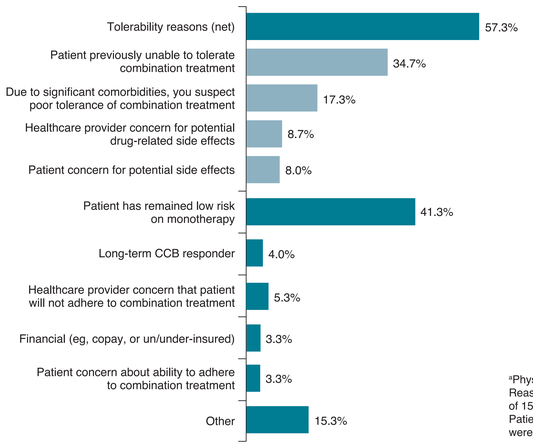
[a]REVEAL Lite 2 risk status calculated from chart data; percentages may not total 100% due to rounding. [b]n = 1 (0.1% of overall population and 0.4% of high-risk patients) received 5 therapies (combination PDE-5i/ERA, sGC, ASI, prostacyclin pathway agent). [c]"No PAH treatment" includes patients who were on CCB for PAH only.

ASI, activin signaling inhibitor; CCB, calcium channel blocker; ERA, endothelin receptor antagonist; PAH, pulmonary arterial hypertension; PDE-5i, phosphodiesterase type 5 inhibitor; REVEAL, Registry to Evaluate Early and Long-term PAH Disease Management; sGC, soluble guanylate cyclase stimulator.

Monotherapy Use

- Of 159 patients receiving monotherapy (**13.1%**), 152 had non-mild disease
- PDE-5 inhibitors were the most frequently used monotherapy agents (76.7%), followed by ERAs (16.4%), prostacyclin pathway agents (5.7%), and sGC stimulators (1.3%) (data not shown)
- The most frequently reported reasons for monotherapy were tolerability-related or because the patient was perceived to be "low risk on monotherapy" (**Figure 4**). Of these, REVEAL Lite 2 scores did not always confirm low-risk status (22.6%)
- Independent predictors of monotherapy use included Functional Class I and older age at diagnosis (data not shown)

Figure 4. Reasons for monotherapy use among patients with non-mild PAH (n = 150)[a]



[a]Physicians could choose more than one reason. Reasons for monotherapy were available for 150 of 152 non-mild patients receiving monotherapy. Patients receiving a CCB for PAH only (n = 12) were excluded. CCB, calcium channel blocker.

Limitations

- Cross-sectional assessment of prevalent patients limited insight into treatment history, prior treatment response, and disease trajectory
- Risk stratification was based solely on REVEAL Lite 2 score and may not generalize to other risk assessment tools
- Treatment patterns were described rather than evaluated, and the clinical rationale for treatment decisions beyond the use of monotherapy was not captured for all patients

CONCLUSIONS

- Widespread use of contemporary combination therapy did not eliminate the burden of elevated REVEAL Lite 2 risk, highlighting an ongoing unmet need in PAH
- Monotherapy was uncommon in expert PAH centers, suggesting that persistent disease burden cannot be explained by undertreatment alone
- Although expert recommendations emphasize risk-based treatment intensification, real-world therapeutic decision making extends beyond risk status alone, reflecting considerations such as tolerability, comorbidities, patient factors, and physician judgment
- Few patients meeting hemodynamic criteria for mild PAH were identified, highlighting the difficulty of generating evidence to guide management of this subgroup

References: **1** Reinders S, et al. *Respir Res.* 2024;25(1):373. **2** Humbert M, et al. *Eur Respir J.* 2023;61(1):2200879. **3** Leary PJ, et al. *Am J Respir Crit Care Med.* 2025;211(4):619-627. **4** Hoeper MM, et al. *Eur Resp J.* 2022;59:2102024. **5** Kovacs G, et al. *Eur Respir J.* 2024;64(4):2401324. **6** Benza RL, et al. *Chest.* 2021;159(1):337-346.

Research supported by: Gossamer Bio, Inc., and Chiesi Farmaceutici S.p.A.