Provider preferences regarding the use of combination ERA+PDE5i for the treatment of pulmonary arterial hypertension: Results from a discrete choice experiment.

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Poster # P270

Key Takeaway

Single-tablet combination therapy may help providers initiate patients on ERA+PDE5i sooner, improve compliance, and simplify delivery of dual and triple therapy. Ensuring coverage and affordability is key to unlocking these benefits.

Background

- Upfront combination therapy with ERA+PDE5i is considered standard of care for patients with pulmonary arterial hypertension (PAH) due to improved patient outcomes.[1,2]
- Despite guidelines recommending combination therapy, many continue to be treated with monotherapy at 6-months post-initiation.[2,3]
- The reasons for this disconnect in real-world vs. recommended prescribing practices are unclear.
- We examined several treatment-level attributes that relate to healthcare providers' (HCPs) decisions to adopt dual-combination of ERA+PDE5i when treating PAH patients.
- We also explored if a single tablet combination therapy (STCT) might increase adoption practices.

Methods

- A cross-sectional online survey of eligible 195 US-based HCPs specializing in cardiology or pulmonology
  - All HCPs had to have treated ≥ 5 PAH patients (WHO Group 1) in the past year.
  - HCPs must currently be practicing as a board-certified physician, nurse practitioner, or physician assistant.
  - This ensured minimum familiarity while allowing for real world variations in expertise / volume.
- Participants were excluded if they did not meet eligibility requirements.

- Nine attributes associated with ERA+PDE5i therapy were explored as part of a discrete choice experiment (DCE) to assess prescribing patterns (**Table 1**).
  - Selected attributes and levels were obtained via literature review and input from clinical advisors.
- Perceptions of a STCT of ERA-PDE5i were explored via supplemental questionnaire.

Table 2. Treatment Attributes and Levels in the DCE

Attribute	Level 1	Level 2	Level 3	Level 4	Level 5
Cause of PAH	Idiopathic / heritable	Connective tissue disease	Drug-induced	Congenital heart disease	NA
Comorbidities	Without comorbidities	With cardiopulmonary comorbidities	With renal comorbidities	With obesity	NA
Hospitalized due to PAH in last 6 months	Yes	No	NA	NA	NA
REVEAL 2.0 risk status[4]	Low	Intermediate	High	NA	NA
Current treatment	Newly diagnosed, treatment naive	Monotherapy PDE5i	Monotherapy SGCs	Monotherapy ERA	Dual oral combination therapy ERA+PDE5i
Symptom progression in last 3 months	Progressed	Unchanged	NA	NA	NA
Functional class	WHO II	WHO III	NA	NA	NA
Medication persistence	History of non-persistence	No history of non-persistence	NA	NA	NA
Side effects	History of extensive side effects	No history of extensive side effects	NA	NA	NA

Selected attributes and levels were obtained via literature review and input from clinical advisors. WHO, World Health Organization; REVEAL, Registry to Evaluate Early and Long-Term PAH Disease Management; SGC, soluble guanylate cyclase stimulators; ERA, endothelin receptor antagonists; PDE5i, phosphodiesterase type 5 inhibitors.

- Using an adaptive choice-based conjoint methodology, HCPs were asked to select the patient profile best served by dual-combination ERA+PDE5i (see **Table 2** for an example choice trial).
- These iterative choice trials were used to calculate preference weights (PW) for each individual level for each attribute measured. These preference weights were used to calculate the relative importance of each attribute. The larger the differences across preference weights within a single attribute, the greater that attribute's influence in determining HCP decision making.
- Relative importance scores summarized the most/least influential attributes.
- Bivariate statistics were used to explore how practice setting impacted ERA+PDE5i adoption practices (i.e., comparing HCPs from centers of excellence (CoE) vs. other institutions (non-CoE).

Table 3. Example of a Choice Task From the DCE

"Which PAH patient would be most optimally treated with a dual combination of ERA and PDE5i? Please assume that all treatments are similarly efficacious. *(Note: May be considered as part of a broader regimen that includes prostacyclin and/or selexipag)"*

Hypothetical Patient Characteristics	Patient A	Patient B	Patient C
Cause of PAH	Idiopathic / heritable	Connective tissue disease	Drug-induced
Comorbidities	With cardiopulmonary comorbidities	With cardiopulmonary comorbidities	Without comorbidities
Hospitalized due to PAH in last 6 months	Yes	No	No
Reveal 2.0 risk status	High	Intermediate Low	Low
Current treatment	Dual oral combination therapy ERA+PDE5i	Monotherapy PDE5i	Newly diagnosed, treatment naive
Symptom progression in last 3 months	Progressed	Unchanged	Unchanged
Functional class	WHO III	WHO II	WHO III
Medication persistence	History of non-persistence	No history of non-persistence	History of non-persistence
Side effects	History of extensive side effects	History of extensive side effects	No history of extensive side effects

Results

- Of the 195 respondents, most were physicians (73.3%) from centers of excellence (63.1%), treating a mean of 117.4 PAH patients in the past year (**Table 4**).

Table 4. HCP Characteristics

Characteristic	N=195*
Provider Type, n (%)	
Physician	143 (73.3%)
Nurse Practitioner	37 (19.0%)
Physician Assistant	15 (7.7%)
Specialty, n (%)	
Cardiology	103 (52.8%)
Pulmonology	92 (47.2%)
Centers of Excellence, n (%)	
Yes	123 (63.1%)
No / Don't Know	72 (36.9%)
Patient Volume per Year	
Mean (SD)	117.4 (189.4)
Median (Range)	50 (5 – 1500)

* Among 202 total survey respondents, 195 met data quality standards for inclusion in the final analysis. SD; standard deviation

Factors influencing ERA+PDE5i Adoption

- The most important factors influencing ERA+PDE5i adoption were the patient's current treatment (17.9), PAH etiology (16.2), existing comorbidities (14.1), and history of side effects (12.7) (**Figure 1**).
  - Individual preference weights confirmed providers were more likely to select ERA+PDE5i for patients treated with PDE5i monotherapy, with idiopathic PAH, and without comorbidities or side effects.
- Functional status, risk of no*n-persistence, and disease escalation (i.e., hospitalization) were less important.

Fig 1. Relative Importance Scores of Each Attribute

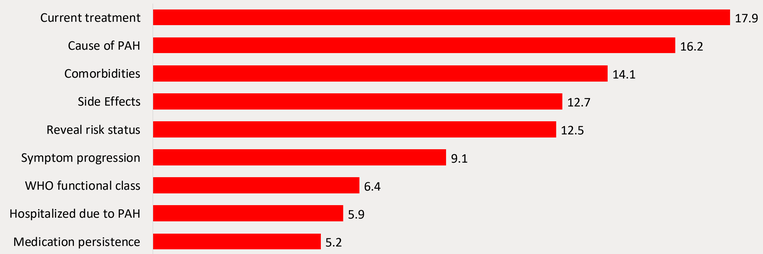
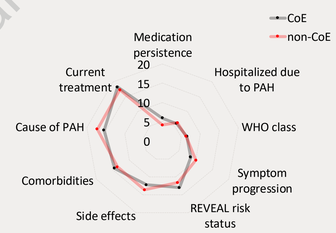


Fig 2. Role of Practice Setting



- Relative importance scores (**Figure 2**) indicated broadly similar prioritization of treatment attributes across practice settings.
- **However**, an exploration of the individual levels within each attribute (*results not shown*) revealed nuances in how practitioners reacted to certain information:
  - HCPs from a **center of excellence** were most likely to select ERA+PDE5i for patients with cardiopulmonary comorbidities (PW: CoE=26.7 vs. non-CoE=10.8).
  - HCPs from **other institutions** most often selected ERA+PDE5i to patients without comorbidities (PW: CoE=18.2 vs. non-CoE=32.6).

Blinded Choice of PAH Therapies

- When asked which of four hypothetical therapies best suited the patient profile presented, HCPs preferred a STCT of macitentan-tadalafil (59.6%) over traditional "loose dose" macitentan-tadalafil (21.1%) (**Table 4**).

Table 5. Blinded Choice Exercise

Treatment Profiles	Treatment A	Treatment B	Treatment C	Treatment D
Dosing frequency	1 tablet once daily	3 tablets per day	Up to 10-13 tablets per day	Up to 3 tablets per day
Adjustable dosing and/or titration	Not adjustable	Adjustable	Adjustable	Adjustable
Safety / tolerability[5-8]	22% chance of peripheral edema	28% chance of peripheral edema	20% chance of peripheral edema	45% chance of peripheral edema
Side effect management	Side effects are difficult to distinguish between ERA and PDE5i	Side effects are difficult to distinguish between ERA and PDE5i	Side effects can be distinguished between ERA and PDE5i	Side effects are difficult to distinguish between ERA and PDE5i
Number of steps required to reach max dose	2 steps	2 steps	4-5 steps	4 steps
Prior authorization	Requires 1 prior authorization	Requires 2 prior authorizations	Requires 2 prior authorizations	Requires 2 prior authorizations
Refers to Blinded Real-World Therapy	**Macitentan + Tadalafil Fixed Dose Combination (STCT)**	**Macitentan + Tadalafil Loose Dose Combination**	**Macitentan + Sildenafil Loose Dose Combination**	**Ambrisentan + Tadalafil Loose Dose Combination**
Mean percent of trials (%)*:	59.6	21.1	13.6	5.7

Treatment profiles were based on existing PAH dual oral combination therapies; safety is reported as the unadjusted proportion of participants who experienced edema in the available clinical trials. All therapies were presented in blinded (unbranded) fashion (e.g., "Treatment A").
*Results reflect the proportion of treatment choice trials (Mean±SD=9.8±0.8 per respondent) in which HCPs selected each therapy as the optimal choice for managing PAH.
SD, Standard Deviation

Perceptions of a STCT of ERA+PDE5i

- Most HCPs were willing to switch patients to STCT (76.9%) and noted that STCT would enable faster initiation on dual combination ERA+PDE5i (76.4%) and would improve medication compliance (82.6%) (**Table 6**).
- Over half of HCPs were willing to implement STCT as upfront and/or triple therapy.
- Cost and/or insurance issues (63.6%) and patient side effects (50.8%) were limitations to adopting a STCT.

Table 6. Perceptions of STCT

Influence of STCT on Treatment Behavior	Respondents Reporting "Always/Often"
Would allow you to initiate ERA+PDE5i sooner	76.4%
Would improve your patients' compliance	82.6%
Willing to switch a current dual patient to STCT	76.9%
Willing to use as upfront therapy	57.9%
Willing to use in triple therapy	54.4%
Limitations of STCT	**>50% Respondents Selected**
Cost and/or insurance issues	63.6%
History of extensive side effects	50.8%

When calculating percentages, the total study sample size (N=195) was used as the denominator.

Presented at the 2024 American Thoracic Society
May 12–22, 2024; San Diego, CA, USA

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