Patient 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 Number

Key Takeaway

Patients prefer a single-tablet combination therapy (STCT) over traditional multi-pill regimens, mostly due to its ability to streamline their prescriptions and reduce pill burden. Costs remain a significant factor in determining whether patients can afford the convenience an STCT offers.

Background

- Upfront combination therapy with ERA+PDE5i is the standard of care for patients with pulmonary arterial hypertension (PAH) due to improved patient outcomes.[1,2]
- Despite guidelines, many continue to be treated with monotherapy at 6-months post-initiation.[2,3]
- Reasons for this disconnect in real-world vs. recommended prescribing practices are unclear.
- In this study, we examined treatment-level attributes affecting patients' perceptions and willingness to adopt dual combination of ERA+PDE5i.
- We also explored if a single tablet combination therapy (STCT) might provide additional benefits and enhance patient participation in treatment choices.

Methods

- This was an online survey of N=201 self-reported PAH patients in the US from PHAR, the largest active longitudinal registry tracking PAH patients across the country.
  - Patient must have used an oral PAH medication for 3+ months in the past year
  - Patient with a self-reported diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH), interstitial lung disease (ILD), or diastolic heart failure were excluded
- Seven attributes associated with ERA+PDE5i therapy were explored as part of a discrete choice experiment (DCE) to assess patients' willingness to adopt ERA+PDE5i **(Table 1).**
  - Attributes and levels were obtained via literature review and input from clinical advisors.
- Additional exploration of STCT on ERA-PDE5i acceptance was assessed via supplemental questionnaire.

Table 1. Treatment Attributes and Levels in the DCE

Attribute	Level 1	Level 2	Level 3	Level 4	Level 5
Out-of-pocket costs	<$20	$20-$50	$50-$100	$100-$200	$200+
Dosing Frequency	One pill, once daily	Three pills, multiple times a day	Four pills, multiple times a day	Ten to thirteen pills, multiple times a day	NA
Discontinuation due to side effects*	7% of patients	8% of patients	9% of patients	12% of patients	NA
Prior authorization	Requires 1 prior authorization	Requires 2 prior authorizations	NA	NA	NA
Pharmacies	Requires 1 pharmacy	Requires 2 pharmacies	NA	NA	NA
Dose increase (titration)	2 steps to reach goal dose	3 steps to reach goal dose	4-5 steps to reach goal dose	NA	NA
Patient support program	Available	Not available	NA	NA	NA

Selected attributes and levels were obtained via literature review and input from clinical advisors. * Presented to respondents in the DCE as "the percentage of patients that stopped medication due to side effects"

- We utilized adaptive choice-based conjoint analysis methodology to ask patients to select the treatment profile they found most attractive (see **Table 2** for an example choice trial).
- These iterative choice trials calculated preference weights (PW) for each individual level for each attribute measured. These preference weights were used to calculate the relative importance of each attribute.
  - Larger differences across preference weights within a single attribute indicated greater influence in shaping patients' willingness to adopt ERA+PDE5i.
- Relative importance scores summarized the most/least influential attributes driving patients' willingness to adopt ERA+PDE5i.
- Patient characteristics and attitudinal beliefs were analyzed descriptively and in aggregate across the total sample

Table 2. Example of a Choice Task From the DCE

"Please indicate whether each PAH treatment below is a possibility or not for you. Please assume that all treatments are similarly effective at treating PAH."

Therapy characteristics	Therapy A	Therapy B	Therapy C
Out-of-Pocket Costs	<$25	$50-100	$50-100
Dosing	One pill, once daily	Three pills, multiple times a day	Ten to thirteen pills, multiple times a day
Prior Authorizations	Requires 1 prior authorization	Requires 2 prior authorizations	Requires 1 prior authorization
Pharmacies	Requires 1 pharmacy	Requires 1 pharmacy	Requires 2 pharmacies
Discontinuation Due to Side Effects	8%	7%	9%
Dose Increase	2 steps to reach goal dose	3 steps to reach goal dose	4-5 steps to reach goal dose
Patient Support Program	Available	Available	Not available

Results

- Respondents were primarily White (86.1%) and female (88.6%). A majority were not employed (70.2%), with over one-third reporting a disability (38.3%).
- The most common regimens at the time of the survey were triple therapy PDE5i+ERA+prostacyclin (36.8%), double therapy PDE5i+ERA (17.9%), and monotherapy PDE5i (15.4%). (**Table 3**).

Table 3. Patient Characteristics

Characteristic	N=201
Sex, n (%)	
Female	178 (88.6)
Race, n (%)	
White	173 (86.1)
Black or African American	10 (5.0)
Asian	6 (3.0)
Native Hawaiian or Other Pacific Islander	1 (0.5)
Two or More Races	5 (2.5)
Prefer Not to Answer	6 (3.0)
Employment, n (%)	
Employed full time	35 (17.4)
Self-employed	11 (5.5)
Employed part time	14 (7.0)
Manage family / household	21 (10.5)
Not employed and looking for work	3 (1.5)
Not employed and not looking for work (e.g., student)	33 (16.4)
Not employed and unable to work (e.g., disability)	77 (38.3)
Prefer not to answer	7 (3.5)
Current Treatment*, n (%)	
PDE5i + ERA + prostacyclin	74 (36.8)
PDE5i + ERA	36 (17.9)
PDE5i monotherapy	31 (15.4)
ERA monotherapy	22 (11.0)
Other	16 (8.0)
sGC + ERA + prostacyclin	15 (7.5)
sGC + ERA	7 (3.5)
Time Since Diagnosis, years	
Mean (SD)	10.6 (8.0)
Median (Range)	9 (1 – 38)

*PDE5i (sildenafil or tadalafil); ERA (bosentan, ambrisentan, or macitentan); prostacyclin (selexipag, treprostinil, epoprostenol, or iloprost); sGC (riociguat)
SD; standard deviation

- The 2 most important factors influencing ERA+PDE5i adoption were the out-of-pocket costs (33.7) and dosing frequency (31.5) (**Figure 1**).
  - Individual preference weights confirmed that patients were most accepting of ERA+PDE5i therapies when available at the lowest out-of-pocket cost and the least frequent dosing regimen (i.e., 1 pill, once daily) (**Figure 2**).
- Availability of patient support programs, discontinuation due to side effects, number of pharmacies, number of prior authorizations, and dose increase (titration) were less important.

Fig 1. Relative Importance Scores of Each Attribute

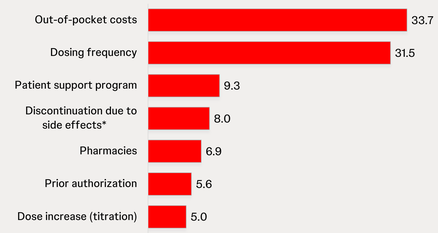
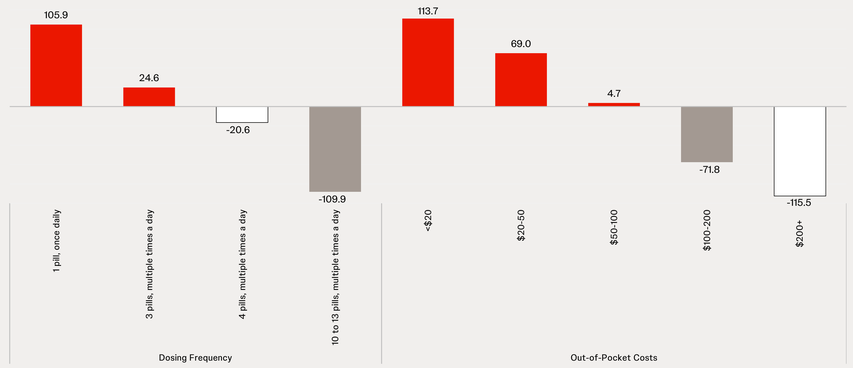


Fig 2. Individual Preference Weights – Top 2 Attributes*



Blinded Choice of PAH Therapies

- After each DCE trial, patients were asked to select their preferred therapy from an array of four blinded (unlabeled) treatment profiles (**Table 4**).
- Patients displayed an overwhelming preference for a STCT of macitentan-tadalafil (96.0%) over alternative traditional "loose dose" profiles (<5%) **(Figure 3).**

Fig. 3 Blinded Choice Exercise – STCT Preference

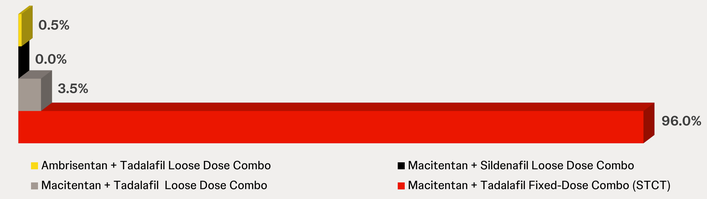


Table 4. Blinded Choice Exercise – STCT Preference

Treatment Profiles Shown	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
Dose increase (titration)	Available	Available	Available	Available
Discontinuation due to side effects[4-6]	8%	7%	9%	12%
Pharmacies required	Requires 1 pharmacy	Requires 2 pharmacies	Requires 2 pharmacies	Requires 2 pharmacies
Prior authorizations	Requires 1 prior authorization	Requires 2 prior authorizations	Requires 2 prior authorizations	Requires 2 prior authorizations

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"). SD, Standard Deviation. CI, Confidence Interval.

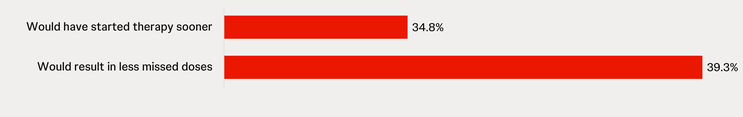
*Presented to respondents in the DCE as "the percentage of patients that stopped medication due to side effects."
** Assumes max dose of 60-80 mg sildenafil.

Perceptions of a STCT for ERA+PDE5i adoption

- Results from a supplemental questionnaire confirmed that most patients believed that a STCT would reduce pill consumption (83.1%) and time spent managing prescriptions (68.7%) (**Figure 4a).**
- Over one-third of patients identified benefits to compliance (42.3%), cost (39.8%), and dose burden (37.3%)
- Approximately a third of patients reported benefits to treatment initiation (34.8%) followed by adherence (39.3%) **(Figure 4b).**

Fig 4a. Perceptions of STCT – Pros

Fig 4b. Influence of STCT on treatment behavior



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