

A Qualitative Interview Study to Evaluate Single-tablet Combination Therapy (STCT) within a Phase 3 Pulmonary Arterial Hypertension (PAH) Clinical Trial – Interim Analysis

PCR57

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INTRODUCTION

- Pulmonary arterial hypertension (PAH) is a rare, chronic, and progressive disease leading to right ventricular (RV) failure and death.¹⁻³
- PAH should be treated with double/triple therapy in most cases, requiring multiple tablets.¹ Patients often have co-morbidities and can be on multiple treatments,⁴ which can impact adherence to medication.⁵⁻⁷
- A single-tablet combination therapy (STCT) of macitentan 10 mg and tadalafil 40 mg compared with corresponding monotherapies is being evaluated in a Phase 3 trial (A DUE, NCT03904693, AC-077A301): patients received 4 tablets during the double-blind period to maintain blinding (Various arms: 1 STCT + 3 placebos; 1 macitentan 10 mg + 3 placebos; 2 tadalafil 20 mg + 2 placebos) and 1 tablet (STCT) during open-label treatment.
 - During the clinical trial double-blind portion STCT led to a highly significant and marked improvement in primary endpoint pulmonary vascular resistance (PVR)-reduction vs macitentan and tadalafil monotherapies⁸
 - A trend for clinically relevant improvement in 6 Minute Walk Test in favour of STCT was observed⁸
- Interviews during the ongoing open-label extension are being conducted to **explore patients' and clinicians' experience with the STCT**, specifically the **adherence and convenience of this medication**.

METHODS

- Qualitative, one-on-one, semi-structured web-assisted interviews are being conducted across multiple countries with A DUE trial patients and clinicians.
- Interviews asked both patients and clinicians about their experience with the STCT, adherence, convenience, and the impact of a reduction in pill count. In addition, clinicians also discussed STCT in relation to treatment-naïve patients and the ESC/ERS guidelines.¹
- All data was analyzed using Thematic analysis⁹ which was conducted using NVivo v14.
- To be eligible for the study, patients had to be currently receiving the STCT during the open-label treatment period of the clinical trial, or the continuous access program, or recently stopped taking the STCT (in the last 2 weeks). Patients had to have taken the STCT for at least 6 months prior to the interviews.
- Clinicians are investigators from the A DUE clinical study sites. There were no additional clinician eligibility requirements.
- A total of 9 countries (Brazil, Germany, Mexico, Poland, South Africa, Spain, Taiwan, Turkey, United States) have been identified for participation in this study.
- This report is based on interim data and analysis from 14 patient and 13 clinician interviews conducted up to the 13th of October 2023 (Germany: 1 clinician; Mexico: 1 clinician; Poland: 1 patient; 1 clinician; South Africa: 2 patients, 1 clinician; Spain: 2 patients, 1 clinician; Taiwan: 2 patients, 1 clinician; Turkey: 2 patients, 1 clinician; and US: 5 patients, 4 clinicians).
- Recruitment and interviews are ongoing across multiple countries, due to complete in Q1 2024.

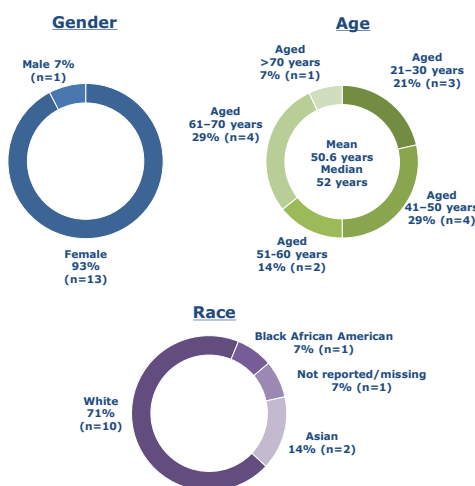
RESULTS

- All 27 participants (14 patients and 13 clinicians) provided **positive feedback on the STCT** and preferred the single tablet in the open-label extension to the four tablets in the double-blind period **regardless of the country** or treatment in the double-blind period.

RESULTS CONTINUED

- Patients stated the **STCT** was **convenient, aided adherence**, and had a positive impact on their **day-to-day lives**. Patients discussed how taking more tablets made them feel "sicker" compared with STCT.
- Patients noted the **STCT improved their psychological well-being and reduced the stress** of managing multiple tablets.
- Clinicians noted that the typically high pill burden in PAH can cause emotional distress in their patients, whereas patients had higher treatment satisfaction with the STCT.
- Clinicians predict the STCT will be well received in clinical practice and endorsed prescribing STCT for their patients, with the majority also endorsing use for treatment-naïve patients.

Patient Demographics, N=14



Clinician Profiles

- Most of the clinicians were cardiologists who worked in multi-disciplinary hospitals, and all had at least 5-9 years of experience working in PAH, seeing at least 5-10 PAH patients each month.
 - Several clinicians had many more years of experience and saw a greater number of patients with PAH per month.
- All clinicians saw patients with a similar spread of disease severities based on World Health Organization functional class evaluation categories.

Clinician Quotes

Overall STCT Feedback

"Uh, I have a **very positive opinion [of STCT]**. I think they [patients] are experiencing... all the benefits of the medication And the fact of taking it **one single tablet is absolutely positive.**" (Spain)

Adherence

"I believe that it [STCT] will **improve adherence** of patient, and **will make their life easier.**" (Germany)

Reduction in Pill Burden

"If you **reduce a pill burden in a patient** who's taking at baseline, you know, five or six tablets, yeah, uh, **it makes a big difference.**" (South Africa)

First Line Treatment

"Yeah, I, I think so. I mean **especially the treatment-naïve**, idiopathic PAH patient or patients with not a lot of comorbidities. I think definitely... It [STCT] can be, uh, **the upfront, uh, combination therapy for these patients.**" (United States)

Suitable for all Patients

"I think it will be **absolutely suitable [for everyone]**, and it will be, uh, an interesting improvement in... if we can offer them a combination in a single tablet, this is... this is positive, of course." (Spain)

Patient Quotes

Overall STCT Feedback

"Yeah. **It's really nice to take only one tablet-** Yes. So many times, I just wanted to tell the doctors like, you know, "I don't want to take all these tablets now." (South Africa)

Better Mental Health

"It's a good thing. **Psychologically it's a good thing.** Uh... now I'm taking one pill instead of three or four. The **brain tells you that it's... Well... it tells you that it's better.** I feel better. I'll tell you that. **It's better for me.**" (Turkey)

Convenience

"I would **honestly be ecstatic** [to continue taking the single tablet] Um, a **lot easier to fit just one pill for something,** um, **into my rotation or my schedule.** Um, I wish I could do that for all of my stuff." (United States)

Adherence

"The **fewer the tablets, it's always better** [for adherence]." (United States)

Better Mental Health

"Um, **every pill makes me a little bit more sad that, you know, I'm, I'm sick,** and it's just a re-, a daily reminder that I'm sick, and **having fewer pills just makes me feel better about myself.**" (United States)

Reduction in Pill Burden

"... **it's better to take one, right?** Rather than 4 and having to remember the timings. Because as I mentioned, even if you go out or meet friends or family, ... **you don't have to remember and keep track of taking the pill.**" (Poland)

Convenience

"Um, it, it **simplifies things.** It simplifies my life. It is, um, **much more convenient,** and, um, it **gives me confidence** that I'm doing something good for myself." (United States)

Adherence

"**For me, it's easy.** I have already a routine and I have... I wake up, have breakfast, my pill, you know? Once I had my routine established, I already... And as it is working fine, **I don't forget to take it. That's for sure.**" (Spain)

CONCLUSION

- Interim analysis suggests that the **STCT** was well **received by patients and clinicians regardless of the country**.
- The qualitative insights from this study show, directly from the patients living with PAH, that reducing the number of tablets needed to treat PAH would be **highly valued by patients** and would have a **positive effect on patients' well-being**.
- The participants in this study highlighted how the **STCT reduced pill burden, minimised stress, improved adherence to treatment and simplified the treatment regimen**, which could improve patient outcomes and health-related quality of life (HRQoL).
- These findings align with previous research** that has also provided strong evidence that reducing the tablet count and frequency has a major impact on patient adherence to PAH therapies, and subsequently clinical outcomes.^{6,7}
- Limitations: The study has been conducted on limited interim data, and interviews are ongoing.

References

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