Worldwide Clinical Trials

Case Study

Innovation in a PAH Phase III Study:
Enhancing Patient Recruitment & Retention

Worldwide was selected by a sponsor to conduct a Phase III, placebo-controlled, double-blind, randomized clinical study of pulsed inhaled nitric oxide targeting the rare cardiovascular disease, pulmonary arterial hypertension (PAH). Worldwide leveraged our innovative rare disease patient recruitment and retention strategies, operational expertise, and flexibility to overcome study challenges and achieve trial success.

Study Design

18
Countries

103
Sites

160
Randomized Patients
18-85 Years Old

Patients were randomized into two groups:

Active Drug

Placebo

The study was divided into two distinct parts:

1. **Week 0-18:** One blinded treatment group compared to the placebo
2. **Week 0-52 (or end-of-study):** Open-label treatment provided

Study Challenges

Patients with PAH are a unique population with symptoms that can impact trial participation and require greater support from sites. The study faced three main challenges that Worldwide would have to account for:

Designing a Successful Retention Plan

PAH patients often quickly tire and become breathless with physical movement. Our team needed to develop a retention plan and design a study that ensured patients would not drop out due to the indication's symptoms.

01

Creating a Custom Site Management Model

With this indication, sites required more frequent attention, support, and visits than the number of patients per site would suggest in an average rare disease site management model. Regional differences in PAH patient profiles, site profiles, regulatory strategies, and standards of care all required effective relationships between site personnel and our CRAs. Additionally, our team needed to find a new approach to manage the competing priorities of tailoring site management to account for regional variances while standardizing global operations for efficiency and performance.

02

Amending a Limiting Protocol

The original study protocol excluded patients with unrepaired congenital heart disease, a condition prevalent in Europe. Since a considerable segment of the PAH population is affected by congenital disease, both unrepaired or repaired, the exclusions limited the study's enrollment.

03

Worldwide's Solutions

Overcoming Operational Study Complexities

To overcome operational study complexities, including barriers to patient recruitment and retention, Worldwide implemented the following:

- **Regional Training for Recruitment Traction:** We interviewed and identified sites in each region most likely to respond to retraining to implement regionally tailored recruitment strategies.
- **Early Site Interaction for Reliable Recruitment:** Worldwide crafted transparent and reliable recruitment forecasts by tracking potential patients from the initial point of identification to randomization/screen failure. This approach promoted patient retention before and during screening and allowed us to anticipate enrollment patterns to proactively direct resources where needed.
- **PAH Expert Utilization:** PAH assessment criteria, oxygen therapy standards, and standard of care vary between countries. To ensure the various standards were met, we provided the sponsor with knowledge of the local standards of care and facilitated physician-to-physician communication with PAH experts. We also held frequent calls with the principal investigators to answer questions about the protocol.

Close physician-to-physician communication, frequent calls with investigators, and local resources presented by our strong, qualified, and dedicated people gave the sponsor confidence in having accurate, complete, and verifiable data. It helped to ensure that appropriate steps were taken for the care and management of study patients. Overall, the collaboration with the sponsor within the study helped to get an innovative vision in patients' recruitment and retention strategies for PAH studies."

Eteri Tsetskhladze MD, PhD, FESC
Vice President, Therapeutic Area Medical Lead, Medical Affairs
Worldwide Clinical Trials

Partnering with Patient Advocacy Organizations

To address patient retention concerns, Worldwide partnered with a PAH-focused patient organization to better understand PAH patient perspectives and resolve day-to-day challenges. Our partnership deepened our understanding of the PAH patient population, which allowed us to anticipate retention risks, improve our screening and enrollment strategies, and offer means to reduce the burden of participation for this community.

Providing Hands-On Site Support and Sponsor Communication

Due to the recruitment challenges faced by the sites in this study, Worldwide rapidly restructured our site management team to address the changing needs. We mobilized a site-focused team restructure within four weeks, enabling a swift conduct of intensive site interviews and analyses that contributed to significant momentum in patient recruitment. To further support the sites, our CRAs facilitated and coordinated multiple on-site visits to provide communication and translation support and to share site-specific insights with the sponsor.

The Results

Our solutions not only resulted in a sustainable 50% increase in the study's randomization rate, but also a 128% increase (9.6 vs. 3.2 patients per month) in average global monthly enrollment during the last seven months of the study. We also promoted patient retention before and during the screening process, which was more effective than initiating retention strategies after randomization. Knowing early in the process when and where potential patients were identified allowed us to anticipate enrollment patterns and proactively direct resources where needed.

Solutions lead to a **128% increase** in enrollment

Thanks to the partnership with the PAH-focused patient organization, we advocated sponsor support of the community through:

- Taxis for patient transportation to site visits
- Additional clinic/hospital visits for patients
- Travel vouchers to reimburse patients for travel expenses
- Patient-centric solutions when travel to the study center was not possible

The sponsor implemented all recommendations, playing a crucial role in recruitment and retention success.

Based on the collaborative evolution and flexibility throughout our partnership, the sponsor stated they want to work with Worldwide again on their expanding cardiopulmonary pipeline.

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Why Worldwide?

Worldwide is a leading full-service global CRO that offers innovative end-to-end customized solutions in partnership with biotechnology and pharmaceutical companies. Founded on an unwavering commitment to therapeutic excellence and personalized attention, we bring scientific expertise, a specialized and flexible cardiovascular team, and a shared passion for advancing new medicines from discovery to reality.

If you're interested in learning how Worldwide can help support your drug development program, contact us today.

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