PLAIN LANGUAGE SUMMARY[1]

SERALUTINIB FOR THE TREATMENT OF PULMONARY ARTERIAL HYPERTENSION. RESULTS FROM THE PHASE 2 TORREY STUDY

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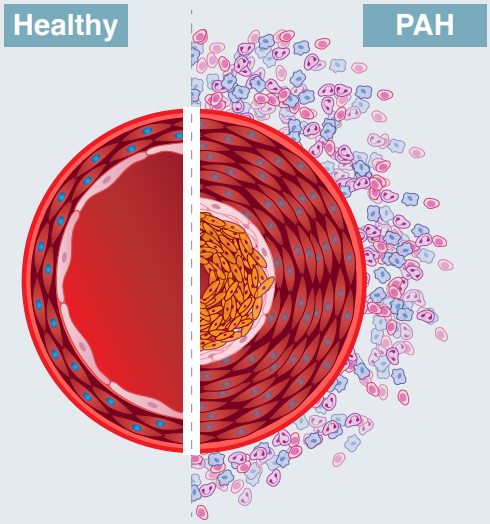
BACKGROUND

Pulmonary arterial hypertension, or PAH, is a rare, progressive disease that occurs when the small arteries in the lungs become thickened and narrowed (see Figure 1), causing pressure in those arteries to build, and putting a strain on the heart. Three connected processes contribute to PAH disease:

1. inflammation
2. cell growth (called proliferation) and
3. scarring (called fibrosis)

These processes play a role in the thickening, narrowing, and stiffening of the small arteries in the lungs, often referred to as "vascular remodeling."

Figure 1. Cross-section of a small pulmonary artery in the lung, healthy (left) and constricted due to PAH (right)



Approved PAH treatments act primarily as vasodilators; these treatments work to open up the blood vessels but cannot reverse the vascular remodeling brought on by inflammation, proliferation, and fibrosis. Seralutinib is a new molecule under study, specifically developed to treat PAH. By blocking inflammation, proliferation, and fibrosis responsible for PAH, seralutinib works in a different way than vasodilators. Seralutinib is formulated as a fine dry powder for inhalation and is administered using a small hand-held device. This dry powder inhaled formulation was specifically designed to reach deep into the lungs to the site of disease.

The goal of the phase 2 TORREY study was to help researchers determine if inhaled seralutinib may be an effective and safe treatment in PAH. This summary aims to explain the results of the TORREY study in plain language.

METHODS

The TORREY study enrolled 86 adults with PAH already taking two or three PAH medicines; 44 were given seralutinib and 42 were given placebo for 24 weeks. Researchers wanted to understand if seralutinib could decrease the resistance to blood flow through the lungs (measured as pulmonary vascular resistance or PVR), and improve other measures related to PAH.

TORREY STUDY

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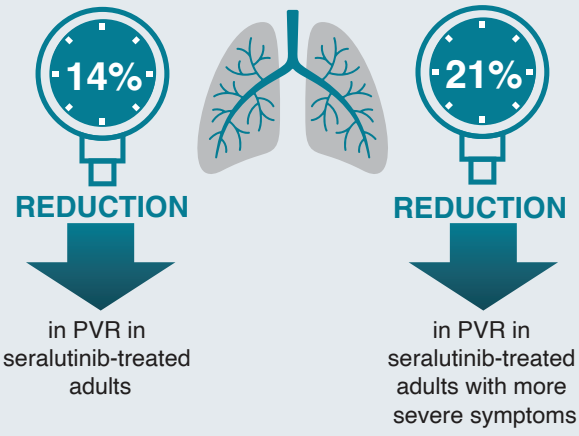
RESULTS

On average, after 24 weeks in the study, adults taking inhaled seralutinib lowered their pulmonary vascular resistance by 14% more than adults taking placebo, which was statistically significant (p=0.0310) (see Figure 2 below). A subset of adults with more severe PAH symptoms had an even greater reduction in pulmonary vascular resistance (21%) (p=0.0427).

Figure 2.



Seralutinib-treated participants also had significantly lower (improved) NT-proBNP levels compared to participants who received placebo. NT-proBNP is a protein marker in the blood that goes up when the heart is under stress. Lowered NT-proBNP levels suggest that seralutinib may have decreased stress on the heart. Positive changes in other measures of heart function were also observed.

While the TORREY study was not designed to show a difference in 6-minute walk distance, meaningful improvement was seen in a subset of participants with more severe PAH symptoms, with an increase of 37 meters compared to placebo.

Seralutinib was generally well tolerated. Cough was the most common side effect in participants receiving seralutinib or placebo (see table below), not unexpectedly, as cough is often reported for medicines given by dry powder inhalation. Three participants who received seralutinib and two participants who received placebo had an increase in liver function enzymes (markers of possible liver injury).

Side Effects Reported More Frequently in Study Participants Taking Seralutinib vs. Placebo

Side Effect	Seralutinib (N=44)	Placebo (N=42)
Cough	19 (43.2)	16 (38.1)
Diarrhea	6 (13.6)	3 (7.1)
Dizziness	5 (11.4)	2 (4.8)
Nightmare	4 (9.1)	1 (2.4)
Abdominal pain lower	3 (6.8)	0
Nasopharyngitis	3 (6.8)	0
Throat irritation	3 (6.8)	0

The numbers in the table are the number of participants (percentage of participants) for whom the side effect was reported.

CONCLUSIONS

The TORREY study met its primary objective; that is, participants with PAH who took seralutinib had lowered resistance to blood flow in the lungs to a greater extent than those who took placebo. Seralutinib was generally well tolerated. Based on these positive results, research on inhaled dry powder seralutinib will continue in a global Phase 3 clinical study of adults with PAH, starting late 2023. We thank all participants, their families, and all investigators and coordinators for their involvement in the TORREY study.

[1]Frantz RP et al. *Am J Respir Crit Care Med*. 2023;207:A6726.