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SUSTAINED BENEFIT WITH SERALUTINIB TREATMENT: A POST-HOC ANALYSIS OF THE TORREY OPEN-LABEL EXTENSION



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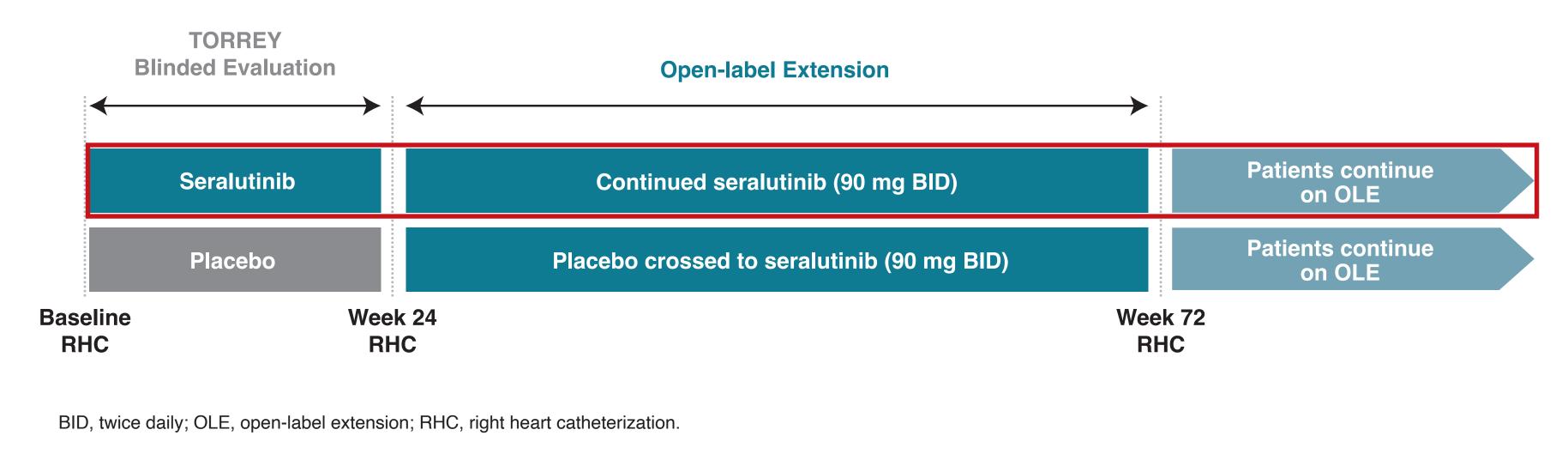
BACKGROUND

- Seralutinib is a novel inhaled platelet-derived growth factor receptor α/β, colony stimulating factor 1 receptor, and mast/stem cell growth factor receptor kit kinase inhibitor currently in phase 3 development in Group 1 pulmonary hypertension (PAH)^{1,2}
- In the open-label extension (OLE) of the phase 2 TORREY study, longer-term treatment with seralutinib through Week 72 resulted in continued improvements in pulmonary vascular resistance (PVR) and six-minute walk distance (6MWD)3
- To further characterize the efficacy profile of seralutinib, we undertook a more detailed analysis of the patients with PVR improvements from TORREY Baseline through Week 72 of the OLE study

METHODS

- 74 patients enrolled in the OLE study, with hemodynamic data available for 55 patients at Week 72
- This analysis is focused on patients treated with seralutinib for 72 weeks (n=28) (**Figure 1**)
- Patients demonstrating a >15% PVR reduction from TORREY Baseline to Week 72 were considered "responders" (n=17)
- Results are descriptive

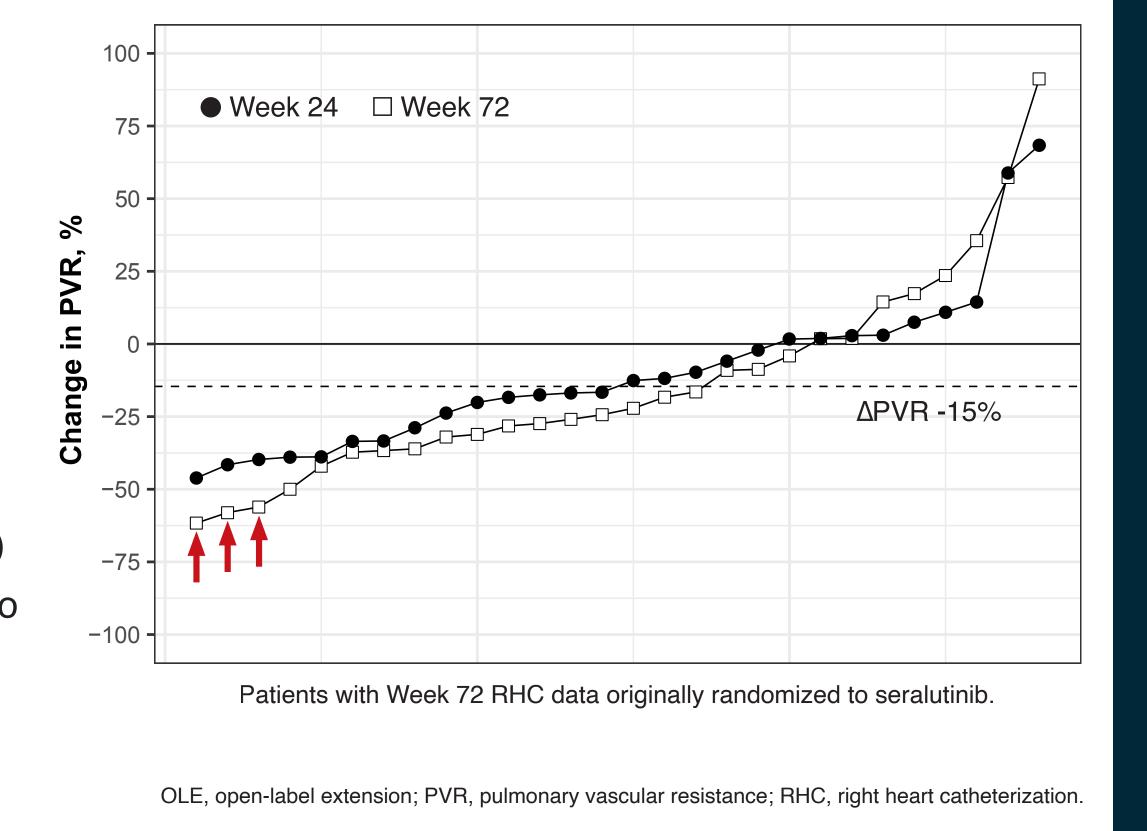
Figure 1. Study Design.



RESULTS

Figure 2. Change in PVR in Seralutinibtreated Patients Over 72 Weeks in the **OLE.** Sorted distribution of % change from Baseline in the continued-seralutinib population (n=28). Arrows indicate patients with PVR <200 dyne*s/cm⁵ at Week 72.

- In the TORREY open-label continuedseralutinib group treated for 72 weeks, PVR improved in 20 (of 28) patients
- In PVR responders (n=17), the median change was -32% (range: -17% to -62%)
- 3 patients had a Week 72 PVR reduction to <200 dyne*s/cm⁵ (arrows)



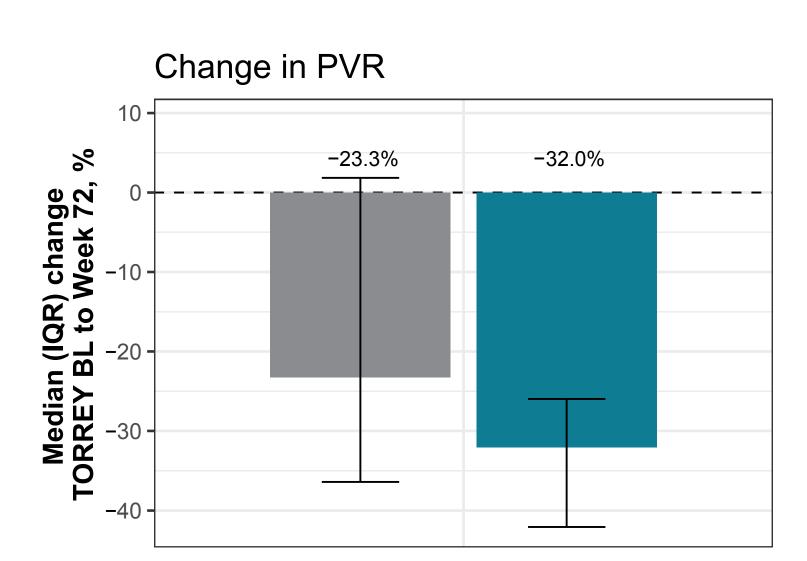
RESULTS (continued)

Table 1. Baseline Disease Characteristics of OLE Patients With 72-Week Pulmonary Hemodynamic Data. Characteristics are at TORREY Baseline. Data presented as mean (SD) unless otherwise noted.

	RHC overall (n=55)	Continued seralutinib (n=28)	Continued seralutinib >15% PVR decrease (n=17)
Age at PAH diagnosis, y	44.0 (12.90)	45.9 (14.43)	46.6 (13.71)
Years since PAH diagnosis	7.2 (6.34)	6.4 (6.17)	4.8 (4.93)
PAH classification, n (%)			
Idiopathic/Heritable	27 (49.1)/13 (23.6)	14 (50.0)/9 (32.1)	10 (58.8)/4 (23.5)
CTD / D and T, repaired CHD	9 (16.4)/6 (10.9)	2 (7.1)/3 (10.7)	0/3 (17.6)
Background PAH treatment, n (%)			
Triple therapy	34 (61.8)	16 (57.1)	7 (41.2)
Parenteral prostacyclins/PRA	24 (43.6)	12 (42.9)	6 (35.3)
WHO FC II, n (%)	29 (52.7)	17 (60.7)	10 (58.8)
WHO FC III, n (%)	26 (47.3)	11 (39.3)	7 (41.2)
REVEAL 2.0 risk score ≥6, n (%)	26 (47.3)	13 (46.4)	6 (35.3)
PVR, dyne*s/cm⁵	646.8 (162.71)	620.9 (156.17)	628.4 (152.17)
6MWD, m	398.6 (92.74)	403.6 (81.66)	400.9 (88.75)
NT-proBNP, ng/L	612.0 (1000.53)	550.8 (720.74)	500.4 (753.13)

6MWD, six-minute walk distance; CHD, congenital heart disease; CTD, connective tissue disease; D and T, drugs and toxins; FC, Functional Class; NT-proBNP, N-terminal pro-brain natriuretic peptide; OLE, open-label extension; PAH, pulmonary arterial hypertension; PRA, prostacyclin receptor agonist; PVR, pulmonary vascular resistance; REVEAL, Registry to Evaluate Early and Long-term PAH Disease Management; RHC, right heart catheterization; SD, standard deviation; WHO, World Health Organization.

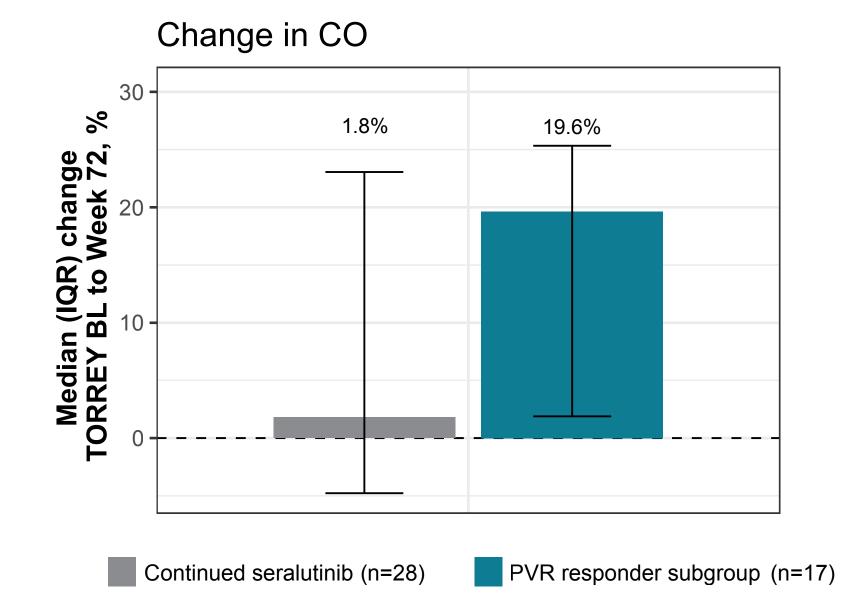
Figure 3. Mean Pulmonary Arterial Pressure and Cardiac Output Contributed to Hemodynamic Improvement in Patients Treated With **Seralutinib for 72 Weeks.**

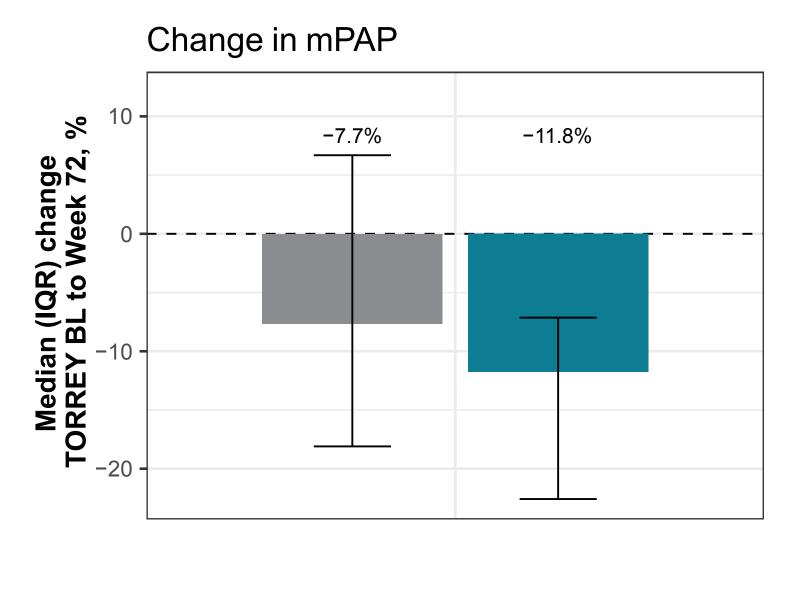


Plot shows patients in the continued-seralutinib group

6MWD, six-minute walk distance; SE, standard error;

PVR, pulmonary vascular resistance

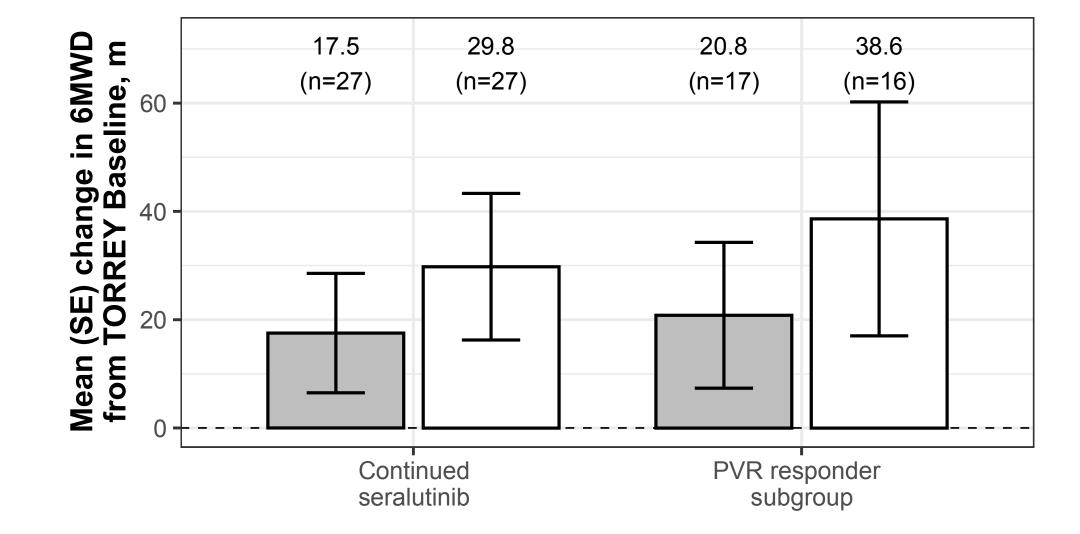




■ Week 24 □ Week 72

BL, Baseline; CO, cardiac output; IQR, interquartile range; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance.

Figure 4. PVR Responders Showed Improved Functional Capacity. 6MWD increased 38.6 m from TORREY Baseline in PVR responders treated with seralutinib for 72 weeks.



Seralutinib was generally well tolerated during the OLE treatment period (Table 2), with no new safety signals emerging

Table 2. Treatment-emergent Adverse Events (TEAEs) With an Incidence ≥10% During the OLE.*

Incidence of TEAEs by preferred term: ≥10%	RHC overall (n=55)	Continued seralutinib (n=28)	Continued seralutinib >15% PVR decrease (n=17)
Patients with a TEAE, n (%)	53 (96.4)	28 (100)	17 (100)
COVID-19	15 (27.3)	8 (28.6)	4 (23.5)
Headache	15 (27.3)	7 (25.0)	5 (29.4)
Cough	11 (20.0)	5 (17.9)	2 (11.8)
Nausea	11 (20.0)	6 (21.4)	3 (17.6)
Diarrhoea	10 (18.2)	4 (14.3)	1 (5.9)
Dyspnoea	10 (18.2)	4 (14.3)	2 (11.8)
Arthralgia	8 (14.5)	2 (7.1)	2 (11.8)
Influenza	8 (14.5)	5 (17.9)	2 (11.8)
Nasopharyngitis	8 (14.5)	3 (10.7)	3 (17.6)
Pain in extremity	8 (14.5)	3 (10.7)	2 (11.8)
Epistaxis	7 (12.7)	6 (21.4)	4 (23.5)
Fatigue	7 (12.7)	1 (3.6)	0
Rash	7 (12.7)	3 (10.7)	3 (17.6)
Flushing	6 (10.9)	2 (7.1)	2 (11.8)
Hypokalaemia	6 (10.9)	4 (14.3)	1 (5.9)
Palpitations	6 (10.9)	4 (14.3)	2 (11.8)

TEAE results as of 26 July 2024. OLE, open-label extension; PVR, pulmonary vascular resistance; RHC, right heart catheterization

CONCLUSIONS

- Acknowledging the limitations of an open-label study and post-hoc analysis, longer-term treatment with seralutinib resulted in continued PVR improvement through 72 weeks of treatment in a low-risk, heavily treated population
- In the PVR responder group, median PVR improvement was 32% (range: -17% to -62%) and three patients achieved an absolute PVR <200 dynes*s/cm⁵
- Improvements in mPAP and CO contributed to the PVR improvement
- PVR responders showed concordant improvements in functional capacity (6MWD)
- Seralutinib was well tolerated, with no new safety signals emerging over the OLE treatment period to date

References: 1 Galkin A, et al. Eur Respir J. 2022;60(6):2102356. 2 Pullamsetti SS, et al. Int J Mol Sci. 2023;24(16):12653. 3 Sitbon O, et al. Am J Respir Crit Care Med. 2024;209:A1011.

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