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

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TORREY STUDY

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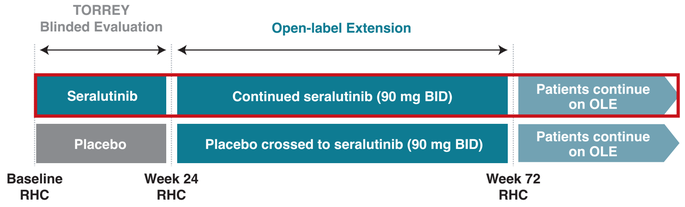
BACKGROUND

- Seralutinib is a novel inhaled platelet-derived growth factor receptor α/ß, 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

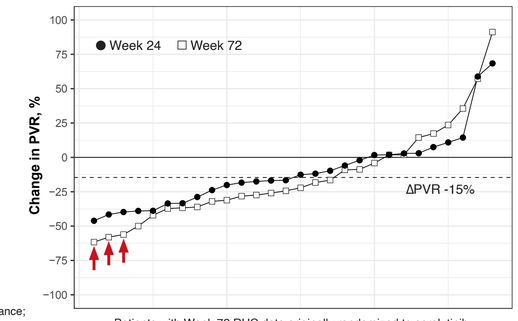
Figure 1. Study Design.



BID, twice daily; OLE, open-label extension; RHC, right heart catheterization.

RESULTS

Figure 2. Change in PVR in Seralutinib-treated 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/cm^5 at Week 72.



OLE, open-label extension; PVR, pulmonary vascular resistance; RHC, right heart catheterization.

Patients with Week 72 RHC data originally randomized to seralutinib.

- In the TORREY open-label continued-seralutinib 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/cm^5 (arrows)

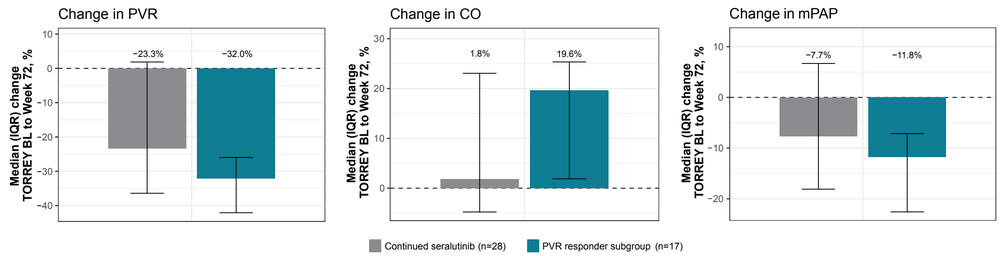
RESULTS (continued)

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/cm^5	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)

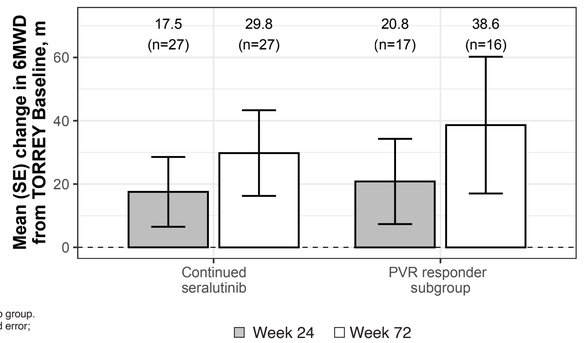
6MWD, six-minute walk distance; CHD, congenital heart disease; CTD, connective tissue disease; D and T, drugs and toxins; FC, Functional Class; NT-proBNP, N-terminal pro-brain natriuretic peptide; OLE, open-label extension; PAH, pulmonary arterial hypertension; PRA, prostacyclin receptor agonist; PVR, 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.



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.



Plot shows patients in the continued-seralutinib group. 6MWD, six-minute walk distance; SE, standard error; PVR, pulmonary vascular resistance.

- 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/cm^5
- 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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