



Seralutinib improves pulmonary arterial blood vessel volume distribution in pulmonary arterial hypertension (PAH): Results of the TORREY Phase 2 imaging substudy

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Conflict of Interest Disclosure



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Affiliation / Financial interest	Commercial company
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CT Imaging to Assess Pulmonary Vascular Remodeling in the Phase 2 TORREY Substudy of Inhaled Seralutinib for PAH



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Background

- Seralutinib: a novel PDGFR α/β , CSF1R, and c-KIT kinase inhibitor with anti-inflammatory, anti-proliferative, and anti-fibrotic properties
- Phase 2 TORREY study met primary end point of reduction in PVR at Week 24 (14.3%, $p = 0.0310$)
 - Reduction in mPAP ($p = 0.0094$)
 - Improved PAC ($p = 0.0410$)
- Reduction in NT-proBNP at Week 12 (LSMD -309.6 ng/L, $p = 0.0116$) and Week 24 (LSMD -408.3 ng/L, $p = 0.0012$)

CT imaging substudy

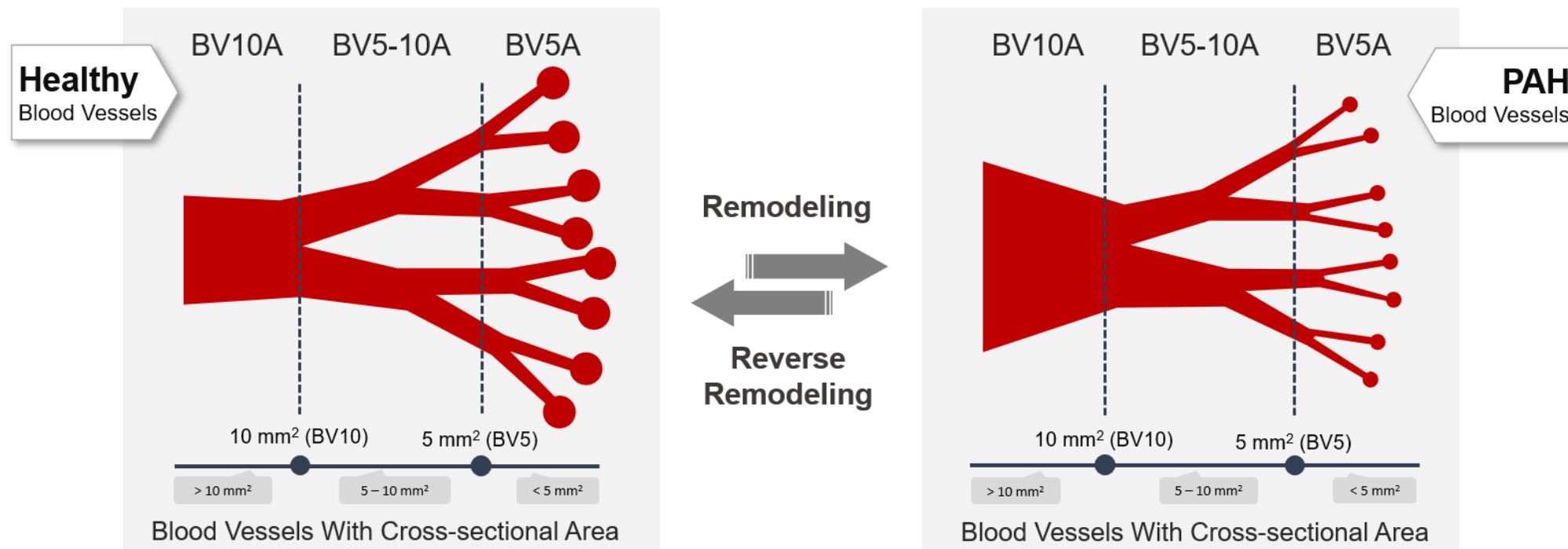
- Thin slice non-contrast CTs obtained at baseline and Week 24
- Arterial venous segmentation performed and blood vessel volumes quantified
- Data available for seven seralutinib-treated patients and twelve placebo patients (18 females, average age 49 years, on double or triple therapy)

Pulmonary Vascular Volume of Small Distal Arterial Vessels Is Decreased in PAH, Leading to Enlargement of Proximal Vessels



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CT imaging can quantify these changes: BV5A: BVV of pulmonary arteries with a CSA $< 5 \text{ mm}^2$; BV5-10A: BVV of pulmonary arteries with a CSA between $5-10 \text{ mm}^2$; BV10A: BVV of pulmonary arteries with a CSA $> 10 \text{ mm}^2$; BV510ARatio: BV5A/BV10A

- Pulmonary vascular pruning on CT correlates with histologic pulmonary vascular remodeling¹

1. Synn AJ, et al. *Pulm Circ.* 2021;11(4):20458940211061284. Histologic remodeling correlation shown is based on a study in patients undergoing resection for early-stage adenocarcinoma.¹ Illustration adapted from FLUIDDA, Inc. BV5A, blood vessel volume (BVV) of pulmonary arteries with a cross-sectional area (CSA) $< 5 \text{ mm}^2$; BV5-10A: BVV of pulmonary arteries with a CSA between $5-10 \text{ mm}^2$; BV10A: BVV of pulmonary arteries with a CSA $> 10 \text{ mm}^2$; BV510ARatio: BV5A/BV10A; CT, computed tomography; PAH, pulmonary arterial hypertension

Patient Characteristics



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Characteristic	Total
N	19
Age, mean (SD), y	49.26 (12.07)
Sex, n (%)	
Female	18 (94.7)
Male	1 (5.3)
BMI, mean (SD)	30.42 (7.59)
Treatment, n (%)	
Seralutinib	7 (36.8)
Placebo	12 (63.2)

Characteristic	Total
PAH classification, n (%)	
Idiopathic	10 (52.6)
Heritable	2 (10.5)
Associated with CTD	3 (15.8)
Drug- or toxin-induced	3 (15.8)
Associated with congenital shunts	1 (5.3)
WHO FC, n (%)	
Class II	7 (36.8)
Class III	12 (63.2)

Seralutinib Treatment Increases the BV5A/BV10A Ratio and Supports Reverse Remodeling Hypothesis

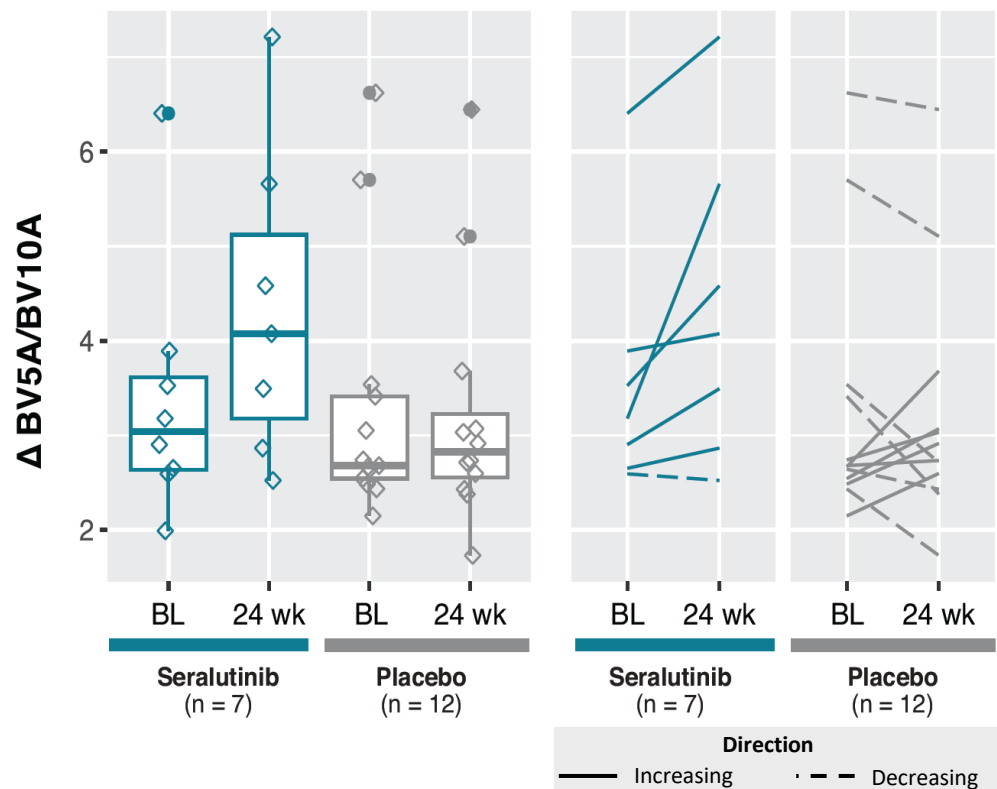


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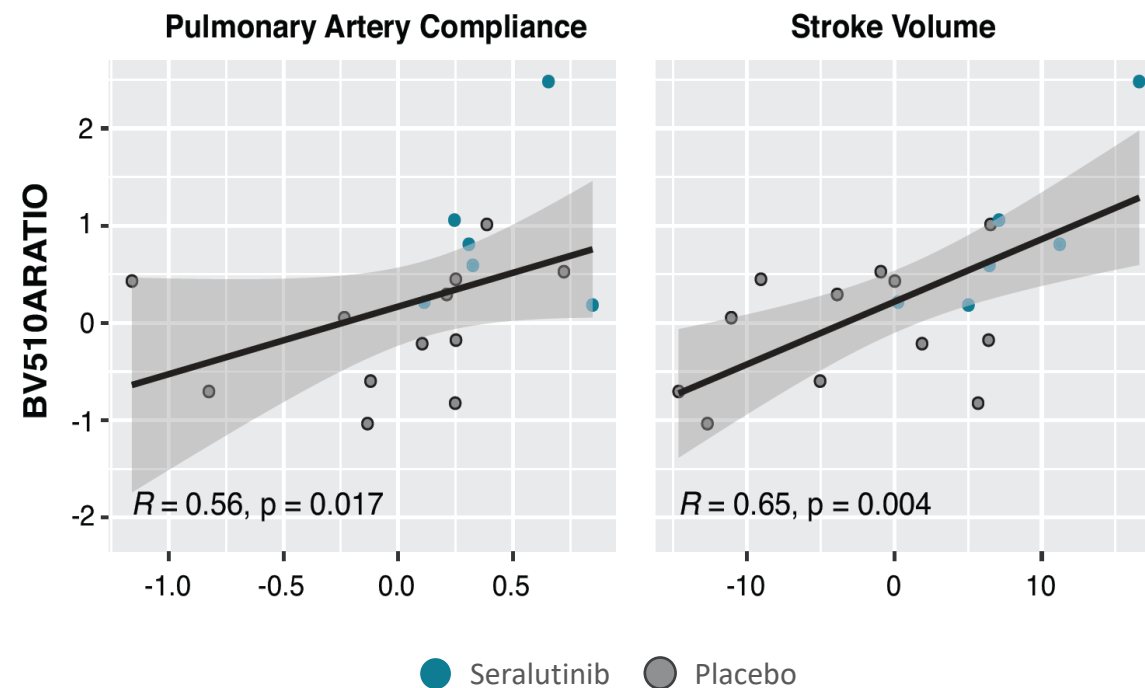
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Seralutinib increases BV5A/BV10A ratio

Parameter	LSMD Estimate (95% CI)	p-value
BV5A/BV10A ratio	0.845 (0.105, 1.585)	0.028



Change in BV5A/BV10A ratio from BL to Week 24 correlates with change in hemodynamics

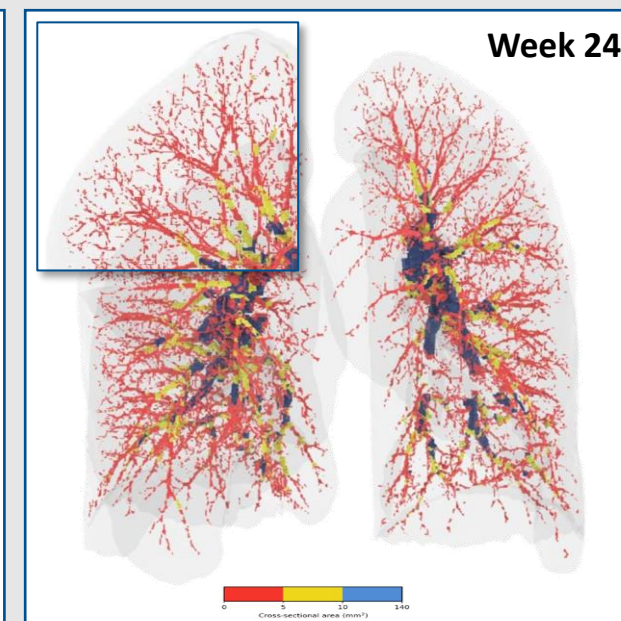
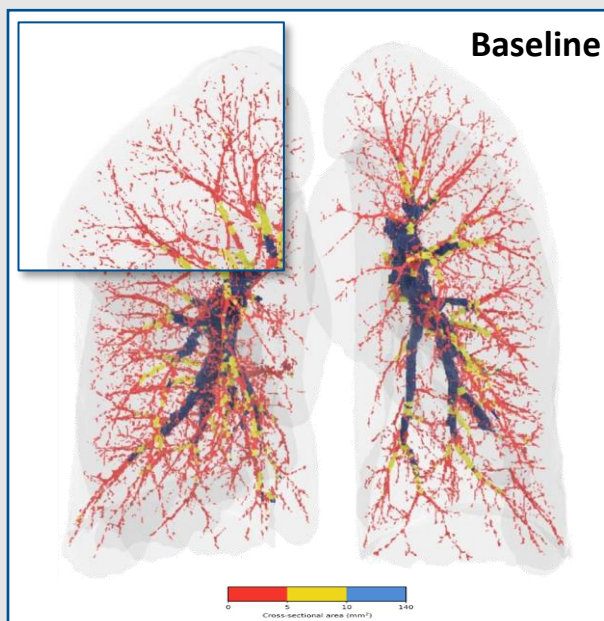
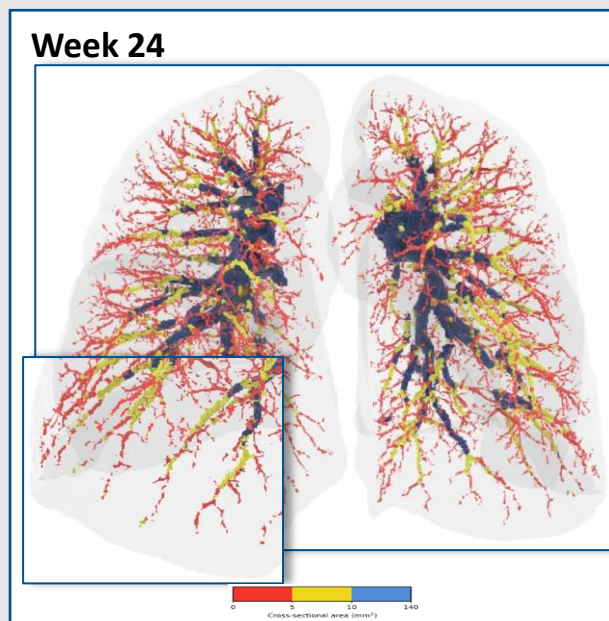
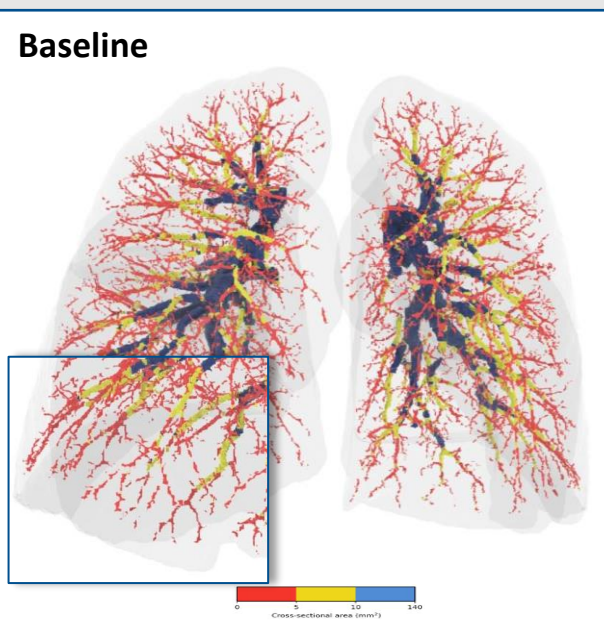


Linear regression models adjusted for BL values and treatment arm. BL, baseline; LSMD, least squares mean difference; BV510ARatio, ratio of pulmonary arteries smaller than 5 mm² in cross-sectional area (BV5A) compared to pulmonary arteries larger than 10 mm² in cross-sectional area (BV10A).

Examples of Imaging: Placebo vs. Seralutinib



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Placebo patient

Female, 24 y, iPAH, FC II, treated with PDE5-i + prostacyclin

PVR change, $\text{dyne}\cdot\text{s}/\text{cm}^5$ (%) 283 (+65.4)

$\Delta\text{BV510ARatio}$ (% change) -0.70 (-28.9)

Seralutinib patient

Female, 58 y, iPAH, FC II, treated with ERA + PDE5-i + prostacyclin

PVR change, $\text{dyne}\cdot\text{s}/\text{cm}^5$ (%) -159 (-39.0)

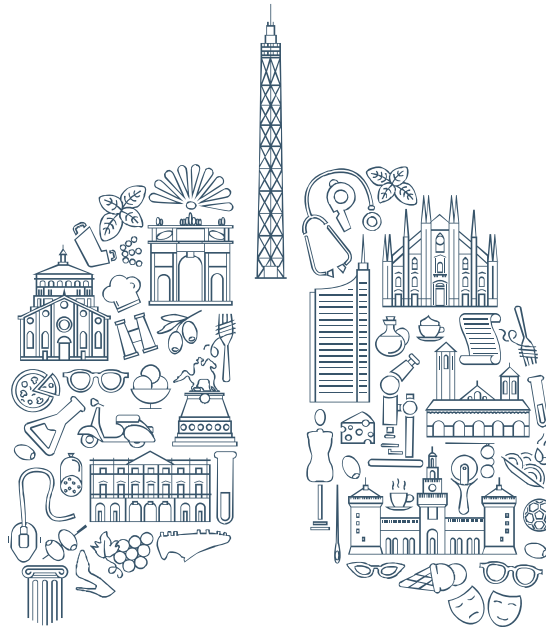
$\Delta\text{BV510ARatio}$ (% change) +2.5 (+78.0)

- Seralutinib treatment resulted in a significant improvement in the ratio of blood vessel volume in distal vessels relative to larger vessels (BV510ARatio), consistent with a reverse remodeling effect
- The BV510ARatio correlated with important measures of right ventricular-pulmonary artery coupling as measured by pulmonary artery compliance and stroke volume
- To increase our understanding of the effect of seralutinib on pulmonary vascular remodeling, a CT substudy is planned for the phase 3 PROSERA trial (NCT05934526)



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