PA5143

Seralutinib reduces vessel wall volume and increases small pulmonary artery vessel volume: Insights from AI-driven CT imaging analysis

Raúl San José Estépar[1], Pietro Nardelli[1], Robin Osterhout[2], Jean-Marie Bruey[2], Thao Duong-Verlé[2], Richard Aranda[2], Roham T. Zamanian[3], Lawrence S. Zisman[2], Farbod N. Rahaghi[1]

[1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; [2]Gossamer Bio, Inc., San Diego, CA, USA; [3]Stanford University School of Medicine, Stanford Medicine, Stanford, CA, USA

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BACKGROUND

- Seralutinib, an inhaled PDGFR, CSF1R, and c-KIT kinase inhibitor, demonstrated significant improvements in pulmonary vascular resistance in the phase 2 TORREY study in patients with WHO Group I pulmonary hypertension[1]
- In a quantitative computed tomography (CT) substudy of TORREY, seralutinib improved the ratio of blood vessel volume (BVV) of pulmonary arteries (PAs) with a cross-sectional area (CSA) <5 mm^2 to those with a CSA >10 mm^2 (BV5A/BV10A) after 24 weeks of treatment vs. placebo[2]
- Changes in pre-acinar vessel wall volume as a reflection of wall thickness may be a complementary measure of potential reverse remodeling effects in addition to changes in BVV of PAs with smaller CSA
- In a post-hoc analysis of the TORREY CT imaging data set, we applied a novel, artificial intelligence (AI)-derived CT imaging analysis method to quantify changes, for the first time, in vascular wall volumes and BVV ratio in smaller vessels associated with seralutinib treatment

METHODS

- Arterial reconstructions and vascular wall metrics were computed from non-contrast chest CT scans using a neural network regressor trained on synthetic vascular trees (**Figure 1**)
- Key AI-based vascular metrics included wall-volume ratio (WVR)3-4 and BV1/BV20 (**Figure 2**)
- Linear mixed models evaluated treatment effects of seralutinib (n=7) vs placebo (n=12) at 24 weeks in the TORREY study
- Spearman correlations assessed relationships between changes in vascular metrics and changes in right heart catheterization parameters from baseline to week 24

Figure 1. Vascular analysis pipeline and primary vascular imaging metrics.

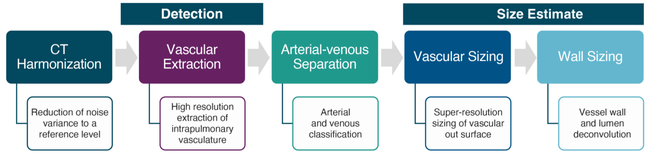
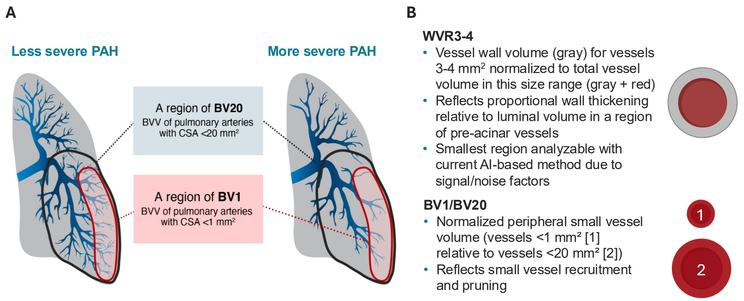


Figure 2. Changes in the pulmonary vasculature quantifiable by CT imaging (A) and redefinition of primary vascular imaging metric cut-offs (B).



B(V)V, blood (vessel) volume; CSA, cross-sectional area; PAH, pulmonary arterial hypertension; WVR, wall-volume ratio.

RESULTS

Table 1. Patient baseline characteristics.

Characteristic	Total
N	19
Age, mean (SD), y	49.3 (12.1)
Sex, n (%)	
Female	18 (94.7)
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)

BMI, body mass index; CTD, connective tissue disease; FC, functional class; PAH, pulmonary arterial hypertension; SD, standard deviation; WHO, World Health Organization.

Figure 3. Seralutinib reduced WVR3-4 (p=0.021) (A) and increased arterial BV1/BV20 (p=0.02) (B) vs placebo.

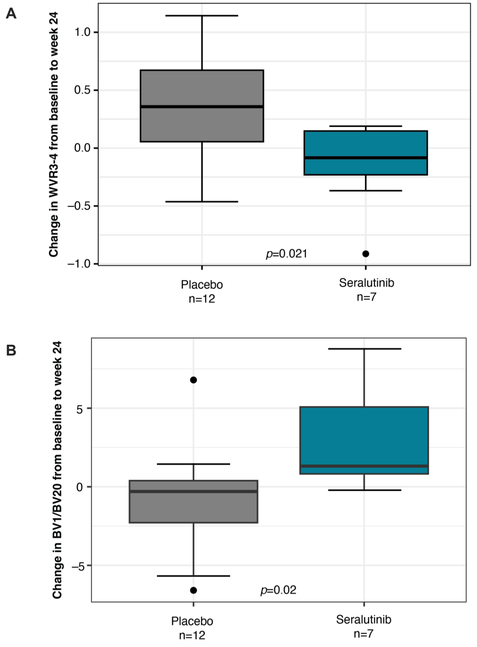
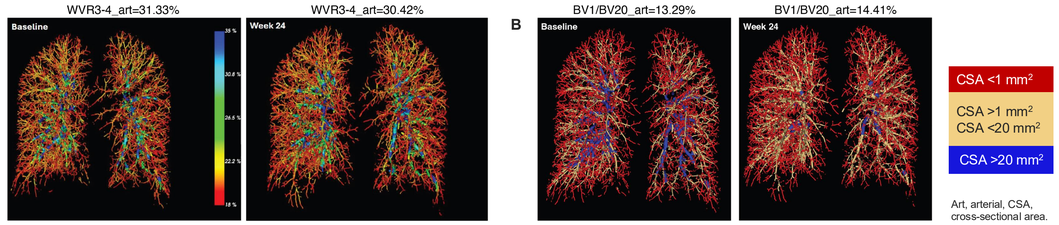
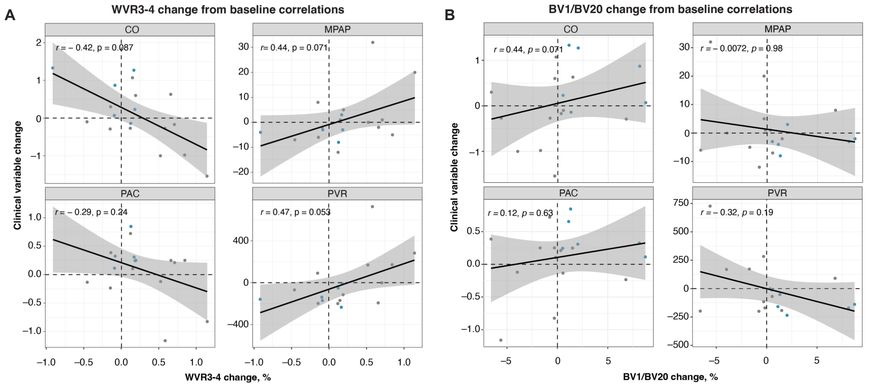


Figure 4. 3D renderings illustrating 24-week changes in arterial WVR3-4 (A) and BV1/BV20 (B) with seralutinib treatment. A. Vascular tree color-coded by wall-to-vessel ratio percentage, with yellow-to-red shading indicating reduced vessel wall thickness, consistent with treatment response. **B.** Visualization of changes in peripheral small vessels, color-coded by vessel CSA. 24-week response showed an increase in normalized peripheral small vessel volume (BV1/BV20) and a corresponding decrease in proximal vessels (CSA >20 mm^2), potentially reflecting reduced distal vascular resistance.



Art, arterial, CSA, cross-sectional area.

Figure 5. Correlations were observed between changes in WVR3-4 with changes in PVR (r=0.47), CO (r=−0.42), and MPAP (r=0.44) (A), and changes in BV1/BV20 with PVR (r=−0.32) and CO (r=0.44) (B).



CO, cardiac output; MPAP, median pulmonary arterial pressure; PAC, pulmonary arterial compliance; PVR, pulmonary vascular resistance; WVR, wall-volume ratio.

CONCLUSIONS

- In this exploratory post-hoc analysis, seralutinib improved metrics of vascular remodeling, correlating with hemodynamic changes
  - The measure of blood vessel wall volume in pre-acinar vessels supports a reverse remodeling effect of seralutinib
  - Improved BV1/BV20 suggests increased blood volume of smaller pulmonary arteries
  - WVR3-4 and BV1/BV20 correlated with relevant measures of cardiopulmonary hemodynamics
- These results support the effect of seralutinib on pulmonary vascular remodeling and highlight the utility of AI-driven CT imaging in treatment evaluation in PAH

References: 1 Frantz RP, et al. *Lancet Respir Med.* 2024;12(7):523-534. **2** Zamanian RT, et al. *Eur Respir J.* 2023;62(suppl 67):OA742.

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