



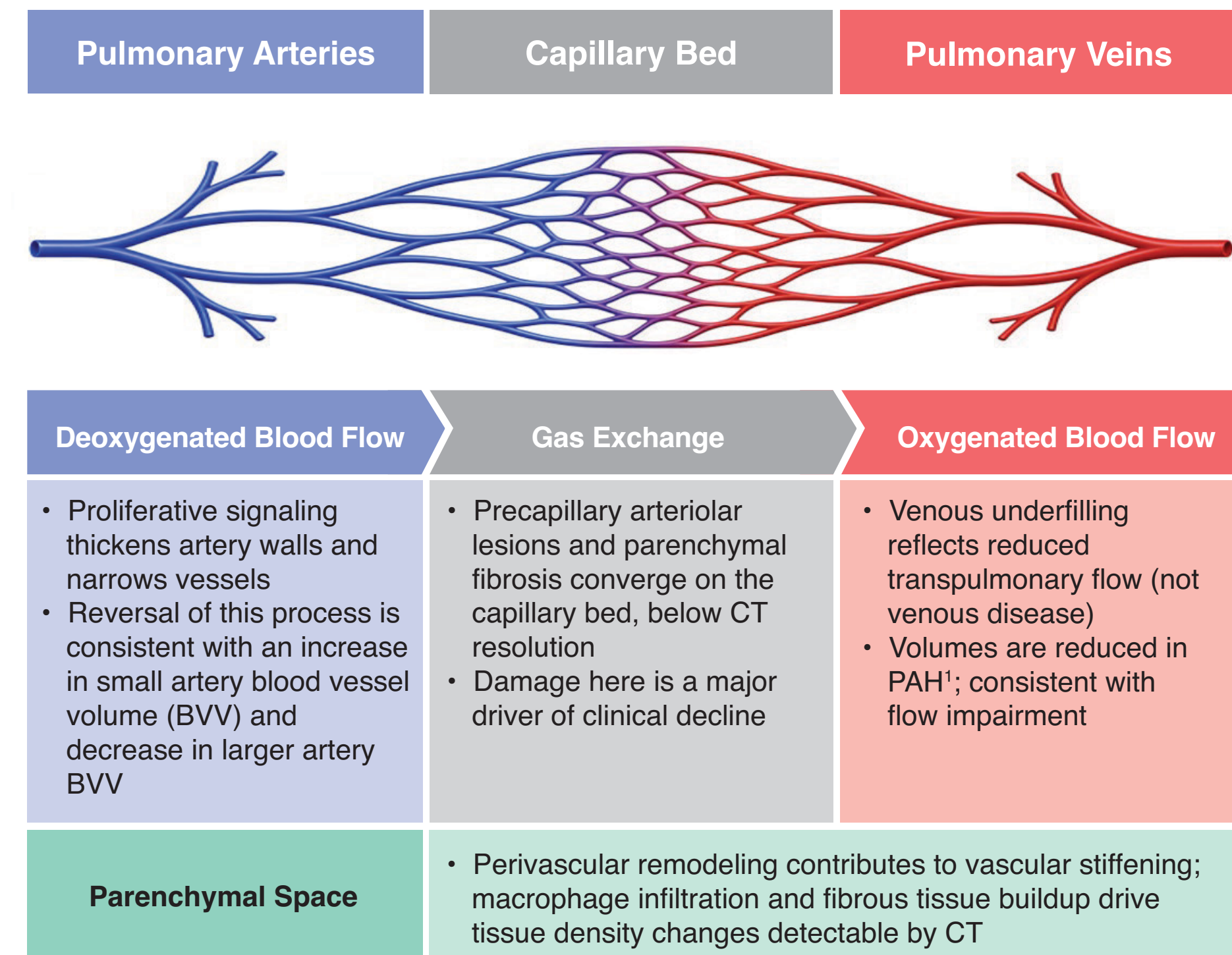
Effects of seralutinib on pulmonary vascular remodeling assessed by quantitative CT: A randomized, double-blind, placebo-controlled imaging substudy of the phase 3 PROSERA trial

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BACKGROUND

- Pulmonary arterial hypertension (PAH) is characterized by progressive remodeling of the distal pulmonary vasculature, resulting in increased pulmonary vascular resistance (PVR), reduced microvascular perfusion, and venous underfilling
- Quantitative CT imaging has demonstrated that PAH is associated with loss of small arterial and venous vessel volume relative to large vessels, reflecting distal vascular pruning and proximal redistribution¹
- Functional Respiratory Imaging (FRI) quantifies pulmonary blood vessel volumes (BVV) and lung structure from high-resolution CT scans
- Seralutinib, an inhaled tyrosine kinase inhibitor targeting PDGFR α / β , CSF1R, and c-KIT pathways implicated in PAH,² demonstrated FRI-detected changes consistent with reduced vascular remodeling in the phase 2 TORREY study of seralutinib in PAH (NCT04456998)^{3,4}
- The effect of seralutinib on FRI-derived measures of distal pulmonary vasculature was evaluated in a prospective, exploratory substudy of the phase 3 PROSERA study



PROSERA Study (NCT05934526)⁵

- PROSERA is a global phase 3 study of inhaled seralutinib in patients with WHO Group 1 PH, FC II–III, with prevalent disease on standard of care therapy and limited functional capacity
- Seralutinib increased 6MWD from baseline to week 24 in the overall population by 28.2 m compared with 13.5 m in the placebo group, yielding a placebo-corrected effect of 13.3 m (p=0.0320), which did not meet the prespecified $\alpha=0.025$, but remains relevant under conventional p<0.05 criteria
- Seralutinib treatment effects on 6MWD were directionally consistent across clinically relevant prespecified subgroups, with greater benefits observed in patients with higher baseline disease burden, including REVEAL Lite 2 ≥ 6 and CTD-PAH
- Gossamer Bio is preparing to file an NDA submission in September 2026 following recent discussion with the FDA

METHODS

- Participation in the FRI substudy was optional and was a randomization stratum in the study to ensure balance across treatment arms
- HRCT scans were acquired at baseline and week 24 per CT protocol
- CT scans were analyzed using FRI (FLUIDDA, Inc.), quantifying lung volume, blood vessel volumes, artery-vein segmentation and fibrosis volume⁶
- Scan quality control, review, and processing were blinded to visit and treatment
- Statistical analysis followed a prespecified statistical analysis plan; treatment effects were determined with linear models adjusted by baseline FRI values
- All p-values are nominal and unadjusted for multiplicity

References: 1 Rahaghi FN, et al. *Chest*. 2021;160(6):2220–2231. 2 Pullamsetti SS, et al. *Int J Mol Sci*. 2023;24(16):12653. 3 Zamanian RT, et al. *Eur Respir J*. 2023;62(suppl 67):OA742. 4 San José Estépar R, et al. *Eur Respir J*. 2025;66(suppl 69):PA5143. 5 Ghofrani HA, et al. *Am J Resp Crit Care Med*. 2026;212(suppl 2):a2mag286.279. 6 Church C, et al. *Pulm Circ*. 2026;16(2):e70322. 7 Aerts G, et al. *Eur Respir J*. Published online May 21, 2026. doi:10.1183/1993003.02118-2025.

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RESULTS

Characteristics of substudy participants from 40 global sites

- Baseline characteristics were well balanced between treatment arms (placebo, n=78; seralutinib, n=84) and consistent with the overall PROSERA population
- Participants were predominantly female (87.7%), with a mean age of 50.5 years. Most had idiopathic (60.5%) or CTD-associated PAH (21.0%), WHO FC III (73.5%), and were receiving double or triple background PAH therapy (>92%)
- Mean baseline 6MWD, NT-proBNP, and PVR were 378.3 m, 1000.5 ng/L, and 821.3 dyn·s/cm², respectively
- Paired week 24 data were available for 125 participants (placebo, n=61; seralutinib, n=64)

Pulmonary vasculature CT FRI imaging parameters

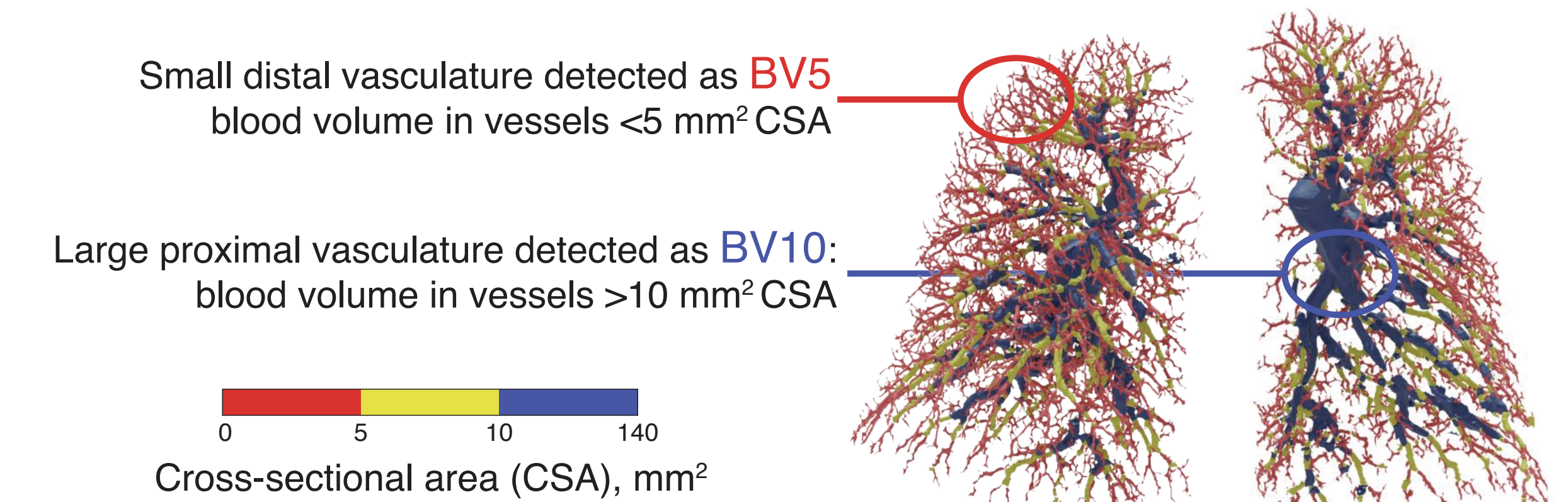


Figure 1. BV5 (red): Small distal arterial and venous vessel blood volumes (BV5A, BV5V, respectively) are decreased in PAH relative to healthy controls¹
BV10 (blue): Large proximal arterial vessel blood volumes (BV10A) are increased in PAH¹

FRI parameters correlated with physiology at baseline

- Arterial and venous BVV proportions correlated with PVR, mean pulmonary arterial pressure (mPAP), cardiac output (CO), 6MWD, NT-proBNP, and risk strata (REVEAL Lite 2 [REVLITE2] and ESC/ERS risk scores)

Baseline Correlations Spearman ρ							
BV5A%	-0.19*	-0.26**	-0.01	0.11	-0.24**	-0.18*	-0.23**
BV5V%	-0.22**	-0.26***	0.07	0.08	-0.08	-0.11	-0.14
BV10A%	0.25**	0.28***	-0.05	-0.05	0.16*	0.11	0.18*
BV10V%	-0.39***	-0.29***	0.26***	-0.17*	-0.24**	-0.16*	-0.08
FV%	0.07	0.10	0.02	-0.13	0.18*	0.12	0.19*
	PVR	mPAP	CO	6MWD	NT-proBNP	REVLITE2	ESC/ERS

Figure 2. Baseline correlations between selected FRI parameters and clinical variables, pooled across treatment groups (n=156). Pulmonary hemodynamic variables were measured only at baseline. *p<0.05, **p<0.01, ***p<0.001.

DISCUSSION

- In a heavily treated PAH population, prespecified FRI imaging endpoints showed a statistically significant, multi-compartment effect of seralutinib
- FRI imaging changes correlated with clinical endpoint changes in a direction of improvement, including 6MWD, NT-proBNP, and REVEAL Lite 2 and ESC/ERS risk scores, reinforcing clinical relevance and linking structural effects to clinical benefit

Seralutinib showed multi-compartment treatment effects

- Arterial compartment:** Seralutinib decreased and placebo increased BV10A%, supporting proximal arterial decompression. BV5A% increased directionally in both seralutinib and placebo arms
- Venous compartment:** Seralutinib increased venous blood volume (TVV, BV5V, BV5-10V, BV5V%) and venous vascular complexity (FDOVP) vs placebo, supporting improved microvascular flow and perfusion

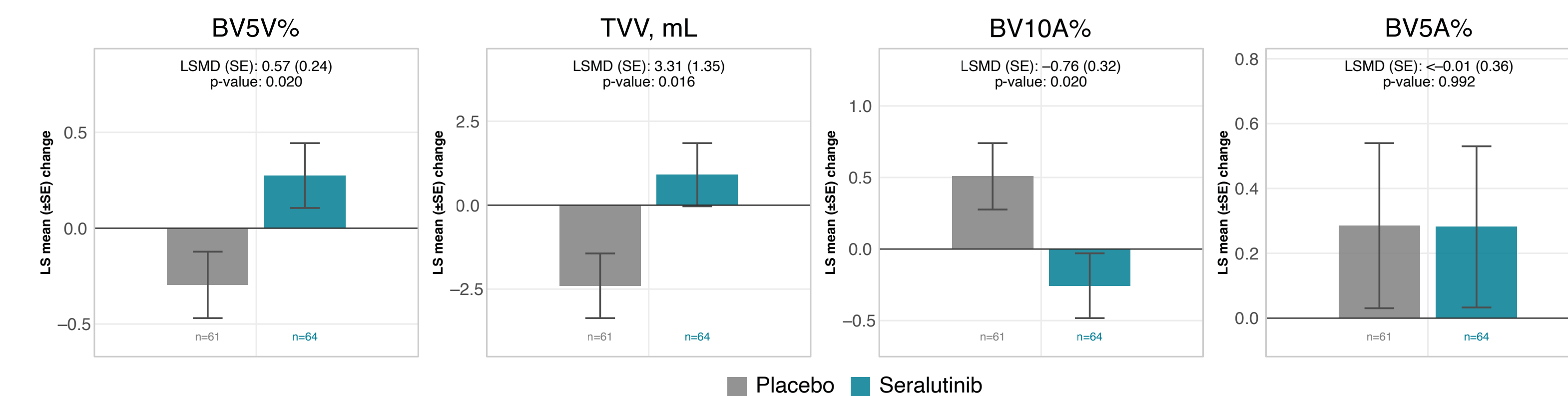


Figure 3. LS mean changes from baseline to week 24 on BV5V%, TVV, BV10A%, and BV5A%. LSMD, least squares mean difference; SE, standard error.

Compartment	Parameter	Description	LSMD	95% CI	p-value
Arteries	BV5A%	Blood vessel volume in arteries <5 mm ² / TBV	< -0.01	-0.71, 0.70	0.992
	BV10A%	Blood vessel volume in arteries >10 mm ² / TBV	-0.76	-1.41, -0.12	0.020*
	BV5A/BV10A	Small / large arterial vessel ratio	0.01	-0.03, 0.06	0.556
	TVV	Total venous vessel volume, mL	3.31	0.64, 5.98	0.016*
Veins	BV5V	Blood vessel volume in veins <5 mm ² , mL	1.59	0.12, 3.06	0.034*
	BV5V%	BV5V / TBV	0.57	0.09, 1.05	0.020*
	BV5-10V	Blood vessel volume in veins 5–10 mm ² , mL	0.51	0.02, 1.00	0.041*
	BV10V%	Blood vessel volume in veins >10 mm ² / TBV	0.19	-0.12, 0.50	0.231
Total	FDOVP	Venous blood vessel complexity	0.01	<0.01, 0.01	0.044*
	TVV	Total blood volume, mL	2.06	-5.10, 9.21	0.570
Parenchyma	FV%	Fibrosis-like volume / total lung volume	-0.44	-0.82, -0.06	0.025*

Table 1. Treatment effects of selected FRI parameters at week 24 (placebo, n=61; seralutinib, n=64). BVV sizes refer to vessel cross-sectional areas. LSMD, least-squares mean difference (seralutinib–placebo). FRI FV quantifies CT voxel-level features characteristic of fibrotic ILD (eg, reticulation, ground-glass), using FibroNet algorithm. *Nominal p<0.05.

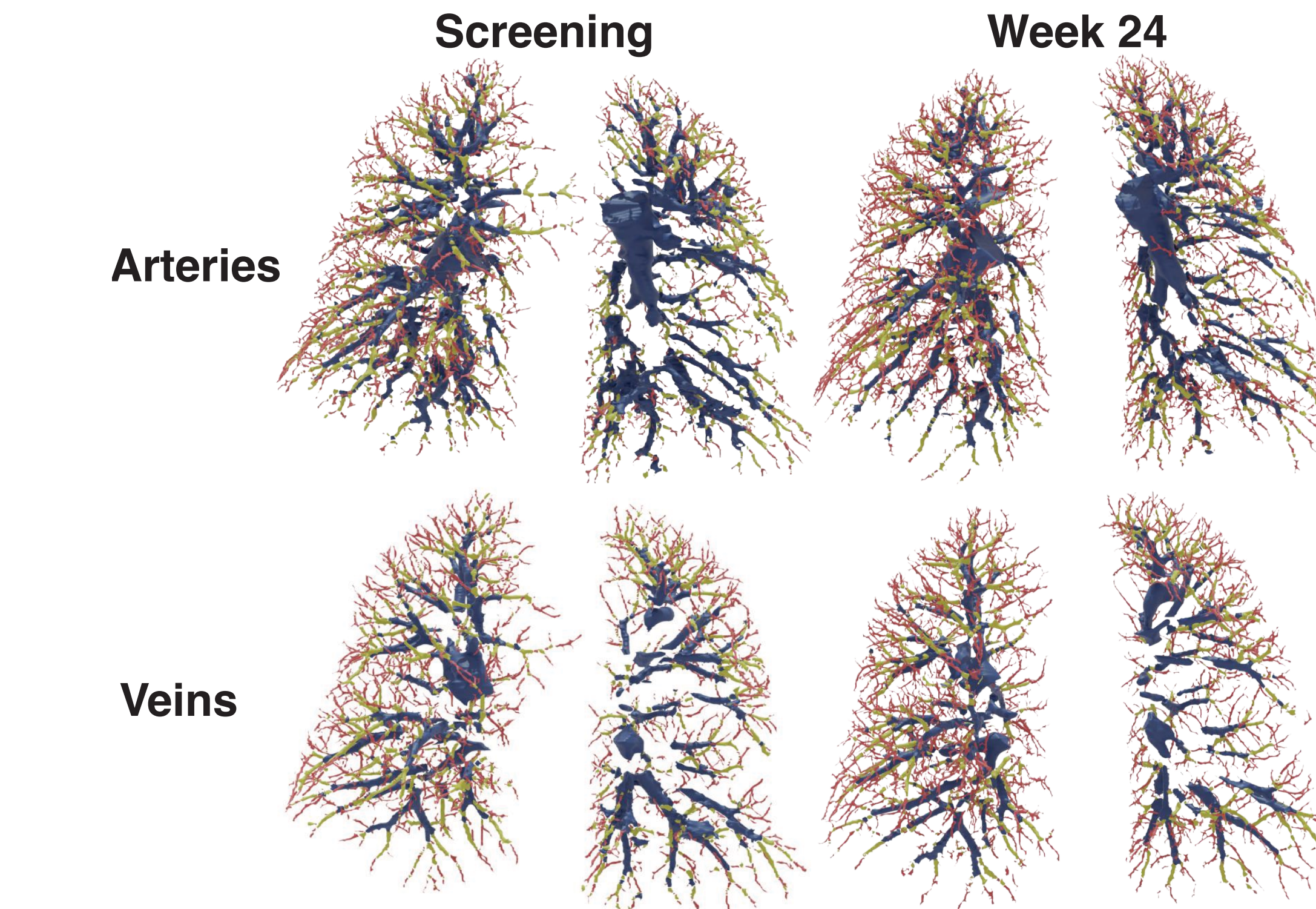
Week 24 FRI changes correlated with clinical endpoints

Change Correlations Week 24 Spearman ρ				
BV5A%	0.14	-0.28**	-0.18*	-0.21*
BV5V%	0.12	-0.20*	-0.20*	-0.17
BV10A%	-0.33***	0.29**	0.24**	0.29**
BV10V%	0.13	-0.08	-0.25**	-0.20*
FV%	-0.12	0.28**	0.21*	0.17
	6MWD	NT-proBNP	REVLITE2	ESC/ERS

Figure 4. Change correlations between week 24 FRI and clinical variables, pooled across treatment groups (n=125). *p<0.05, **p<0.01, ***p<0.001.

Arterial and venous FRI changes after 24 weeks of treatment

A. Seralutinib



B. Placebo

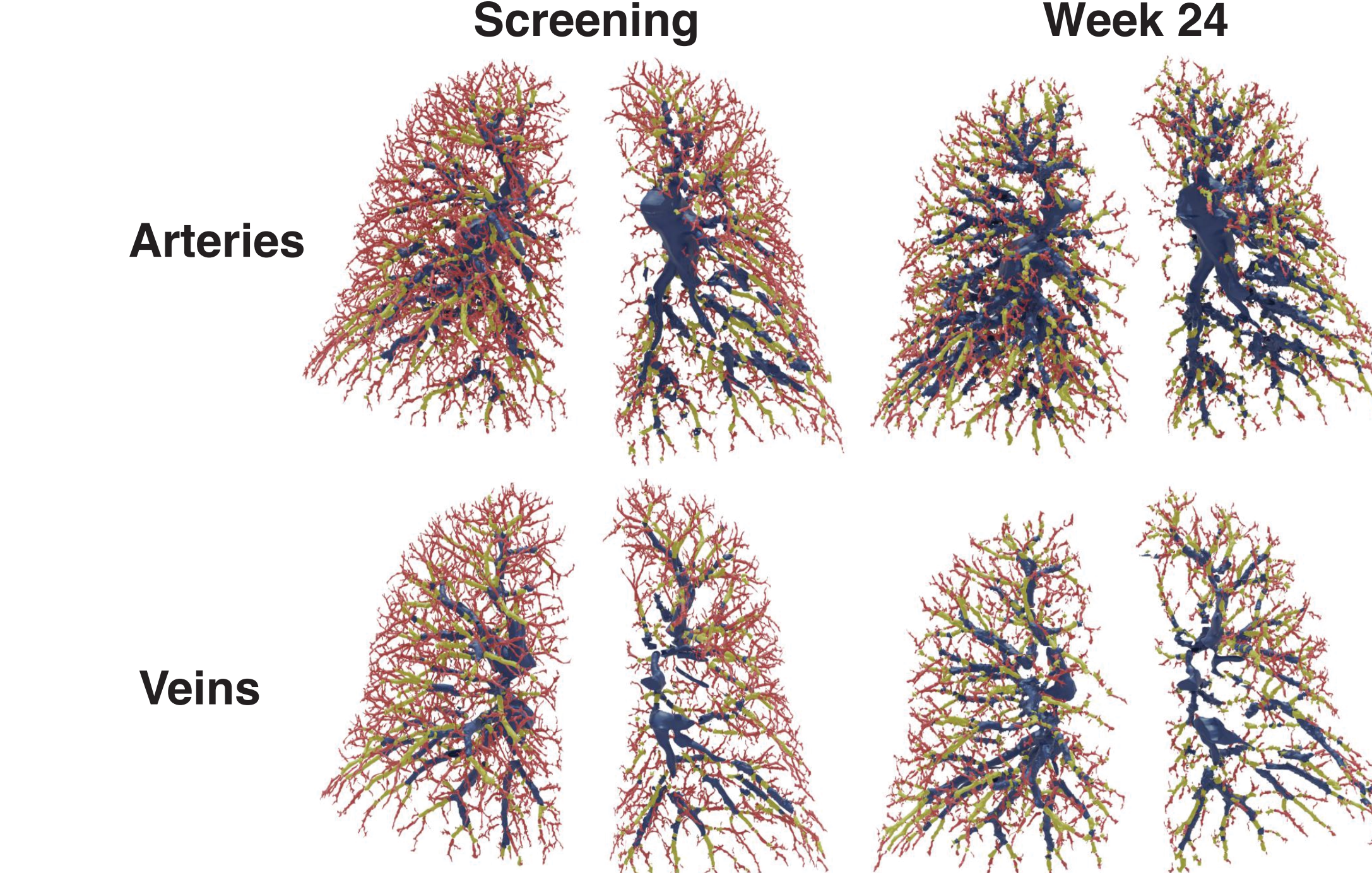


Figure 5. BVV reconstructions of representative patients after 24 weeks of treatment with **A)** seralutinib and **B)** placebo. Red = small distal vessel blood volumes; blue = large proximal vessel blood volumes (see Figure 1).

Treatment effects were consistent in prespecified subgroups

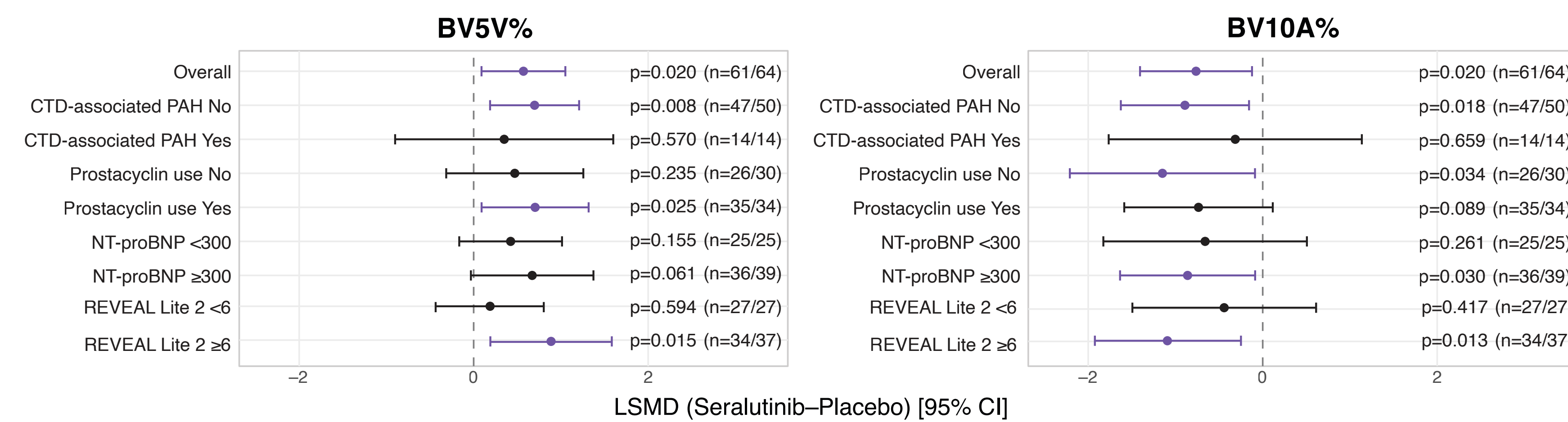


Figure 6. Treatment effects in BV5V% and BV10A% in prespecified subgroups. Purple denotes subgroups with a nominally significant treatment effect (p<0.05). N-values indicate sample sizes (placebo/seralutinib). BV5V% is reduced and BV10A% is increased in PAH vs controls.¹ CI, confidence interval; CTD, connective tissue disease; LSMD, least squares mean difference; NT-proBNP, N-terminal pro-B-type natriuretic peptide (ng/L).