



PULSED INHALED NITRIC OXIDE HAS THE POTENTIAL TO IMPROVE EXERCISE TOLERANCE IN SEVERE COPD SUBJECTS WITH PULMONARY HYPERTENSION



B. Hajian¹, B. Shivalkar¹, F. Ferreira², C. Van Holsbeke², W. Vos², J. De Backer², D. Quinn³, A. Hufkens¹, P.M. Parizel¹, J. Clukers¹, W. De Backer¹

¹Antwerp University Hospital, Antwerp, Belgium; ²FLUIDDA nv, Kontich, Belgium; ³Bellerophon Therapeutics, Warren, NJ, USA

Introduction

In a previous Functional Respiratory Imaging (FRI) trial (Int J Chron Obstruct Pulmon Dis. 2016;11:1533-1541), pulsed inhaled nitric oxide (iNO) was shown to cause an acute vasodilating effect in 6 severe World Health Organization Group 3 pulmonary hypertension (PH) associated with COPD patients on long-term oxygen treatment (LTOT). In a follow up telephone call patients reported improvement in their symptoms up to 24 hours after a one-time 20-minute treatment with pulsed iNO. Therefore, a follow up study was designed to investigate the clinical relevance of this vasodilation with respect to changes in exercise tolerance and hemodynamics after chronic treatment with iNO.

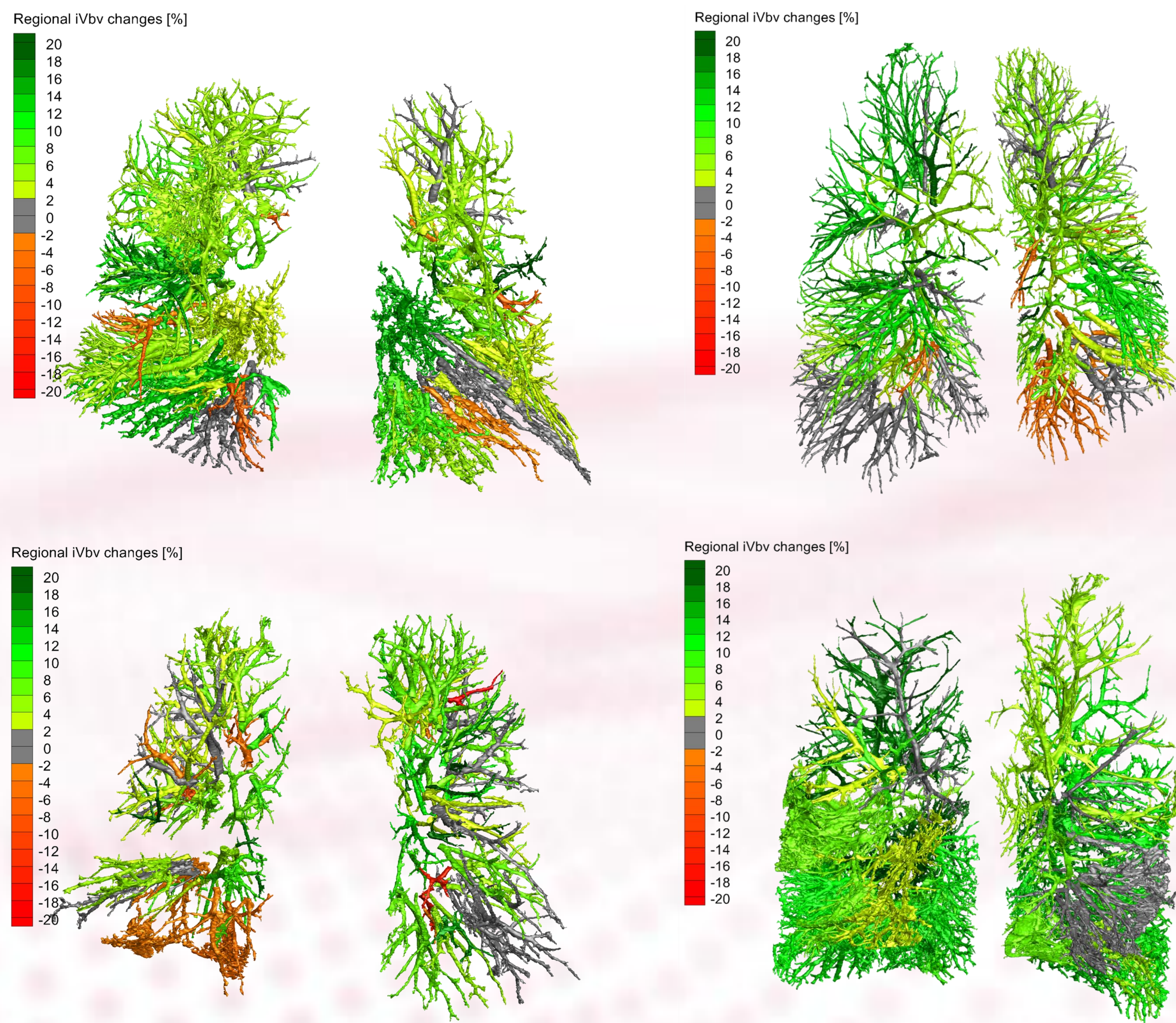
Methods

This ongoing study is recruiting 10 PH-COPD patients on long-term oxygen therapy (LTOT). Pulsed iNO was provided by the INOpulse® delivery system. For all patients, acute vasodilation under pulsed iNO, is assessed by FRI before starting a 4-week treatment with iNO (>12h/day). Exercise tolerance and hemodynamics are measured at baseline and after 4 weeks treatment with iNO. Interim data from the first four study patients who completed four weeks of treatment on iNO are summarized.

Table 1: Summary of Results

	Patient 1	Patient 6	Patient 7	Patient 12
Age (years)	52	59	62	60
Acute Change Blood Vessel Volume (%)	6.2±1.6	6.6±4.5	3.3±2.1	9.7±3.5
Chronic Change SPAP (%)	-26.6	-16.7	-21.3	-5.1
Chronic Change SPAP (mmHg)	-25.0	-8.0	-10.0	-4.0

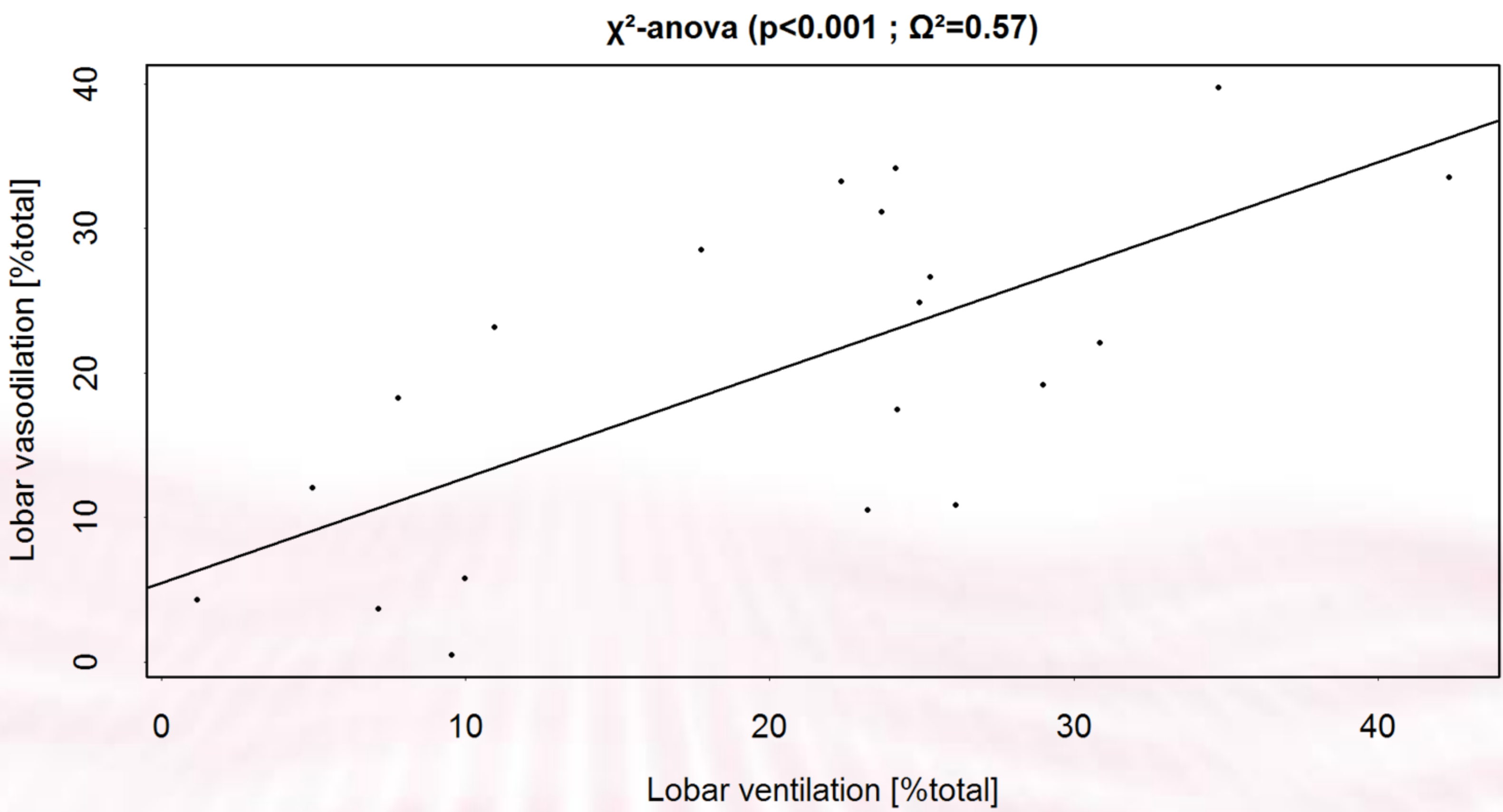
Figure 1: Acute Changes in Blood Vessel Volume During iNO Administration Compared to Baseline for first four patients who completed four weeks of treatment on iNO



Results

All four patients experienced acute increases in blood vessel volumes following iNO treatment (6.45±2.62%; Figure 1). A significant association ($p<0.001$) was also found between ventilation and vasodilation during iNO therapy, suggesting that regions with better ventilation experience more vasodilation (Figure 2). All patients experienced reductions in pulmonary arterial pressure after four weeks (-17.42±9.16%). To date, iNO has been well tolerated in the study.

Figure 2: Correlation between Lobar Ventilation and Lobar Vasodilation



Conclusion

- FRI analyses demonstrate regional dilatation of blood vessels in the lungs following acute pulsed iNO treatment.
- Vasodilation occurs in well-ventilated areas as supported by the correlation with lobar ventilation.
- Preliminary results appear to support a meaningful reduction in pulmonary artery pressures with four weeks of treatment with iNO.
- Full results including exercise tolerance will be provided upon completion of the study.

This study is supported by Bellerophon Therapeutics
B. Hajian and W. De Backer have no relevant financial interests