# High-Resolution Computed Tomography (HRCT) chest scans to examine the association between regional drug deposition of LIQ861 (YUTREPIA™) and vasodilation in PH-ILD population.

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## INTRODUCTION

- Pulmonary hypertension (PH) is a frequent complication of interstitial lung disease (ILD) and is associated with substantially increased morbidity and mortality.
- PH associated with ILD (PH-ILD) arises due to a combination of vascular remodeling and rarefaction and chronic vasoconstriction[1].
- Quantitative CT (qCT) analysis of the pulmonary vasculature in PH-ILD has shown utility as a prognostic tool, and as a marker of therapy response to PH-specific therapies[2-5].
- Misclassification of interstitial markings as vessels on CT is common in ILD patients[6].
- Inhaled treprostinil is the only approved therapy indicated for treatment of PH-ILD. YUTREPIA is an investigational dry powder inhaled (DPI) formulation of treprostinil.
- YUTREPIA is formulated using Liquidia's proprietary PRINT™ technology which ensures particles of uniform size and shape to enhance distal lung drug deposition.

## OBJECTIVES

- To evaluate the use of dry powder treprostinil in PH-ILD.
- To assess the localized and dose-dependent vasodilatory effects of YUTREPIA on the pulmonary vasculature and other lung structures using qCT and computational fluid dynamics.
- To minimize the misclassification of fibrosis as vasculature and to improve the accuracy and interpretability of qCT via a reduced-contrast-dose CT pulmonary angiogram protocol and respiratory gating.

## METHODS

**STUDY OVERVIEW** **The ASCENT study is an open-label, multicenter, prospective study that will enroll approximately 60 subjects with PH-ILD to be treated with YUTREPIA for up to 52 weeks.**

### CT Protocol

Participants will receive inspiratory/expiratory, thin-slice, volumetric chest CT with low-dose intravenous contrast at baseline prior to initial dosing and at Week 24 following dosing. Hand-held spirometry equipment will be used to monitor breathing signal.

### Quantitative CT Analysis

Functional Respiratory Imaging™ (FRI) will be used to quantify pulmonary vascular volume distribution, extent of fibrosis, and airway and lobar volumes:

- **BV5%TBV**: Fraction of pulmonary blood in vessels <5 $mm^2$
- **BV10%TBV**: Fraction of pulmonary blood in vessels >10 $mm^2$
- **siVfib**: Quantitative extent of fibrosis
- **iVlobe**: Imaging-based lung volume
- **iVaw**: Volume of airways >2 mm in diameter

### HRCT Methodology Overview

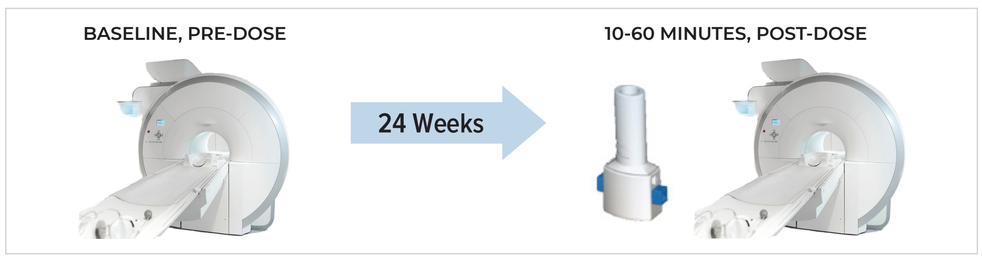



**FIGURE 1:** Schematic of CT Acquisition Schedule

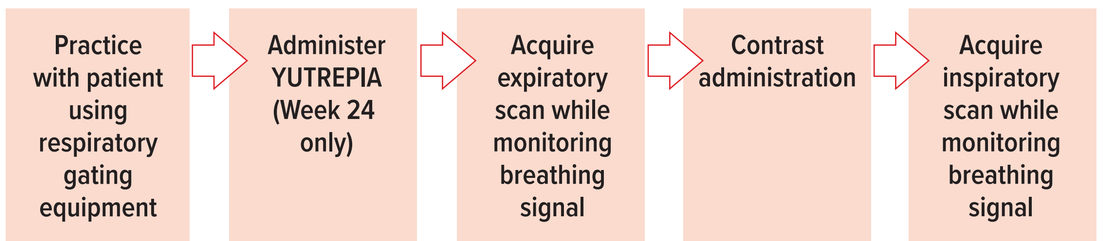


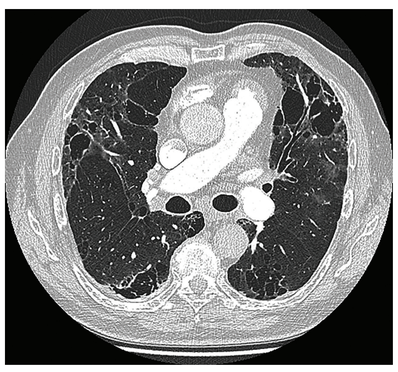

**FIGURE 2:** Schematic of CT Visit

### Blinded visual read by thoracic radiologist

- Assessment of ILD pattern
- Semiquantitative fibrosis scoring

### In-silico deposition analysis

- Computational fluid dynamics will be used to model deposition of YUTREPIA[7]
- Uses measured aerosol characteristics and patient-specific airway measurements, extracted via qCT analysis
- No radio label is used
- Used to assess: 1) adequate delivery of YUTREPIA to the distal lung and 2) quantify the spatial relationship between exposure (deposition) and response (vasodilation)



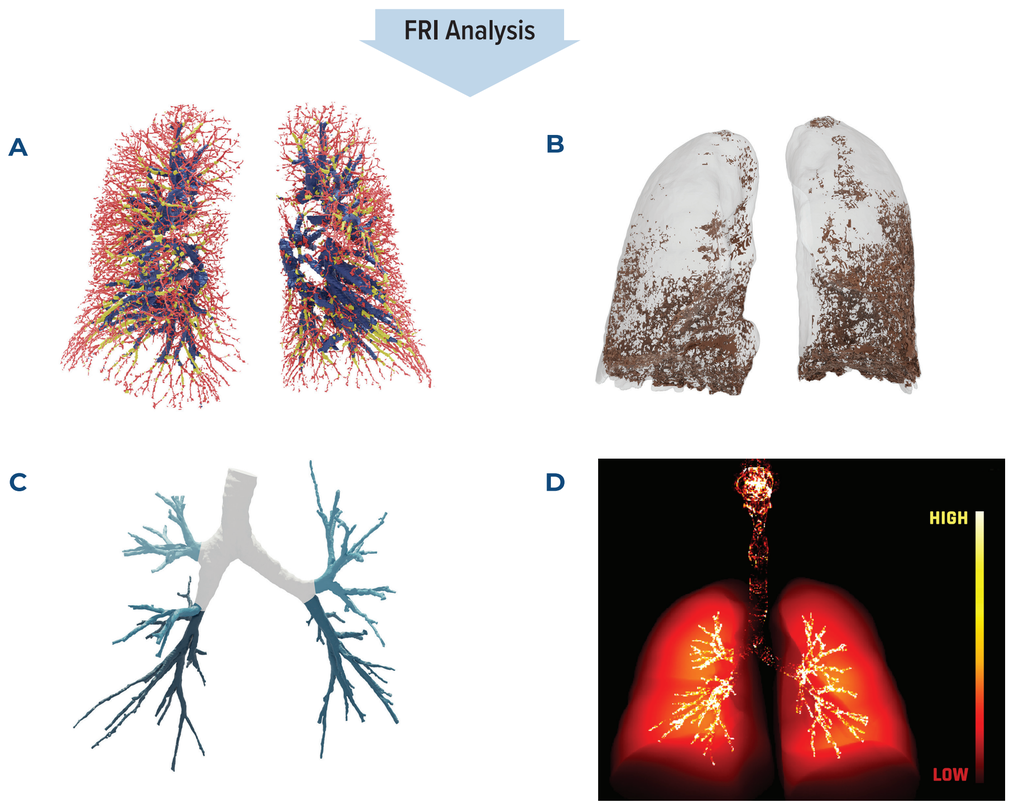



**FIGURE 3:** Representative FRI Workflow and Output
**A.** Reconstructed vascular tree of a subject with PH. Red represents BV5-sized vessels and blue represents BV10-sized vessels. **B.** Detected fibrotic regions in a subject's lungs. **C.** An example segmented airway tree. **D.** Heatmap of modeled particle deposition.

## CONCLUSIONS

**ASCENT is the first study to use quantitative CT imaging to examine the association between regional drug deposition of YUTREPIA™ and its potential effects in a PH-ILD population.**

**The use of intravenous contrast will improve the accuracy of vascular analysis by improving the detection of the pulmonary vasculature.**

**References:**

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**Disclosures:**
**B. R. Lavon:** Employee of Fluidda, NV
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