A PROOF OF CONCEPT STUDY OF LTB4 INHIBITION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION (WHO GROUP 1) (LIBERTY)

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PURPOSE
To conduct a clinical proof of concept study to test the role of inhibition of leukotriene B4 (LTB4) in patients with Pulmonary Arterial Hypertension (WHO Group 1).

BACKGROUND
Pulmonary Arterial Hypertension (PAH) is a progressive and life-threatening disease characterized by increased pulmonary vascular resistance, heart failure, and premature death. Although management of PAH has improved significantly with the development of multiple drugs targeted on 3 pathways, the mortality rate remains high, with a life expectancy of 7 years after diagnosis (McGeon 2014). Thus, new approaches are needed, and in particular, approaches which may modify disease progression.


The current study was designed to test the role of inhibition of LTB4 in patients with PAH (WHO Group 1).

METHODS

**Design**
Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group proof of concept study in patients with PAH (WHO Group 1).

**Study Population**
All patients with WHO Group 1 PAH on at least one PAH-specific drug. All PAH-specific drugs were allowed as background therapy.

**Open Label Extension**
Patients who complete the randomized, double-blind study may be eligible to enroll in an open label extension study.

**Study Sites**
45 clinical study sites in North America

**Randomization**
2:1 active:placebo

**Study Drug**
Ubenimex 150 mg TID or matching placebo for 24 weeks.

RESULTS
We describe the key eligibility criteria and enrollment of a proof of concept study conducted entirely in North America. Sixty-one PAH patients were enrolled in a 10-month period across 45 clinical sites in the United States and Canada.

**LIBERTY Study Sites - USA and Canada**

**Key Eligibility Criteria**

**Inclusion Criteria**
- Informed consent
- Male or female, 18–75 years
- WHO Group 1 PAH
- WHO/NYHA-FC II or III
- FVC > 50% of predicted
- 6MWD > 150 m
- Pulmonary Vascular Resistance (PVR) > 4 Wood units
- WHO Group 1 PAH
- Standard of Care + Placebo for 24 weeks
- WHO/NYHA-FC II or III
- FVC > 50% of predicted
- 6MWD > 150 m
- Pulmonary Vascular Resistance (PVR) > 4 Wood units

**Exclusion Criteria**
- HIV-associated PAH
- Newly diagnosed with PAH
- Chronic infection related to TB, fungal, or mycobacterial disease
- PVOD or pulmonary capillary hemangiomatosis or persistent pulmonary hypertension of the newborn; or WHO Groups 2-5
- Pulmonary Disease and Other Medical Conditions
- Chronic infection related to TB, fungal, or mycobacterial disease
- Newly diagnosed with PAH
- HIV-associated PAH
- Other Medical Conditions
- Active infection requiring IV or oral antibiotics
- Pregnancy or breastfeeding
- Prior treatment with B cell or lymphocyte-depleting agents
- Substance abuse within 6 months before Screening
- Concomitant Medications
- Regular use of a leukotriene pathway inhibitor

**References**