A Phase 1B, Multi-Center, Randomized, Placebo-Controlled Trial of Inhaled Seralutinib in Subjects With WHO Group 1 Pulmonary Arterial Hypertension (PAH)


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BACKGROUND

- Abnormal signaling of PDGFα/β, CSF1R, and c-KIT as well as BMPR2 deficiency drive cellular overgrowth in the lung vasculature and play key roles in the development of PAH1-3
- Seralutinib (formerly GB0002) is a new chemical entity delivered via dry powder inhalation that inhibits PDGFRα/β, CSF1R, and c-KIT, and modulates BMPR2 (Figure 1)
- Studies of inhaled seralutinib in animal models showed
  - Higher lung exposure than that of plasma by 30x
  - Reversal of pulmonary vascular remodeling, improved hemodynamic parameters, increased lung BMPR2 and reduced circulating pro-inflammatory cytokines

METHODS

- Phase 1 studies in healthy volunteers demonstrated
  - That seralutinib was well tolerated at doses up to 90 mg BID
  - This study is the first clinical experience reported

OBJECTIVES

- Primary: Determine the safety and tolerability of seralutinib when administered via dry powder inhalation for 14 days in subjects with WHO Group 1 PAH
- Secondary: Assess pharmacokinetic parameters of inhaled seralutinib

RESULTS

- 8 subjects enrolled and completed the 2-week study
- N=6, seralutinib; N=2, placebo
- 4 seralutinib-treated subjects received an escalated dose (90 mg BID) starting at day 8
- No serious adverse events were reported
- Most frequently reported AEs were mild-moderate cough and mild headache
- No AEs resulted in dose reduction, interruption, or discontinuation of seralutinib
- No clinically significant changes in laboratory parameters, electrocardiograms, pulmonary function tests, or vital signs occurred

REFERENCES


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