CONTROL ID: 2811023

PRESENTATION TYPE: Slide

CURRENT CATEGORY: Pulmonary Vascular Disease

TITLE: Hemodynamic Effects of the Oral Prostacyclin (IP) Receptor Agonist Ralinepag in Pulmonary Arterial Hypertension (PAH)

Presenting Author: Fernando Torres

All Authors/Institutions: F. Torres[1], H. W. Farber[2], A. D. Ristić[3], V. V. McLaughlin[4], J. Adams[5], J. Zhang[5], P. Klassen[5], P. Escribano Subías[6], N. Sood[7], A. Keogh[8], L. Rubin[9]

ABSTRACT BODY:

PURPOSE: Targeting the prostacyclin pathway is a central part of PAH management, although inconvenience and side effects remain issues. Ralinepag is an oral, non-prostanoid, IP receptor agonist with optimized receptor activation and a half-life of ~24 hours. Ralinepag has antiproliferative and vasodilatory activities on pulmonary smooth muscle cells and pulmonary arteries. We evaluated the efficacy, safety, and tolerability of ralinepag in a multinational double-blind Phase 2 study.

METHODS: Adults with stable functional class (FC) II–IV PAH and 6-minute walk distance (6MWD) of 100–500 m were enrolled. All subjects were receiving background PAH treatment with an endothelin receptor antagonist, phosphodiesterase type-5-inhibitor, or soluble guanylate cyclase activator, alone or in combination. Subjects were randomized 2:1 to receive ralinepag (40 subjects) or placebo (21 subjects) in a 9-week titration phase followed by 13-week maintenance. Treatment was initiated at 10 µg twice daily (bid) and titrated weekly up to 300 µg bid, as tolerated. Right heart catheterization was performed at baseline (BL) and at the end of treatment. The primary efficacy endpoint was change in pulmonary vascular resistance (PVR) from BL to Week 22. Additional analyses included changes in 6MWD, hemodynamics, and safety and tolerability.

RESULTS: Enrolled subjects had FC II/III/IV (56%/42%/2%) PAH and mean (standard deviation) 6MWD of 378 m (104 m). BL median PVR was 705 (ralinepag) and 480 (placebo) dyn.s.cm^{-5}. Thirty-five percent of ralinepag subjects and 52% of placebo subjects were receiving background monotherapy; 65% and 48%, respectively, were receiving dual combination therapy. Ralinepag improved median PVR by 163.9 dyn.s.cm^{-5} from BL, compared with 0.7 dyn.s.cm^{-5} worsening with placebo (P=0.02). Subjects receiving ralinepag had a 29.8% improvement in PVR compared with placebo (P=0.03) and a 20.1% improvement from BL. 6MWD increased by 36.2 m in the ralinepag group, which was not significantly different from placebo. There were 2 deaths, both in the placebo group. Serious adverse events (AEs) occurred in 10% of ralinepag subjects and 28.6% of placebo subjects. The most common treatment-emergent AEs were as expected for prostacyclin receptor agonists.

CONCLUSIONS: Ralinepag significantly improved PVR compared with placebo in subjects with FC II–IV PAH on single or dual background therapy.

CLINICAL IMPLICATIONS: Targeting the IP receptor with ralinepag may provide clinical benefit in patients with PAH.

Grant Identification Information:

Presenter Disclosure of Product Research or Unlabeled Uses of Products: **YES**, the Presenter will be discussing information about a product/procedure/technique that is considered research and is NOT yet approved for any purpose.

Additional Details (All): Ralinepag is being investigated for the treatment of pulmonary arterial hypertension

INSTITUTIONS (ALL):

1. UT Southwestern Medical Center, Dallas, TX, United States.
2. Boston University School of Medicine, Boston, MA, United States.
3. Belgrade University School of Medicine, Belgrade, Serbia.
4. University of Michigan, Ann Arbor, MI, United States.
5. Arena Pharmaceuticals, San Diego, CA, United States.
6. Hospital 12 de Octubre, Madrid, Spain.
7. University of Texas Health Science Center of Houston, Houston, TX, United States.
8. St Vincent's Hospital, Darlinghurst, NSW, Australia.
9. University of California, San Diego School of Medicine, La Jolla, CA, United States.

CURRENT SUB-CATEGORY: Pulmonary arterial hypertension (WHO Classes I-V)