

## HEMODYNAMIC ASSESSMENT OF PATIENTS (PTS) WITH INOPERABLE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH) IN THE CHEST-1 STUDY

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**Objective:** To evaluate the correlation between clinical outcome and hemodynamic changes with riociguat in CHEST-1.

**Methods:** This was a 16-week, randomized, double-blind, placebo (pbo)-controlled study investigating riociguat in pts with inoperable CTEPH or persistent/recurrent CTEPH after pulmonary endarterectomy (PEA). The primary endpoint was change in 6-minute walking distance (6MWD). Hemodynamic parameters included pulmonary vascular resistance (PVR), right atrial pressure (RAP), cardiac index, and mean pulmonary arterial pressure (mPAP).

**Results:** In total, 261 pts received riociguat (n=173) or pbo (n=88): 189 were deemed inoperable and 72 had post-operative CTEPH. Mean ( $\pm$ standard deviation) PVR at baseline in the riociguat arm was 791 ( $\pm$ 432) dyn·s·cm<sup>-5</sup> in the total population, 867 ( $\pm$ 471) dyn·s·cm<sup>-5</sup> in pts with inoperable CTEPH, and 618 ( $\pm$ 252) dyn·s·cm<sup>-5</sup> in pts with post-operative CTEPH. Riociguat reduced PVR by  $-226$  ( $\pm$ 248) dyn·s·cm<sup>-5</sup> (least-squares [LS] mean difference  $-246$  dyn·s·cm<sup>-5</sup>; p<0.0001) compared with an increase of  $+23$  ( $\pm$ 274) dyn·s·cm<sup>-5</sup> in the pbo group. In the riociguat arm at baseline, mean RAP was 9 ( $\pm$ 5) mmHg, cardiac index was 2.3 ( $\pm$ 0.6) L/min/m<sup>2</sup>, and mPAP was 45 ( $\pm$ 13) mmHg. Riociguat provided a change (LS mean difference) of  $-0.6$  mmHg in RAP (95% confidence interval [CI]:  $-1.7$  to 0.6 mmHg; p=0.36),  $+0.5$  L/min/m<sup>2</sup> in cardiac index (95% CI: 0.3 to 0.6 L/min/m<sup>2</sup>; p<0.0001), and  $-5$  mmHg in mPAP (95% CI:  $-7$  to  $-3$  mmHg; p<0.0001). Riociguat significantly improved 6MWD (LS mean

difference +46 m;  $p < 0.0001$ ) which correlated with improved hemodynamics (6MWD vs PVR:  $r = -0.28$  [ $p < 0.0001$ ]; 6MWD vs CI:  $r = 0.22$  [ $p < 0.001$ ]).

**Conclusions:** Riociguat is the first compound to demonstrate significant improvements in hemodynamics and exercise capacity in pts with inoperable or post-operative CTEPH.

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