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 (±standard deviation) PVR at baseline in the riociguat arm was 791 (±432) dyn·s·cm⁻⁵ in the total population, 867 (±471) dyn·s·cm⁻⁵ in pts with inoperable CTEPH, and 618 (±252) dyn·s·cm⁻⁵ in pts with post-operative CTEPH. Riociguat reduced PVR by −226 (±248) dyn·s·cm⁻⁵ (least-squares [LS] mean difference −246 dyn·s·cm⁻⁵; p<0.0001) compared with an increase of +23 (±274) dyn·s·cm⁻⁵ in the pbo group. In the riociguat arm at baseline, mean RAP was 9 (±5) mmHg, cardiac index was 2.3 (±0.6) L/min/m², and mPAP was 45 (±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/m² in cardiac index (95% CI: 0.3 to 0.6 L/min/m²; 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.

**Character count:** 2478; *Maximum 2600 including spaces, abstract title, authors and affiliations*