RIOCIGUAT FOR THE TREATMENT OF INOPERABLE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH) OR PERSISTENT/RECURRENT CTEPH AFTER PULMONARY ENDARTERCTOMY (PEA): A RESPONDER ANALYSIS FROM THE PHASE III CHEST-1 STUDY

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Objective: PEA is the treatment of choice for CTEPH, but a proportion of patients (pts) are ineligible or have persistent/recurrent CTEPH after PEA. Data from the CHEST-1 study showed that riociguat is a promising therapy for such pts, as it improved 6-minute walking distance (6MWD), hemodynamics, World Health Organization functional class (WHO FC), and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels. The aim of this analysis was to determine the proportion of pts in CHEST-1 at baseline (BL) and after targeted therapy who reached responder thresholds shown previously to correlate with improved outcome in pts with other forms of pulmonary hypertension.

Methods: In this randomized, double-blind, Phase III study, pts received placebo (pbo) or individually adjusted riociguat (up to 2.5 mg three times daily) for 16 weeks. The criteria taken to suggest a positive response were: 6MWD increase ≥30 m and ≥40 m, 6MWD ≥380 m, cardiac index (CI) ≥2.5 L/min/m^2, pulmonary vascular resistance (PVR) <500 dyn·s·cm^{-5}, venous oxygen saturation (SvO_2) ≥65%, WHO FC I/II, and NT-proBNP <1800 ρg/mL.

Results: The proportion of pts meeting the above criteria at BL and Week 16 is shown below. At BL, the proportions were similar in the pbo and riociguat arms. Riociguat increased the proportion of pts achieving these criteria at Week 16; minimal improvements or decreases were seen in the pbo arm for most parameters.

Criteria	Riociguat			Pbo		
	n	BL, %	Wk 16, %	n	BL, %	Wk 16, %
6MWD increase ≥30 m	173	n/a	63	88	n/a	30
6MWD increase ≥40 m	173	n/a	53	88	n/a	24
6MWD ≥380 m	173	37	58	88	43	44
CI ≥2.5 L/min/m^2	155	32	58	83	29	28
PVR <500 dyn·s·cm^{-5}	151	25	50	82	27	26
SvO_2 ≥65%	145	42	55	77	42	35
WHO FC I/II	173	34	57	87	29	38
NT-proBNP <1800 ρg/mL	150	73	81	73	71	63

n/a, not applicable

Conclusions: Riociguat increased the proportion of pts with CTEPH who met criteria that demonstrate a positive response to therapy.