Riociguat for the treatment of chronic thromboembolic pulmonary hypertension: 1-year results from the CHEST-2 long-term extension study

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BACKGROUND: In the 16-week Phase III CHEST-1 study, riociguat, a novel soluble guanylate cyclase stimulator, significantly improved 6-minute walking distance (6MWD) and a range of secondary endpoints in patients with chronic thromboembolic pulmonary hypertension (CTEPH). These improvements were maintained for a further 12 weeks in the CHEST-2 long-term extension study. Here we present 1-year data from CHEST-2.

METHODS: Patients with inoperable CTEPH or persistent/recurrent CTEPH after pulmonary endarterectomy (PEA) could enter CHEST-2 after successfully completing CHEST-1 and if they were without ongoing riociguat-related serious adverse events. During the initial 8-week blinded dose-adjustment period of CHEST-2, patients originally randomized to the riociguat arm continued on their optimum dose (up to 2.5 mg three times daily [tid]) while receiving sham dose adjustment; patients originally randomized to the placebo arm were adjusted to their optimum dose of riociguat (up to 2.5 mg tid). The primary endpoints were safety and tolerability; secondary endpoints included change in 6MWD and World Health Organization functional class (WHO FC).

RESULTS: Of the 261 patients enrolled in CHEST-1, 237 (91%) entered CHEST-2. In this interim analysis (cut-off March 2013), 211 (89%) patients were ongoing and 179 (76%) had received ≥1 year of treatment. Riociguat was well tolerated, with 3% of patients withdrawing due to adverse events. At the end of CHEST-1, 6MWD had increased by +50±59 m (mean±SD) in the riociguat arm and +8±63 m in the placebo arm of the cohort entering CHEST-2. After 1 year of CHEST-2 (overall population; n=172), 6MWD had increased by +51±62 m versus CHEST-1 baseline. At the end of CHEST-1, WHO FC was improved/stabilized/worsened in 35/62/3% of riociguat-treated patients and 16/81/2% of placebo-treated patients; after 1 year of CHEST-2 (overall population; n=178), the proportions were 46/49/3% (data missing for two patients) versus CHEST-1 baseline. At 1 year, 8% of ongoing patients (n=12) were receiving additional PAH medications.

CONCLUSIONS: Riociguat has a good long-term safety profile and is the first therapy to show sustained benefits in 6MWD and WHO FC in patients with CTEPH. Therefore, riociguat is a promising option for the long-term treatment of patients with inoperable CTEPH or persistent/recurrent CTEPH after PEA.

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