

Novel pulmonary hypertension drug proves safe and effective in Phase III Trial

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After a year of being treated with a novel drug, patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) and those with persistent or recurrent pulmonary hypertension after an operation for the disease showed sustained improvement in a multicenter, international trial presented at the 2014 American Thoracic Society International Conference.

The drug, riociguat, is a guanylate cyclase stimulator that works independently and in concert with endogenous nitric oxide to induce vasodilation. A long-term extension study, CHEST-2 enrolled [patients](#) from CHEST-1, which followed these patients for 16 weeks and achieved its primary endpoint: improved six-minute walking distance (6MWD).

"The pivotal study, CHEST-1, showed significant improvements in exercise capacity and hemodynamics in patients treated with riociguat," said principal investigator Marius Hoepfer, MD, of the Hannover Medical School (Germany). "However, the study was relatively short, and CHEST-2 adds important information on the long-term tolerability and efficacy of riociguat in patients with CTEPH."

CTEPH is a relatively rare disease; about 5000 people in the U.S. are diagnosed with the disease each year. It occurs when blood clots from previous episodes of [acute pulmonary embolism](#) do not resolve, causing persistent obstruction of the pulmonary vasculature, which may ultimately lead to [pulmonary hypertension](#).

A surgical procedure called pulmonary endarterectomy (PEA) is the treatment of choice for operable patients with CTEPH. However, not all patients are candidates for PEA, a long and complex operation, and 20 to 30% of those who undergo the surgery are not cured. Thus, there is an urgent medical need to develop effective drugs for patients with inoperable CTEPH or persistent pulmonary hypertension after PEA.

Both groups of patients were part of the CHEST studies. In CHEST-2, 172 patients (73%) had inoperable CTEPH and 65 (27%) had persistent/recurrent PH after PEA. Unlike in CHEST-1, which had a placebo arm, in the extension trial all patients received riociguat.

The primary endpoint of CHEST-2 was safety and tolerability, which riociguat met. The drug was well tolerated by the majority of patients: 4% of inoperable patients and 2% of persistent/recurrent patients withdrew due to adverse events.

The researchers presenting at ATS 2014 also reported data related to the secondary endpoints: change in 6MWD and World Health Organization Functional Class, a means of classifying disease severity in patients with pulmonary hypertension (PHJ). Compared to the baseline established with CHEST-1, after one year of CHEST-2, 6MWD improved by 54 ± 62 m in the inoperable subgroup and 44 ± 64 m in the persistent/recurrent subgroup.

Similarly, when compared to the CHEST-1 baseline, at the first year mark of CHEST-2, the percentage of inoperable patients who improved in WHO FC was 46%. Those stabilized represented 50%. And those whose function worsened was 5%. The comparable percentages for the persistent/recurrent patients were 47, 49, and 0.

Based on the data from CHEST-1 and CHEST-2, Hoepfer noted, riociguat was recently approved in the U.S., Canada, Europe and Japan

for patients with inoperable or recurrent CTEPH, closing an important therapeutic gap for these patients.

More information: Abstract 52139, Effects Of Riociguat In Patients With Inoperable Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Vs Persistent/Recurrent Pulmonary Hypertension (PH) After Pulmonary Endarterectomy (PEA): 1-Year Results From The CHEST-2 Study , Scientific Abstract , 18.10 - Pulmonary Hypertension: Clinical – Treatment and Outcomes (PC) , M. Hoeper¹, N.H. Kim², E. Mayer³, T. Pulido⁴, M.R. Wilkins⁵, G. Simonneau⁶, A. Torbicki⁷, C. Wang⁸, N. Davie⁹, A. Fritsch⁹, H.-A. Ghofrani¹⁰; ¹Hannover Medical School - Hannover/DE, ²Division of Pulmonary and Critical Care Medicine, UCSD School of Medicine - San Diego, CA/US, ³Kerckhoff Heart and Lung Center - Bad Nauheim/DE, ⁴Cardiopulmonary Department, Ignacio Chávez National Heart Institute - Mexico City/MX, ⁵National Institute for Health Research/Wellcome Trust Imperial Clinical Research Facility, Imperial Centre for Translational and Experimental Medicine, Imperial College London - London/UK, ⁶Univ. Paris-Sud; INSERM U999; AP-HP, Hôpital Bicêtre, Service de Pneumologie - Le Kremlin-Bicêtre/FR, ⁷Department of Pulmonary Circulation and Thromboembolic Diseases, Center of Postgraduate Medical Education, ECZ-Otwock - Otwock/PL, ⁸Beijing Institute of Respiratory Medicine, Beijing Chao Yang Hospital, Department of Respiratory Medicine, Capital Medical University, Beijing Key Laboratory of Respiratory and Pulmonary Circulation Disorders - Beijing/CN, ⁹Global Clinical Development, Bayer HealthCare Pharmaceuticals - Wuppertal/DE, ¹⁰University of Giessen and Marburg Lung Center (UGMLC), member of the German Center of Lung Research (DZL); and Department of Medicine, Imperial College London - Giessen/DE

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