# A Study to Test the Effects of Riociguat in Patients With Pulmonary Hypertension Associated With Left Ventricular Systolic Dysfunction (LEPHT)

*Section Editor*
Fernando Torres, MD

The Clinical Trials Update highlights new and ongoing research trials that are evaluating therapies for PAH. In this issue, Fernando Torres, MD, examines a study on patients with pulmonary hypertension associated with left ventricular systolic dysfunction.

Pulmonary hypertension (PH) associated with left heart disease has been a challenge for the PH community. Though most of us have concentrated our efforts on managing the patients who have PH with normal systolic heart function, there is another population of patients with PH with decreased left ventricular heart function who also are at risk of poor survival. It is known that patients with high mean pulmonary arterial pressure (mPAP)
and left ventricular ejection fraction (LVEF) less than 45% carry a high mortality compared to those with normal mPAP. Thus, finding new therapies for this population would be advantageous.

In 2009, a single-dose study with riociguat was found to decrease the mPAP, wedge, and pulmonary vascular resistance (PVR) of patients with high mPAP and left heart failure. This then prompted the design and completion of LEPHT.

LEPHT enrolled about 200 patients worldwide. All patients had a screening right heart catheterization in which the mPAP was higher than 25 mm Hg, and all had an LVEF <45% at inclusion to the study. They were all maximally medically treated, and their heart failure medications could not have changed in the month prior, with the exception of diuretics, which could have been changed up to a week prior to randomization. The patients were randomized to placebo or riociguat of 0.5, 1, or 2 mg TID in four parallel arms. After 16 weeks, the patients had a repeat right heart catheterization and the primary endpoint of decrease in mPAP was evaluated. Secondary endpoints included other hemodynamic parameters, 6-minute walk distance (6MWD), N-terminal pro-brain natriuretic peptide (NT-proBNP) as well as quality of life questionnaire.

The results of the trial were presented recently at the American Heart Association annual meeting in Dallas and showed a decrease in the mPAP that was not statistically significant. The change in cardiac index, systemic vascular resistance, and PVR showed statistically significant improvements. Quality of life markers also were positive and the medication was tolerated well.

Though the primary endpoint was not achieved, there were some markers in the hemodynamics that were favorable. Thus, there is still hope that riociguat may have a role in the treatment of PH associated with left heart disease. A large multicenter clinical trial is now being planned to look at the efficacy and safety of using riociguat for the treatment of patients with PH and preserved LVEF (HFpEF). DILATE is another smaller study finished in Austria with 39 patients looking at the effects of riociguat for the treatment of PH with left heart diastolic dysfunction. The results of these trials are anticipated in the near future.