Purpose: To validate the PAH-SYMPACT™, a novel pulmonary arterial hypertension (PAH)-specific patient-reported outcome (PRO) tool, by demonstrating its final content validity, reliability, construct validity, and responsiveness in patients with PAH. This study will also assess the safety of macitentan and its effect on PAH symptoms and their impacts on patients’ lives.

Background/Significance: PAH remains a progressive, life-threatening condition, which severely impacts patients’ physical and mental quality of life (QoL). Available QoL instruments were either not specifically designed for PAH, and therefore may not capture PAH-specific symptoms and their impacts on patients’ lives, or do not meet the FDA PRO guidance criteria. The PAH-SYMPACT is a novel PRO tool designed to assess the symptoms of PAH and their impacts on patients’ lives and has been developed according to FDA PRO guidance. Evidence from qualitative research in patients with PAH shows that this instrument is relevant and comprehensive for use in PAH, well understood by patients, and easy to complete. Before the instrument can be used in future clinical trials or clinical practice, final content and psychometric validation, including development of a scoring guide, must be completed. The assessment of the instrument’s responsiveness as part of the psychometric validation requires that patients are exposed to a change, ideally due to an intervention with a known treatment effect. Macitentan, a novel, oral dual endothelin receptor antagonist under clinical development for PAH, demonstrated a significant effect on the combined endpoint of morbidity and mortality in the long-term, event-driven SERAPHIN outcomes trial in PAH.

Method: The SYMPHONY study consists of a 2-week screening, a 2-week baseline, and 16-week treatment period, plus a 4-week safety follow-up. Patients with symptomatic PAH in WHO functional class (FC) II–IV who meet the inclusion criteria will undergo screening and baseline assessments and begin treatment with macitentan 10 mg once daily. Patients will be reassessed at weeks 8 and 16. Each visit includes functional assessments (6-minute walk test, FC), patient-completed questionnaires (including Short Form 36 and CAMPHOR), and physician-completed forms (ie, response assessment) used in the validation of the PAH-SYMPACT. Adverse events, vital signs, ECG, laboratory parameters, and concomitant medications will be recorded. The PAH-SYMPACT will be completed by patients prior to the baseline, week 8, and week 16 assessments. Final content validity, reliability, construct validity, and responsiveness to change will be analyzed.

Findings: It is planned to enroll approximately 275 patients from 75 US sites between April 2013 and June 2014. Patients completing the 16-week treatment phase will be given the option of continuing in an extension study during which they will continue to receive macitentan. Results are expected in early 2015.

Implications: SYMPHONY will allow for the final validation and psychometric characterization of the PAH-SYMPACT and will provide additional open-label safety data on macitentan. If successfully validated, the PAH-SYMPACT will enable health care professionals to assess PAH symptoms and their impacts from a patient’s perspective. Further, the PAH-SYMPACT could be utilized as an endpoint in future clinical studies in PAH.

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