Development of the Pulmonary Arterial Hypertension–Symptoms and Impact (PAH-SYMPACT™) Questionnaire: A New Disease-Specific Patient-Reported Outcome Instrument for PAH

D. McCollister, RN, BSN\textsuperscript{1}; S. Kummer Shaffer, BA\textsuperscript{2}; D. Badesch, MD\textsuperscript{1}; A. Filusch, MD\textsuperscript{3}; E. Hunsche, PhD\textsuperscript{4}; R. Schüler, MSc\textsuperscript{4}; I. Wiklund, PhD\textsuperscript{5}; A. Peacock, MD\textsuperscript{6}

\textsuperscript{1}Pulmonary Sciences and Critical Care Medicine, University of Colorado Denver, Aurora, Colo.; \textsuperscript{2}United BioSource Corporation, Bethesda, Md.; \textsuperscript{3}Department of Cardiology, Angiology and Pulmonology, Heidelberg University Hospital, Heidelberg, Germany; \textsuperscript{4}Actelion Pharmaceuticals Ltd, Allschwil, Switzerland; \textsuperscript{5}United BioSource Corporation, London, United Kingdom; \textsuperscript{6}Scottish Pulmonary Vascular Unit, Golden Jubilee National Hospital, Glasgow, United Kingdom

PURPOSE: A qualitative research study was conducted at 5 US sites to develop a new patient-reported outcome (PRO) instrument assessing pulmonary arterial hypertension (PAH) symptoms and the impacts of these symptoms on patients, following the 2009 Food and Drug Administration (FDA) guidance for the development and validation of PROs.

BACKGROUND: Evaluating the effects of therapies on PAH symptoms and their impacts requires patient self-report via PROs. The FDA guidance calls for documentation that a PRO captures all concepts important to patients with the disease, and that patients understand the items as intended. Based on a literature review of currently available PROs used to evaluate PAH symptoms and/or their impacts, it was found that none was developed in accordance with these requirements.

METHODOLOGY: Content development and initial validation for the new PRO consisted of three phases. Phase 1 involved discussions with 5 focus groups of PAH patients to elicit concepts. Once saturation of emergent concepts was reached, a PRO questionnaire assessing PAH symptoms and their impacts on patients’ lives was drafted, considering clinical input from the international Steering Committee (SC) as well as assessments of readability and translatability to other languages. Phase 2 consisted of two rounds of cognitive interviews in PAH patients to assess patient comprehension and the appropriateness of the draft instrument. Phase 3 involved additional interviews to confirm patient interpretation of the revised PRO, followed by additional minor changes. Revisions of the draft PRO after each round incorporated SC input and translatability assessment. All patients were required to be 18–80 years old, with symptomatic PAH (WHO Group 1) confirmed by right-heart catheterization at diagnosis. Recorded interviews were transcribed by a third-party service, and qualitative data from recordings and transcripts were analyzed with ATLAS.ti software. The study was approved by institutional review boards for all 5 sites, and patients provided written informed consent.

FINDINGS: The 55 patients who participated (25 in Phase 1, 20 in Phase 2 [10 per round], and 10 in Phase 3) were generally representative of the PAH population: predominantly female (93%), and diverse in age (mean±SD 53±16 years), race/ethnicity (Caucasian: 67%, African American: 16%, Hispanic: 11%, Other: 7%), WHO/NYHA functional class (FC I/II: 56%, III/IV: 44%), and etiology (associated PAH: 42%, idiopathic PAH: 56%, familial PAH: 2%). The draft Pulmonary Arterial Hypertension-Symptoms and Impact (PAH-SYMPACT™) questionnaire was found to be clear, comprehensive, and relevant to PAH patients in cognitive interviews. Items were organized in a draft conceptual framework with 4 hypothesized symptom domains (respiratory symptoms, tiredness, cardiovascular symptoms, other symptoms) and 5 hypothesized impact domains (physical activities, daily activities, social impact, cognition, emotional impact). The recall period is the past 24 hours for symptom items and 7 days for impact items.

IMPLICATIONS: This qualitative study showed that the draft PAH-SYMPACT™ captures symptoms and their impacts relevant to PAH patients, demonstrating content saturation and concept validity. Final content and psychometric validation of the PAH-SYMPACT™ questionnaire will be performed in an upcoming clinical trial (SYMPHONY) before the tool can be used in clinical practice or studies.

This study was sponsored by Actelion Pharmaceuticals Ltd, Allschwil, Switzerland