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A Preliminary Quality of Life Questionnaire-Bronchiectasis

A Patient-Reported Outcome Measure for Bronchiectasis

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BACKGROUND: The Quality of Life Questionnaire-Bronchiectasis (QOL-B) is the first disease-specific, patient-reported outcome measure for patients with bronchiectasis. Content validity, cognitive testing, responsivity to open-label treatment, and psychometric analyses are presented.

METHODS: Reviews of literature, existing measures, and physician input were used to generate the initial QOL-B. Modifications following preliminary cognitive testing (N = 35 patients with bronchiectasis) generated version (V) 1.0. An open-ended patient interview study (N = 28) provided additional information and was content analyzed to derive saturation matrices, which summarized all disease-related topics mentioned by each participant. This resulted in QOL-B V2.0. Psychometric analyses were carried out using results from an open-label phase 2 trial, in which 89 patients were enrolled and treated with aztreonam for inhalation solution. Responsivity to open-label treatment was observed. Additional analyses generated QOL-B V3.0, with 37 items on eight scales: respiratory symptoms; physical, role, emotional, and social functioning; vitality; health perceptions; and treatment burden. For each scale, scores are standardized on a 0-to-100-point scale; higher scores indicate better health-related quality of life. No total score is calculated. A final cognitive testing study (N = 40) resulted in a minor change to one social functioning scale item (QOL-B V3.1).

RESULTS: Content validity, cognitive testing, responsivity to open-label treatment, and initial psychometric analyses supported QOL-B items and structure.

CONCLUSIONS: This interim QOL-B is a promising tool for evaluating the efficacy of new therapies for patients with bronchiectasis and for measuring symptoms, functioning, and quality of life in these patients on a routine basis. A final psychometric validation study is needed and is forthcoming.

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ABBREVIATIONS: 6MWT = 6-min walk test; AZLI = aztreonam for inhalation solution; CF = cystic fibrosis; CFQ-R = Cystic Fibrosis Questionnaire-Revised; HRCT = high-resolution CT; PRO = patient-reported outcome; QOL-B = Quality of Life-Bronchiectasis; SGRQ = St. George's Respiratory Questionnaire; V = version

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Bronchiectasis, an obstructive lung disease, is defined by dilated airways on high-resolution CT (HRCT) chest scans. The disease is associated with significant morbidity. Symptoms typically include chronic cough, sputum production, dyspnea, fatigue, and persistent lower respiratory tract infections.[1-4] Acute exacerbations of airway infections are common, associated with worsening symptoms, and typically treated with antibiotics, and they sometimes result in hospitalization.

The development of new therapies for treating bronchiectasis has been hampered by the lack of disease-specific, practical, and well-validated primary end points. Commonly used measures have serious limitations in clinical trials.[5] Changes in measures of lung function (eg, FEV_1 %) are often subtle, and FEV_1 is not strongly associated with a reduction in airway bacteria or an improvement in patients' health status after treatment.[6,7] The 6-min walk test (6MWT) has fallen into disfavor because of variability in the way the test is administered and because the results may be confounded by concomitant lung disease or other age-related comorbidities. Radiographic studies (eg, HRCT scans) have been used to develop severity scores, but changes do not correlate strongly with clinical improvement. It has been suggested that their lack of correlation is because some patients with bronchiectasis have debilitating respiratory symptoms with only focal structural airway damage visible by HRCT scans.[8] Use of acute exacerbations as a primary end point is complicated by the lack of a standardized definition and by the requirement for lengthy periods of assessment. Further, analyses could be affected by seasonal differences in exacerbation rates, and using this end point implies that patients feel well between episodes, when in fact most are symptomatic.

Prior to developing the Quality of Life Questionnaire-Bronchiectasis (QOL-B), existing patient-reported outcome (PRO) measures were evaluated; both the Leicester Cough Questionnaire[9] and the St. George's Respiratory Questionnaire[10] (SGRQ) have been studied in bronchiectasis.[11-13] Limitations have included minimal respiratory symptom coverage (Leicester Cough Questionnaire; Chronic Respiratory Questionnaire[14]), variable or lengthy recall intervals (SGRQ), and substantial response burden (some Chronic Respiratory Questionnaire and SGRQ forms).

Our review strongly suggested that a new PRO was needed for bronchiectasis.[15] The Cystic Fibrosis Questionnaire-Revised (CFQ-R)[16,17] contained the most complete and relevant items measuring respiratory symptoms (because of the common occurrence of bronchiectasis in patients with cystic fibrosis [CF]). Therefore, items from the CFQ-R and the relevant literature were used as a starting point for developing the QOL-B, the first bronchiectasis-specific PRO instrument to our knowledge.

Materials and Methods

QOL-B development (Table 1) was based on established processes.[18] Three interview studies (preliminary and secondary cognitive testing and open-ended concept elicitation) and a validation study (open-label, 28-day course of aztreonam for inhalation solution (AZLI) (Cayston; Gilead Sciences, Inc) (e-Fig 1) were conducted. AZLI is approved for treatment of patients with CF with chronic *Pseudomonas aeruginosa* infection.[19,20]

Study Designs

Cognitive testing interviews (lasting approximately 1.5 h) were audio recorded. Interviews used standard cognitive-testing procedures to determine what participants were thinking when responding to each item, how responses were chosen, what would elicit an adjacent response, relevance of items, and need for additional topics.[21-23] Most recent BMI, spirometry (performed during preliminary study[24]), and sputum culture results were obtained (retrospective chart review). In the preliminary cognitive-testing study, revisions were made on the basis of responses and were tested at subsequent sites; QOL-B version (V) 1.0 was developed after analyzing all interviews.

In concept-elicitation interviews (lasting 1-1.5 h), interviewers probed several dimensions of severity: (1) the frequency with which symptoms and other impacts occurred, (2) the level of difficulty managing symptoms, and (3) the extent to which symptoms affected daily activities (work, social roles). Audiotapes were transcribed and responses were coded (Atlas.ti V5.0; Scientific Software Development). Relevant topics were selected based on the frequency of patient endorsement (more than two patients) and physician review.

The phase 2 clinical trial was conducted at 21 centers in the United States (December 2008 to October 2009), with six visits over 70 days,

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