Development of the Ulcerative Colitis Patient-Reported Outcomes (UC-PRO) Questionnaire

PD Higgins; G Harding; DL Patrick; D Revicki; S Tease; G Globe; HK Viswanathan; K Fitzgerald; D Borie; BG Ortmeier; NK Leidy

1University of Michigan Health System School of Public Health, Ann Arbor, MI; 2Evidera, Bethesda, MD; 3University of Washington, Seattle, WA; 4Genentech Inc., South San Francisco, CA; 5Amgen Inc., Thousand Oaks, CA

BACKGROUND
Currently, there is no well-defined and reliable patient-reported outcome (PRO) measure available to provide direct evidence of treatment benefit in clinical trials that evaluate new therapeutic agents for the treatment of ulcerative colitis (UC).

The Ulcerative Colitis Patient-Reported Outcomes (UC-PRO) questionnaire is being developed by the IBD PRO Consortium to assess signs, symptoms, and impacts of UC important to this patient population.

METHODS
The development of the UC-PRO is based on qualitative research conducted among a total of 64 patients with moderate to severe UC, representing a diverse sample in terms of age, gender, ethnicity, and extent of disease (Table 1).

To determine instrument content and structure, 48 patients participated in six concept elicitation focus groups (n=38) or one-on-one interviews (n=10).

Findings were used to generate an item pool, inform response options, and determine appropriate recall.

To ensure clarity and understanding, two rounds of cognitive interviews were subsequently conducted among 16 patients to refine the measure.

Content analyses were performed by independent coders, with data organized in NVivo or Atlas.ti.

Six gastroenterologists (four from North America and two from Europe) were interviewed to obtain their clinical perspective of the important and relevant signs and symptoms of UC.

RESULTS
Table 1. Patient Demographic and Clinical Characteristics, Qualitative Studies

<table>
<thead>
<tr>
<th>Age</th>
<th>Race</th>
<th>Hispanic or Latino</th>
<th>Missing</th>
<th>Extent of Disease, n (%)</th>
<th>Ulcerative colitis (strict)</th>
<th>Crohn’s disease</th>
<th>Ulcerative proctitis (rectum)</th>
<th>Proctosigmoiditis (rectum and the sigmoid colon)</th>
<th>Left-sided colitis (rectum, beyond the sigmoid colon, but not past the splenic flexure)</th>
<th>Extensive disease</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–77</td>
<td>42 (65.6%)</td>
<td>10 (15.6%)</td>
<td>6 (9.4%)</td>
<td>6 (9.4%)</td>
<td>0 (0%)</td>
<td>1 (1.5%)</td>
<td>1 (1.5%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Table 2. Consistency of Concepts by Elicitation Method

<table>
<thead>
<tr>
<th>Concept</th>
<th>Focus Group Symptoms</th>
<th>One-on-one Interviews Symptoms</th>
<th>One-on-one Interviews Current Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood in BM</td>
<td>20 (69%)</td>
<td>8 (69%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Frequency of BM</td>
<td>25 (83%)</td>
<td>6 (83%)</td>
<td>8 (60%)</td>
</tr>
<tr>
<td>Pain in stomach area</td>
<td>24 (83%)</td>
<td>9 (83%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Consistency of BM</td>
<td>23 (81%)</td>
<td>10 (100%)</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>Joint/peri-anal body pain</td>
<td>22 (77%)</td>
<td>3 (30%)</td>
<td>5 (30%)</td>
</tr>
<tr>
<td>Un舒服</td>
<td>17 (60%)</td>
<td>6 (60%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Discharge</td>
<td>10 (42%)</td>
<td>4 (40%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Weakness</td>
<td>11 (42%)</td>
<td>4 (40%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Bowing</td>
<td>9 (40%)</td>
<td>2 (20%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Dehydration</td>
<td>6 (22%)</td>
<td>1 (10%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Lack of appetite</td>
<td>5 (19%)</td>
<td>2 (20%)</td>
<td>2 (20%)</td>
</tr>
</tbody>
</table>

Figure 1. Saturation of Signs and Symptoms of UC

Figure 2. Preliminary Hypothesized Conceptual Framework - Signs and Symptoms of UC

CONCLUSION
The UC-PRO was developed based on input from patients with UC who represent a range of diversity in subcategories of the disease, age, and ethnicity.

Qualitative data were collected to the point of saturation, with comprehensive results obtained using focus groups and one-on-one interviews.

The signs and symptoms scales of the UC-PRO are intended for use as co-primary, key secondary, or secondary endpoints in clinical trials.

The UC-PRO impact scales assess the extent to which UC affects the lives of patients in terms of coping strategies, daily activities, and emotional well-being.

Research examining the quantitative performance properties, including reliability, validity, and ability to detect change, is under way.

The preliminary conceptual framework will be modified based on results of the ongoing study to examine the psychometric properties of the UC-PRO.

ACKNOWLEDGMENTS
The Inflammatory Bowel Disease Patient-Reported Outcomes (IBD PRO) Consortium is an academic-industry consortium funded by Amgen Inc. and Genentech Inc. in collaboration with Dr. Peter Higgins at the University of Michigan Health Systems to develop PRO drug development tools (DDTs) for clinical trials evaluating treatment efficacy of BD, specifically ulcerative colitis (UC) and Crohn’s disease (CD).

The Steering Committee of the IBD PRO Consortium includes members experienced in the therapeutic areas of gastrointestinal disease and PRO development methodology. Members include Peter Higgins, MD, PhD, MSc; Donald L. Patrick, PhD; Danita Reiss, PhD; and Nancy Kline Leidy, PhD.

Figure 3. Preliminary Hypothesized Conceptual Framework - Impact of UC

Item-Level Concept

General Concepts

Coping

Disharmony

Emotional Impact

UC Signs

UC Symptoms

Systemic Symptoms

Systemic Symptoms

UC Signs and Symptoms