Irritable Bowel Syndrome Working Group
Presented at the Seventh Annual PRO Consortium Workshop – Silver Spring, MD – April 27-28, 2016

Background

Rationale for Irritable Bowel Syndrome (IBS) Working Group (WG)

• IBS is one of the most commonly diagnosed GI disorders
• IBS lacks a standard “fit for purpose” PRO instrument for assessing important patient-experienced signs and symptoms of IBS
• PRO Consortium member representatives and FDA advisors identified IBS as a priority area for the development of a PRO instrument

Goal of the IBS WG

• To develop three PRO measures for patient-reported symptoms in IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), and IBS with mixed symptoms (IBS-M) for use in clinical trials as a primary endpoint measure to establish treatment benefit

Targeted Labeling Language

• Product X is indicated in adults for the treatment of symptoms associated with irritable bowel syndrome (IBS-C), IBS with diarrhea (IBS-D), or IBS with mixed symptoms (IBS-M) for use in clinical trials as a primary endpoint measure to establish treatment benefit

Milestones

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<tr>
<th>Milestone</th>
<th>Expected Date</th>
<th>Completed Date</th>
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<tbody>
<tr>
<td>Vendor selection and contracting</td>
<td>10/29/2010</td>
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<tr>
<td>Complete background research (literature review and Expert Panel Meeting)</td>
<td>2/2/2011</td>
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<tr>
<td>Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and two rounds of cognitive interviews)</td>
<td>9/9/2011</td>
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<td>Complete qualitative research phase; submit briefing package to FDA (Final Cognitive Interview Report and updated Briefing Document)</td>
<td>8/15/2014</td>
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<td>Receive FDA response and approval to conduct quantitative pilot study</td>
<td>12/4/2014</td>
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<td>Submit quantitative pilot study protocol and quantitative analysis plan (QAP) to FDA for review (meeting with FDA scheduled for 5/3/16)</td>
<td>12/18/2015</td>
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<tr>
<td>Complete documentation of content validity using quantitative evaluation of item functioning via pilot study</td>
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<td>Q4 2016</td>
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<tr>
<td>Submit exploratory endpoint qualification dossier to FDA</td>
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<td>Q1 2017</td>
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Highlights

Example Endpoint Model for Treatment of IBS-M

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<tr>
<th>Endpoint</th>
<th>Endpoint Concept(s)</th>
<th>Endpoint Type</th>
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<tr>
<td>Primary</td>
<td>Overall response (TBO) indicating improvement in IBS-M symptom severity</td>
<td>PRO</td>
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<tr>
<td>• Improvement in abdominal symptoms (abdominal pain, diarrhea, bloating, cramping)</td>
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<tr>
<td>• Improvement in selected BM-related symptoms (stool consistency, stool frequency, incomplete BMs, straining, rectal urgency)</td>
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<td>Target Population</td>
<td>US-based adult patients (18 years and older; males and non-pregnant females)</td>
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<td>• Diagnosis of IBS of three main subtypes based on Rome III criteria (i.e., IBS-C, IBS-M, and IBS-D)</td>
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<td>• Patients without known or suspected organic disease (e.g., Crohn’s disease) that would better explain symptoms</td>
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<td>• Patients not concomitantly using medications known to affect GI mobility, constipation, or other IBS symptoms</td>
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Hypothesized Conceptual Framework

Bowel movement-related symptoms pertain to the following subtypes:

- Abdominal Pain
- Abdominal Discomfort
- Abdominal Bloating
- Abdominal Cramping
- Stool Consistency
- Stool Frequency
- Incomplete BMs
- Rectal Urgency
- Straining

Draft Instrument – Diary for Irritable Bowel Syndrome Symptoms (C, D, M)

Three instruments developed for each subtype:

- Diary for Irritable Bowel Syndrome Symptoms–C (DIBSS-C) for constipation predominant
- Diary for Irritable Bowel Syndrome Symptoms–D (DIBSS-D) for diarrhea predominant
- Diary for Irritable Bowel Syndrome Symptoms–M (DIBSS-M) for mixed symptoms

Core Items: Bowel Functioning and Stool Consistency; Abdominal Symptoms

Recall Period: Event driven and 24-hour recall period (end of day)

Response Options: Verbal rating scales, bivariate response, 11 point numeric rating scales

Updates

• Quantitative pilot study protocol and quantitative analysis plan (QAP) were submitted to the FDA for review
• Depending on the FDA’s approval of the protocol and QAP, RTI –HS anticipates quantitative pilot study to be completed by Q4 of 2016. Teleconference with FDA’s Qualification Review Team (QRT) is scheduled for 5/3/16
• User agreement in place for use of DIBSS-C in a treatment trial. Data from the trial will support a longitudinal evaluation of measurement properties in an IBS-C patient sample

Working Group Plans

Next Steps

• Initiate quantitative pilot study – 2Q2016
• Review and approve psychometric analysis plan for industry-sponsored longitudinal intervention trial that will generate evidence supporting qualification of the DIBSS-C

Dissemination Plan

• Qualitative research phase manuscript will be submitted to Value in Health in 2Q2016

Topics for Discussion

Unique Issues for the Working Group and Their Resolution

• Continued evaluation during upcoming quantitative pilot study needed to consider potential item reduction around abdominal pain and discomfort and choice of optimal stool consistency item
• Continued evaluation of how the Bristol Stool Form Scale (BSFS) may (or may not) translate across languages and cultures
• Ensure representation of patients who are 18 to 21 years of age in quantitative pilot study
• Evaluate whether there are different symptom experiences by gender, age and race

Lessons learned

• Important to consider and develop hypothesized preliminary scoring algorithm prior to quantitative phase

Working Group Participants

Company/Organization | Name | Affiliation
---|---|---
Allergan (formerly Forest Research Institute) | Robyn T. Carson, MPH (Co-Chair); Steven J. Shiff, MD | International Foundation for Functional Gastrointestinal Disorders (IFFGD)
Ironwood Pharmaceuticals, Inc. | Jennifer Hanlon, MPH (Co-Chair); David Reusser, PhD; Joe Lavins, MD |
Takeda Pharmaceuticals International | Maria Claudia Perez, MD; Amy Duhiq, PhD; Charles Baum, MD; Michelle Luo, PhD |
Bracket Global | Alisandra Johnson, BS | International Foundation for Functional Gastrointestinal Disorders (IFFGD)

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Institute | Name
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International Foundation for Functional Gastrointestinal Disorders (IFFGD) | Nancy Norton, BS

Nonmember Participants

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