Irritable Bowel Syndrome Working Group

Presented at the Sixth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2015

PRO CONSORTIUM CRITICAL PATH INSTITUTE

Background

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

- IBS is one of the most commonly diagnosed GI disorders
- IBS lacks a standard and fit for purpose PRO instrument for measuring 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 to establish treatment benefit

Targeted Labeling Language

- Product X is indicated in adults for the treatment of symptoms associated with irritable bowel syndrome [with constipation (IBS-C), with diarrhea (IBS-D), or mixed (IBS-M)]
- Product X improved abdominal symptoms (as measured by the abdominal symptom severity subscale) and bowel movement-related symptoms (as measured by an appropriate BM-related symptom subscale).

Note: This indication would be supported by an improvement in both abdominal symptoms and bowel movement-related symptoms

Milestones

Milestone	Expected Date	Completed Date
Content Validity Stage		
Vendor selection and contracting		10/29/2010
Complete background research (literature review and Expert Panel Meeting)		02/22/2011
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and two rounds of cognitive interviews)		09/09/2011
Submit Qualitative Research Summary Interim Briefing Document to FDA for review and feedback		09/26/2013
Received comments from FDA		12/6/2013
Teleconference with FDA		12/11/2013
Refine initial instrument (final cognitive interviews on demo ePRO device)		2/21/2014
Complete qualitative research phase; submit briefing package to FDA (final Cognitive Interview Report and updated Briefing Document)		8/15/2014
Complete documentation of content validity via quantitative evaluation of item functioning	Q42016	
Submit exploratory endpoint qualification briefing document to FDA	1Q2017	

Content of Interest

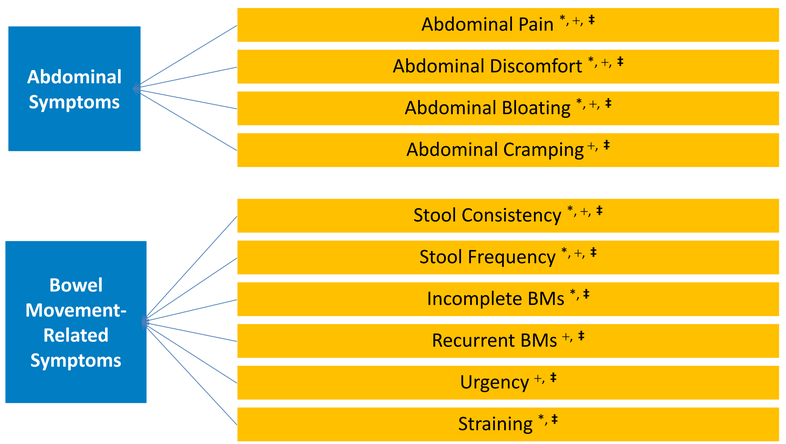
Endpoint Model for Treatment of IBS (Example provided for IBS-M)

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Overall response (TBD) indicating improvement in IBS-M symptom severity •Improvement in abdominal symptoms (abdominal pain, discomfort, bloating, cramping) •Improvement in selected BM-related symptoms (stool consistency, stool frequency, incomplete BMs, straining, recurrent BMs, urgency)	**PRO**

Target Population

- US-based adult patients (18 years and older; males and non-pregnant females)
- Diagnosis of IBS of three main subtypes based on Rome III criteria (i.e., IBS-C, IBS-M, and IBS-D)
- Patients without known or suspected organic disorder (e.g., Crohn's disease) that would better explain symptoms
- Patients not concomitantly using medications known to affect GI mobility, constipation, or other IBS symptoms

Hypothesized Conceptual Framework



Bowel movement-related symptoms pertain to the following subtypes:
* IBS-C; + IBS-D; ‡ IBS-M

Updates

- Conceptual framework confirmed by qualitative research
- Final Qualitative Research Summary Briefing Document for three PRO instruments (IBS-C, IBS-D, and IBS-M) submitted to FDA on August 15, 2014
- Received FDA agreement to advance instruments to quantitative evaluation on December 4, 2014
- Quantitative pilot study proposal finalized and contracts executed

Working Group Plans

Next Steps

- Develop preliminary scoring algorithm and protocol for quantitative evaluation of scale and item functioning
- Quantitative pilot study protocol to be submitted to FDA for review – 3Q2015

Dissemination Plan

- Qualitative research phase manuscript under development for submission to *Value in Health*

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
- 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
Actavis, Inc., an affiliate of Forest Research Institute, Inc.	Robyn T. Carson, MPH (Co-Chair); Steven J. Shiff, MD; Jessica Buono
Ironwood Pharmaceuticals, Inc.	David Reasner, PhD; Jennifer Hanlon, MPH; Joe Lavins, MD
Takeda Pharmaceuticals International	Gianna Rigoni, PharmD (Co-Chair); Maria Claudia Perez; Charles Baum, MD

Nonmember Participants	Affiliation
Nancy Norton, BS	International Foundation for Functional Gastrointestinal Disorders (IFFGD)

Expert Panel Members	Affiliation
Lin Chang, MD	University of California, Los Angeles
William D. Chey, MD	University of Michigan
Douglas A. Drossman, MD	University of North Carolina, Chapel Hill
Mark P. Jensen, PhD	University of Washington
Jeffrey M. Lackner, PsyD	University at Buffalo, SUNY
Brian E. Lacy, MD, PhD	Dartmouth-Hitchcock Medical Center
Brennan M.R. Spiegel, MD, MSHS	University of California, Los Angeles
Contract Research Organization	**Research Team**
RTI Health Solutions	Sheri Fehnel, PhD; Claire Ervin, MPH; Lori McLeod, PhD; Diana Goss