Irritable Bowel Syndrome Working Group

Presented at the Fifth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2014

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 aspects 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
Scoping Stage		04/29/2010
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
QRT written responses		12/6/2013
Teleconference with QRT		12/11/2013
Refine initial instrument (final cognitive interviews on demo ePRO device)	1 Q 2014	2/21/2014
Complete qualitative research phase; submit briefing package to FDA (final Cognitive Interview Report and updated Briefing Document)	3 Q 2014	
Complete documentation of content validity via quantitative evaluation of item functioning	TBD	
Submit exploratory endpoint qualification briefing document to FDA	TBD	

Content of Interest

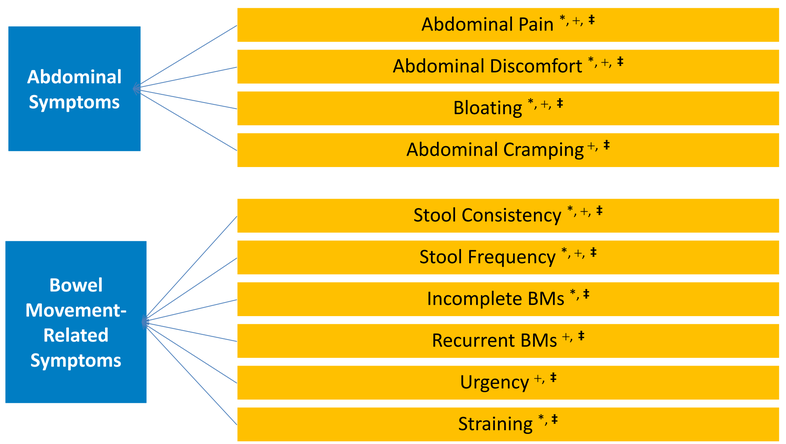
Endpoint Model for Treatment of IBS (Example provided for IBS-M)

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

- Successful teleconference held with QRT and IBS WG on December 11, 2013
- Agreement reached with QRT on current conceptual framework, item sets for IBS-C, IBS-D, IBS-M, endpoint models, and proposed indication statements
- Completed 3rd round of cognitive interviews using demo ePRO device February 21, 2014
- Data analysis complete and draft report under review by WG

Working Group Plans

Next Steps

- Revisions to instrument to be discussed (if any)
- Develop preliminary scoring algorithm and scope for quantitative evaluation for content validity
- Developing data dissemination plan for additional abstracts/manuscripts

Dissemination Plan

- Poster summarizing concept elicitation results presented at Digestive Disease Week, May 17 – 21, 2013
- Dissemination plan under review by WG

Topics for Discussion

Unique Issues for the Working Group and Their Resolution

- Optimal response scales varied across abdominal symptom measures; however, for consistency, a decision was made to use the 0-10 NRS for all abdominal symptom items
- Combination of BM-related symptom measures (e.g., BSFS, CSBM/SBM frequency, straining, urgency) challenging due to differences in response scales and directionality; therefore, key indicators of BM-related symptom improvement will be identified
- Ideal frequency of data capture varied across IBS sub-types; however, for consistency, real-time data capture is being pursued for all sub-types

Lessons learned

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

Working Group Participants

Company/Organization	Name
Forest Research Institute	Robyn T. Carson, MPH (Co-Chair); Steven J. Shiff, MD
Ironwood Pharmaceuticals, Inc.	Brooke Witherspoon; Joe Lavins, MD; David Reasner, PhD
Takeda Pharmaceuticals International	Gianna Rigoni, PharmD (Co-Chair); Karen Lasch, MD; Charles Baum, MD

Nonmember Participants	Affiliation
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Expert Panel Members	Affiliation
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Contract Research Organization	**Research Team**
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