Irritable Bowel Syndrome Working Group

Presented at the Fourth Annual PRO Consortium Workshop – Silver Spring, MD – April 24-25, 2013

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

Goal of the IBS WG

- To develop PRO measures for patient-experienced symptoms in IBS for use in clinical trials as a primary endpoint to establish treatment benefit

Targeted Labeling Language

- Treatment with product [X] results in an improvement in the symptoms of IBS-[diarrhea-predominant, constipation-predominant, or mixed]
  - This indication would have to be supported by an improvement in both abdominal symptoms and bowel movement-related symptoms as described in our conceptual framework.

Milestones

Milestone	Start Date	Completed Date
Establishment of WG		04/2009
Scoping Stage	04/2009	04/29/2010
Content Validity Stage		
Vendor selection and contracting		10/29/2010
Completion of background research (literature review and 1st expert panel)		02/22/2011
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation, patient interviews & expert panels)		09/09/2011
Refining initial instrument (cognitive interviewing, final expert panel, identification of electronic data capture [ePRO] platform, translatability assessment)	2 Q 2013	
Qualitative Research Summary document submitted to FDA for interim review	4 Q 2013	
Quantitative component of Content Validity Stage	TBD	
Content Validity Summary document submitted to FDA	TBD	
Psychometric Testing Stage	TBD	
Qualification of Instrument	TBD	

Content of Interest

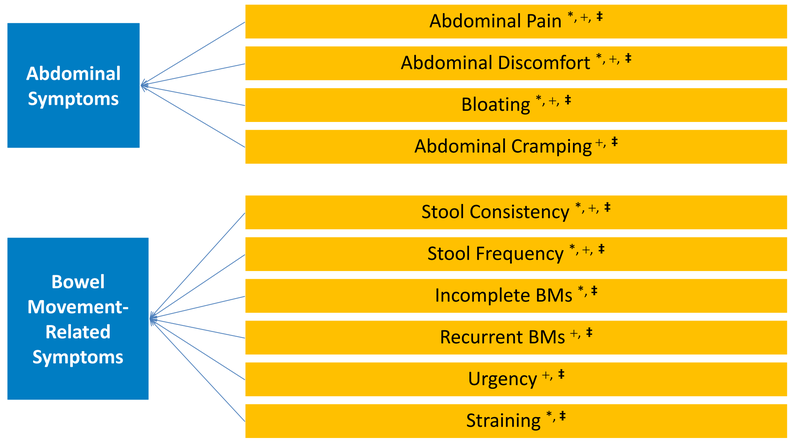
Endpoint Model for Treatment of IBS

Endpoint Hierarchy	Endpoint Concept(s)	Clinical Outcome Assessment (COA)/Biomarker/Survival
Primary	**Relief of IBS symptoms** • Relief of abdominal symptoms • Relief of bowel movement-related symptoms	PRO

Target Population

- US-based adult patients (18 years and older; males and non-pregnant females)
- Diagnosis of IBS of three mail subtypes based on Rome III criteria (i.e., constipation-predominant, mixed pattern, and diarrhea-predominant)
- Patients without known or suspected organic disorder (e.g., Crohn's disease)
- 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

- Draft PRO instruments have been drafted for IBS-C (constipation-predominant) and IBS-D (diarrhea-predominant) and IBS-M (mixed) populations
- Two rounds of cognitive debriefing interviews with IBS-C and IBS-D patients complete
- Translatability assessment complete
- WG and RTI are collaborating with the ePRO Consortium to implement the draft instruments onto PDA style hand-held device
  - Migratability assessment complete
  - Bracket selected as ePRO vendor to implement draft instrument onto device for final round of cognitive debriefing interviews

Updates (cont'd)

- FDA released final guidance: *Guidance for Industry Irritable Bowel Syndrome — Clinical Evaluation of Drugs for Treatment* in May 2012
- New co-chairs: Robyn Carson and Karen Lasch

Working Group Plans

Next Steps

- Pilot testing and final round of cognitive debriefing interviews with IBS-C, IBS-D and IBS-M patients are currently targeted for June 2013

Dissemination Plan

- Abstract accepted and poster in development for Digestive Disease Week, May 17 – 21, 2013
- Additional submissions to be discussed and agreed upon by the IBS WG and RTI-HS

Topics for Discussion

Concerns Worth Noting

- Bi-weekly teleconferences may not afford sufficient time for discussion and decision making among the WG (voting and non-voting) members

Unique Issues for the Working Group and the Resolutions

- In absence of scoring algorithm or metric for endpoint, discussions are ongoing to determine best global symptom assessment item to develop and debrief to use for future evaluation of clinical meaningfulness of instrument

Lessons learned

- Collaboration among KOLs, IBS WG members, and the vendor is critical to the development process of the PRO measure

Working Group Participants

Company/Organization	Name
Forest Research Institute	Robyn T. Carson, MPH (Co-Chair); Steven J. Shiff, MD
Ironwood Pharmaceuticals, Inc.	Brooke Dennee-Sommers; Joe Lavins, MD
Takeda Pharmaceuticals International	Karen Lasch, MD (Co-Chair); Charles Baum, MD

Nonmember Participants	Affiliation
Lin Chang, MD	University of California, Los Angeles
Jeffrey M. Lackner, PsyD	University at Buffalo, SUNY
Nancy Norton, BS	International Foundation for Functional Gastrointestinal Disorders (IFFGD)
Brennan M.R. Spiegel, MD, MSHS	University of California, Los Angeles

Expert Panel Members	Affiliation
William D. Chey, MD	University of Michigan
Douglas A. Drossman, MD	University of North Carolina, Chapel Hill
Mark P. Jensen, PhD	University of Washington
Brian E. Lacy, MD, PhD	Dartmouth-Hitchcock Medical Center

Contract Research Organization	Research Team
RTI Health Solutions	Sheri Fehnel, PhD; Claire Ervin, MPH; Diana Goss