Irritable Bowel Syndrome Working Group

Presented at the Third Annual PRO Consortium Workshop – Silver Spring, MD – April 4, 2012

Background

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

- PRO Consortium member representatives and FDA advisors identified IBS as a priority area
- IBS lacks a standard and fit for purpose PRO instrument for measuring important patient-experienced aspects of IBS
- There is a lack of a PRO instrument developed in accordance with the FDA PRO Guidance for use in clinical trials

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/alternating]
  - 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	Expected Date	Completed Date
Scoping Stage		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 2012	
Quantitative analysis	3 Q 2012	
Content Validity Summary document submitted to FDA for interim review	4 Q 2012	
Psychometric Testing Stage	TBD	

Content of Interest

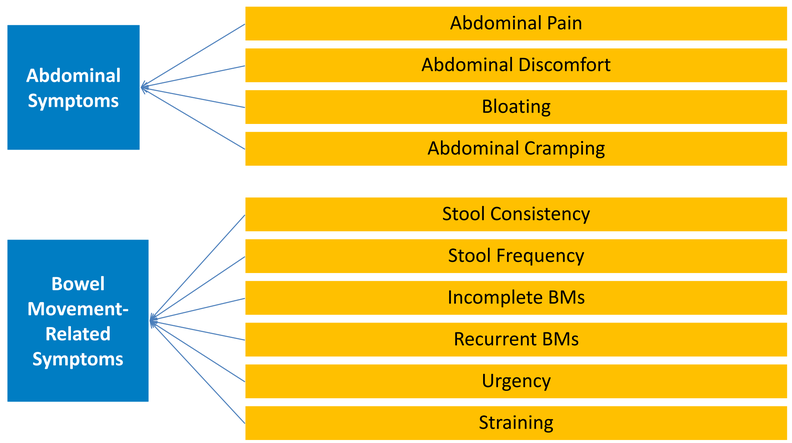
Endpoint Model for Treatment of IBS

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 all subtypes based on Rome III criteria (i.e., constipation-predominant, mixed or alternating 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



Updates

- RTI Health Solutions (RTI-HS) has completed the concept elicitation interviews and delivered final Concept Elicitation Report
- Expert Panel meeting convened on June 10, 2011 (RTI-HS, IBS WG members, and Expert Panel members)
- Draft PRO instruments have been created for IBS-C (constipation-predominant) and IBS-D (diarrhea-predominant) and RTI-HS is currently cognitively debriefing the draft PRO instruments
- Planning for pilot testing of draft instrument and need to select an ePRO vendor

Working Group Plans

Next Steps

- To collaborate with the ePRO Consortium to implement the draft instruments onto an electronic data capture device

Dissemination Plan

- To be developed through discussion and agreement between 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 members
- The approach to the measurement of symptoms in the IBS-mixed/alternating patient population has yet to be fully addressed

Way in Which the Process Might Be Made More Efficient

- FDA/SEALD representative on bi-weekly WG calls to facilitate decision-making

Unique Issues for the Working Group and the Resolutions

- The complexity of defining the relevant concepts and subtypes of IBS (IBS – constipation, and IBS – diarrhea)
  - Through continued communication among the FDA representatives and IBS WG members, it was agreed to develop two IBS PRO measures (IBS-C and IBS-D), and the qualitative phase of content validation informed clarity of a range of complex concepts

Lessons learned

- Collaboration among KOLs, IBS WG members, and the vendor is critical to the development process of the PRO measure
- Giving sponsors an opportunity to observe patient interviews is very helpful and fosters communication, clarity and smooth progression of the WG operations

Working Group Participants

Company/Organization	Name
Ironwood Pharmaceuticals, Inc.	Mollie Baird, MPH (Co-Chair); Jeff Johnston, MD
Forest Research Institute	Robyn T. Carson, MPH; Steven J. Shiff, MD
Takeda Pharmaceuticals International	Charles Baum, MD (Co-Chair)

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

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

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