Functional Dyspepsia Working Group

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

PRO CONSORTIUM CRITICAL PATH INSTITUTE

Background

Rationale for Functional Dyspepsia (FD) Working Group (WG)

- PRO Consortium member representatives and FDA advisors identified FD as an area lacking a "well-defined and reliable" measure of treatment benefit

Goal of the FD WG

- To develop a PRO instrument, in accordance with the FDA PRO Guidance, to measure the symptoms of FD for use in clinical trials as a primary endpoint to establish treatment benefit

Targeted Labeling Language*

- The PRO measure would support an indication of the treatment of the FD subtype as defined by the ROME III diagnostic criteria:
  1) Postprandial distress syndrome (PDS), which includes symptoms such as postprandial fullness and early satiation;
  2) Epigastric pain syndrome (EPS), which involves symptoms such as epigastric pain and burning; or
  3) Co-existing PDS and EPS subtypes

Milestones

Milestone	Start Date	Completion Date
FD WG established		2/7/2011
Scoping Stage	2/21/2011	2/29/2012
Further correspondence with Qualification Review Team to finalize target patient inclusion/exclusion criteria	3/21/2012	4/18/2012
Content Validity Stage		
RFP Issued/Proposals Received	4/2/2012	4/23/2012
Vendor selection	4/23/2012	9/18/2012
Finalization of Proposal/Contracting	9/18/2012	4/5/2013
Kick-off meeting with Adelphi Values	4/17/2013	4/17/2013
Completion of initial qualitative research (concept elicitation, concept selection, item generation, and expert panels)	1 Q 2014	
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)	2 Q 2014	
Quantitative evidence of content validity	3 Q 2014	
Content Validity Summary document submitted to FDA for interim review	4 Q 2014	
Psychometric Analysis Stage	TBD	
Qualification of Instrument	TBD	

Content of Interest

Endpoint model for treatment of FD – Postprandial Distress Syndrome(PDS) Subtype

Endpoint Hierarchy	Concept(s)	Clinical Outcome Assessment (COA)/Biomarker/Survival
Primary	FD-PDS Subtype • PDS Symptoms Score	PRO instrument under development

Endpoint model for treatment of FD – Epigastric Pain Syndrome (EPS) Subtype

Endpoint Hierarchy	Concept(s)	Clinical Outcome Assessment (COA)/Biomarker/Survival
Primary	FD-EPS Subtype • EPS Symptom Score	PRO instrument under development

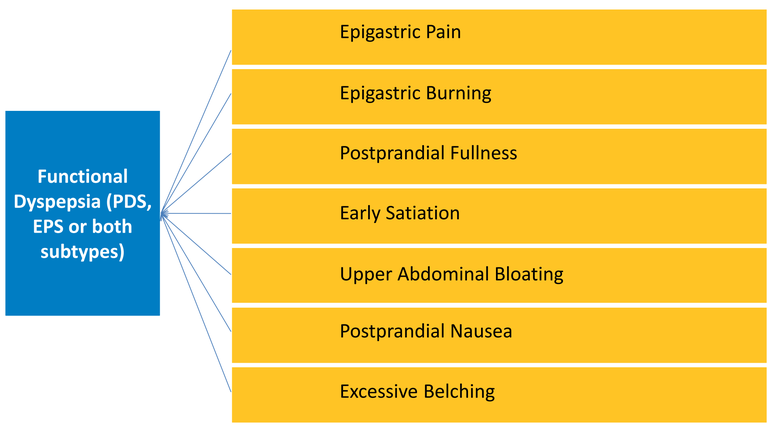
Endpoint model for treatment of FD – Co-existing PDS and EPS symptoms

Endpoint Hierarchy	Concept(s)	Clinical Outcome Assessment (COA)/Biomarker/Survival
Primary	FD • PDS and EPS Symptoms Score	PRO instrument under development

Target Population

- U.S. adult patients aged 18 years and older, with a diagnosis of FD (including PDS, EPS, or both) according to the Rome III diagnostic criteria, inclusive of a recent negative endoscopy
- Exclusion criteria include the following conditions: patients with gastroparesis, active irritable bowel syndrome, active chronic constipation, and active GERD (list not exhaustive)

Hypothesized Conceptual Framework*



- The conceptual framework was developed for the Summary Stage Scoping Document based on a preliminary review of the literature

Updates

- Obtained agreement from the FDA Qualification Review Team (QRT) to enter the qualification program for a PRO measure in FD - February 29th, 2012
- Obtained further clarification on patient inclusion/exclusion criteria from QRT on April 18, 2012
- Scoping Stage Summary Document revised to reflect discussions with QRT
- Vendor selection complete and contracting with Sponsors completed April 5, 2013
  - Adelphi Values selected as vendor collaborator

Working Group Plans

Next Steps

- Kickoff of Content Validity Stage with Adelphi Values held April 17, 2013
- Discussions ongoing regarding identification of key opinion leaders for expert panel engagement

Dissemination Plan

- To be developed

Topics for Discussion

Unique Issues for the Working Group and the Resolution

- Lack of agreement with FDA QRT regarding a consensus definition of FD leading to challenges with defining the target patient population
  - The FD WG was able to negotiate a path forward with the FDA.

Lessons Learned

- Timely feedback from FDA QRT is critical to inform progress of WG
- Composition of working group with both PRO, clinical, and regulatory representatives has been useful in providing different perspectives

Working Group Participants

Organization	Name
Forest Research Institute, Inc.	Robyn Carson, MPH (Co-Chair), Steven J. Shiff, MD
Ironwood Pharmaceuticals, Inc.	Brooke Dennee-Sommers, Gregory Gordon, JD, MD
Shire Development Inc.	Linda Deal, MS (Co-Chair), Debra G. Silberg, MD, PhD

Contract Research Organization	Research Team
Adelphi Values	Alan Shields, PhD; Fiona Taylor, MBiochem; Patrick Marquis, MD, MBA; Farrah Pompilus, MA; Catherine Foley, MPH, MA; Ramon Iovin, PhD; Megan Daggett, BA

* Note: Prior to conducting qualitative research with patients, it is not known whether a separate symptom complex exists between the two individual subtypes of FD (EPS and PDS), nor is it known at this point whether these subtypes would be evaluated in a particular clinical trial. Target labeling language and the conceptual framework will evolve based upon patient feedback and qualitative findings.