Functional Dyspepsia Working Group

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

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

- It is not known if individual subtypes would be evaluated in a particular clinical trial

Milestones

Milestone	Expected Date	Completed Date
Scoping Stage	06/01/2011	02/29/2012
Content Validity Stage		
Vendor selection and contracting	2 Q 2012	
Completion of background research (literature review and 1st expert panel)	TBD once vendor is selected	
Completion of initial qualitative research (concept elicitation, concept selection, item generation, and expert panels)		
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)		
Quantitative analysis		
Content Validity Summary document submitted to FDA for interim review		
Psychometric Testing Stage	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

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

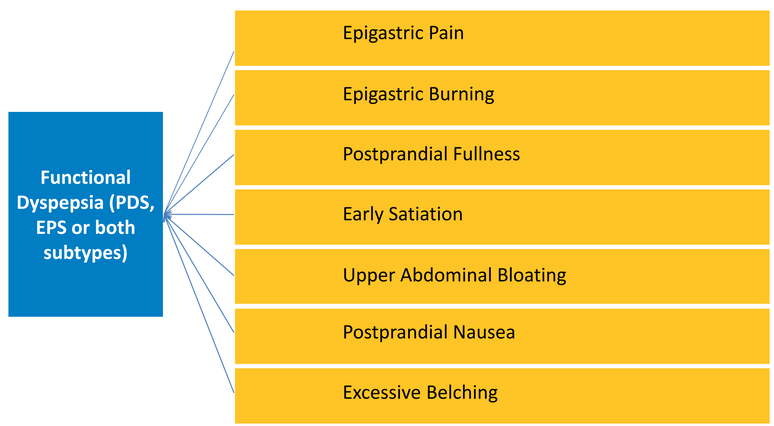
Endpoint model for treatment of FD – Co-existing PDS and EPS symptoms

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

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 (IBS), active chronic constipation, and active GERD (list not exhaustive)

Hypothesized Conceptual Framework



- The conceptual framework was developed for the SSSD based on a preliminary review of the literature

Updates

- Submitted the Scoping Stage Summary Document (SSSD) – June 1st, 2011
- FDA Review/Feedback and Written Correspondence between WG and FDA – July 27th through September 26th, 2011
- Type C face-to-face meeting – October 4th, 2011
- Re-submission of SSSD – January 12th, 2012
- Obtained agreement from the FDA Qualification Review Team (QRT) to enter the qualification program for a PRO measure in FD - February 29th, 2012

Working Group Plans

Next Steps

- Awaiting feedback from FDA for final clarification on one exclusion criterion
- Select vendor, sign project agreements with sponsoring firms, and sign contract with vendor

Dissemination Plan

- To be developed after contract signed with selected vendor

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
  - In its initial feedback on the SSSD, the FDA QRT expressed concerns regarding the ROME III definition of FD pointing out the overlap in the diagnostic signs and symptoms of FD with those of other functional GI disorders, such as gastroparesis, IBS, GERD and chronic constipation. The FD WG was able to negotiate a path forward with the FDA.

Lessons Learned

- Superior collaboration between FDA QRT and FD WG, through a face-to-face Type C meeting, and subsequent written communication led to the definition of robust inclusion/exclusion criteria to clearly define the FD target population for the PRO measure development
- FDA QRT feedback was received in a timely manner
- FDA SEALD fellow on bi-weekly WG calls facilitated decision making (through Nov 2011)

Working Group Participants

Company/Organization	Name
Forest Research Institute, Inc.	Robyn Carson (Co-Chair), Steven Shiff
Ironwood Pharmaceuticals, Inc.	Mollie Baird (Co-Chair), Jeff Johnston
Shire Development Inc.	Debra Silberg, Michael Keith, Juliana Setyawan