Depression Working Group

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

Background

Rationale for the Depression Working Group (WG)

- PRO Consortium members and FDA advisors identified depression as a priority area
- It was unclear whether any existing PRO instruments were 'fit for purpose' as an efficacy endpoint in major depressive disorder (MDD) treatment trials
- There is an apparent lack of a PRO instrument developed in accordance with the FDA PRO Guidance for use in clinical trials

Goal of the Depression WG

- To assess the adequacy of existing PRO instruments for capturing important depressive symptoms information from the patient's perspective and, if there is an unmet need, to either modify an existing instrument or develop a new depression symptom inventory

Targeted Labeling Language (Examples)

- Patients treated with *[drugX]* reported clinically significant reductions in severity of major depression disorder compared with treatment [YY] as assessed by the symptom inventory (*Example based on group comparisons using means*)
- Compared with [YY], significantly more patients treated with *[drugX]* reported clinically significant reductions in severity of major depression disorder as assessed by the symptom inventory (*Example based on group comparison using responder analysis)*
- Compared with [YY], patients treated with *[drugX]* reported significantly fewer days with depression symptoms as assessed by the symptom inventory (*Example based on group comparisons of number of days to meaningful clinical response)*

Milestones

Milestone	Expected Date	Completed Date
Scoping Stage		5/13/2010
Content Validity Stage		
Vendor selection and contracting		10/12/2011
Completion of background research (literature review and 1st expert panel)		3/28/2012
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)	5/18/12	
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)	9/30/12	
Quantitative analysis	1/30/2013	
Content Validity Summary document submitted to FDA for interim review	3/31/2013	
Psychometric Testing Stage	TBD	

Content of Interest

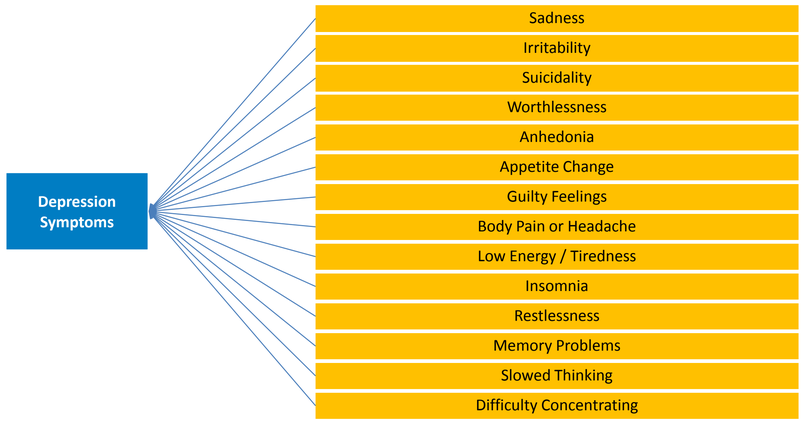
Endpoint Model for Treatment of Depression

Endpoint Hierarchy	Endpoint Concept(s)	Clinical Outcome Assessments (COA) /Biomarker/Survival
Primary	▪ Symptoms of major depressive disorder	PRO
Secondary	▪ Affect ▪ Disease activity	ClinRO

Target Population

- Patients 18 years and older, being treated in ambulatory settings with a clinical diagnosis of major depressive disorder (depression) with or without significant disability that impairs productivity in school, workplace, or in other customary activities, that would be expected to reduce patients quality of life and life satisfaction, and may engender suicidal ideation

Hypothesized Conceptual Framework



Updates

- Zoe Kopp (Pfizer) stepped down as WG co-chair; Steve Blum (Forest) is the new co-chair.
- Bristol-Myers Squibb has joined the WG
- Philip Ninan retired from Pfizer, but will continue on the WG as a non-member participant
- Health Research Associates (HRA) was selected as the vendor for the Content Validity Stage
- Contractor Services Agreement with HRA and Project Agreements with sponsor firms are fully executed
- HRA has completed a literature review and instrument review, as well as, developed the concept elicitation protocol
- The expert panel has been established; the WG held the first expert panel meeting to review the concept elicitation protocol on February 15, 2012.
- HRA has embarked on concept elicitation interviews

Working Group Plans

Dissemination Plan

- WG began work on dissemination plan in November 2011, and a draft version of the Scientific Data Disclosure Plan was completed in January 2012
- Two abstracts submitted to *First Meeting on Patient Reported Outcomes in Mental Health*

Topics for Discussion

Concerns Worth Noting

- Longer than anticipated delays in executing project agreements, potentially due to the process being new to most member firms' legal departments. It is expected that future agreements will not take that long
- WG has had considerable turnover in company representatives, often resulting in revisiting already addressed, and resolved, issues

Ways in Which the Process Might Be Made More Efficient

- Encouraging new company representatives to access the readily available WG document history on SharePoint

Unique Issues for the Working Group and the Resolutions

- The complexity of depression as a disease requires addressing issues related to comorbidity with other psychiatric conditions, depressive subtypes, suicidal ideation, and behavioral concerns
  - The WG has carefully considered the inclusion/exclusion criteria for enrolling patients into the qualitative research
- The need for active member involvement and participation in deciding key issues
  - Encourage open debate among WG members with decisions made by way of vote

Lessons Learned

- Encouraging even distribution of tasks among WG members fosters interaction

Working Group Participants

Company/Organization	Name
Abbott Laboratories	Nicholas Greco (Co-Chair), Steve Hass, Christy Houle
Bristol-Myers Squibb	Justin Doan
Eli Lilly & Company	Susan Ball, Nicki Bush
Forest Research Institute	Abhilasha Ramasamy, Steven Blum (Co-Chair)
Pfizer, Inc	Lucy Abraham, Brendon Binneman
Shire Development Inc.	Dylan Supina, Bryan Dirks, Manisha Madhoo
Sunovion Pharmaceuticals, Inc.	David Reasner, Krithika Rajagopalan
Nonmember Participant	Philip Ninan

Expert Panel Members	Affiliation
Jan Fawcett, M.D.	University of New Mexico
Michael Thase, M.D.	University of Pennsylvania
Madhukar Trivedi, M.D.	UT Southwestern
Linda Carpenter, M.D.	Brown University

Contract Research Organization	Research Team
Health Research Associates (HRA)	Mona Martin, Donald Bushnell, Kelly McCarrier, TeChieh Chen, Cecilia Dedios