Depression Working Group

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

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 symptom 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 measure

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 Symptoms of Major Depressive Disorder Scale (SMDDS) (*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 SMDDS (*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 SMDDS (*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	5/14/2012
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)	9/30/12	9/26/2012
Qualitative Research Summary document submitted to FDA for consultation and advice	4/30/2013	
Quantitative component of the Content Validity Stage	3Q2013	
Psychometric Testing Stage	TBD	

Content of Interest

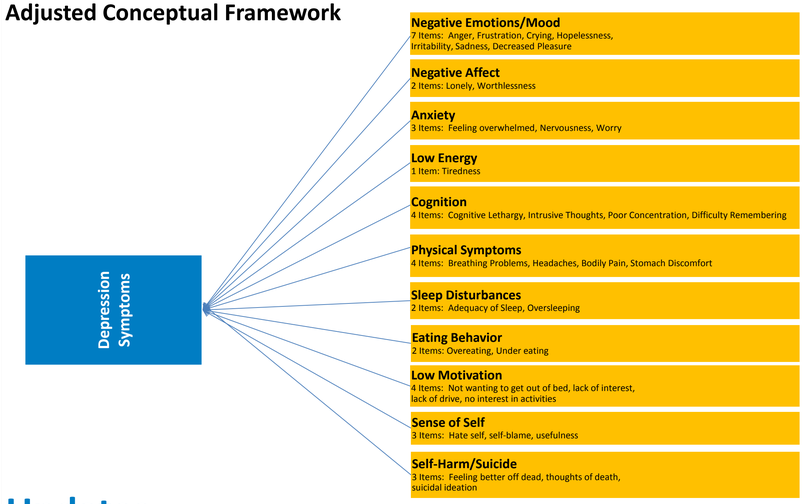
Endpoint Model for Treatment of Depression

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

Target Population

- Patients 18 years and older, being treated in ambulatory settings with a 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

Adjusted Conceptual Framework



Updates

- Bristol-Myers Squibb, Janssen, and Takeda have joined the WG
- Health Research Associates (HRA) completed the qualitative concept elicitation interviews
- In conjunction with HRA and the expert panel, the WG reviewed the results of the concept elicitation interviews and decided to develop a new measure the Symptoms of Major Depressive Disorder Scale (SMDDS)
- The draft measure underwent cognitive interview, translatability assessment and ePRO assessment, and the WG approved the content and name to move forward into the quantitative component of the Content Validity Stage.
- Negotiations are underway to amend contracts per the proposal for the quantitative component of the Content Validity Stage.
- The Qualitative Research Summary document along with the methodology for the quantitative component of the Content Validity Stage was submitted to the FDA in April 2013 for Consultation and advice.

Working Group Plans

Dissemination Plan

- 2012 information dissemination included 2 podium presentations at PRO Mental Health, 1 poster at ISCTM, 2 posters at ISPOR EU, and 1 poster at CNS Summit
- 2013 information dissemination will include 2 posters at ISPOR in May, a poster at NCDEU in May, a panel at DIA in June, and another abstract is pending acceptance for ISOQOL
- Manuscripts are currently under development

Topics for Discussion

Concerns Worth Noting

- 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, and to work with C-Path and the co-chairs to come up to speed

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
  - During the qualitative research, the WG carefully considered the inclusion/exclusion criteria for enrolling patients
  - During the quantitative component of the Content Validity Stage, the WG has decided to used a web-based research panel, which includes a large number of depression patients, but also required a carefully considered approach to address safety issues, in particular ensuring adequate follow-up with patients who may have presence of suicidal ideation
  - WG will also be comparing daily vs weekly recall in the quantitative study

Working Group Participants

Company/Organization	Name
AbbVie	Nicholas Greco (Co-Chair), Steve Hass, Christy Houle
Bristol-Myers Squibb	Justin Doan, David Budd
Eli Lilly & Company	Ellen Dennehy, Susan Ball, Nicki Bush, Risa Hayes
Forest Research Institute	Abhilasha Ramasamy, Maju Mathews, Steven Blum (Co-Chair)
Janssen	Carol Jamieson, Sarah Fleming
Pfizer, Inc	Lucy Abraham, Brendon Binneman
Shire Development Inc.	Linda Deal, Bryan Dirks
Sunovion Pharmaceuticals, Inc.	Mariam Hassan
Takeda Pharmaceuticals	Stephen Sainati, Theresa Vera
Nonmember Participant	Philip Ninan

Expert Panel Members	Affiliation
Michael Thase, M.D.	University of Pennsylvania
Madhukar Trivedi, M.D.	UT Southwestern
Linda Carpenter, M.D.	Brown University / Butler Hospital

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