Depression Working Group

Presented at the Sixth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2015

PRO CONSORTIUM
CRITICAL PATH INSTITUTE

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

Targeted Labeling Language (Examples)

- Patients treated with [*drug X]* reported clinically significant reductions in severity of major depressive 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 [*drug X]* reported clinically significant reductions in severity of major depressive disorder as assessed by the *SMDDS* (*Example based on group comparison using responder analysis)*
- Compared with [YY], patients treated with *[drug X]* 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
Content Validity Stage		
Vendor selection and contracting		Oct2011
Complete background research (Literature Review Report and Expert Panel Meeting)		May2012
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)		Aug2013
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback		Sept2013
Received and responded to written comments from FDA		Nov2013 Apr2014
Received and responded to written comments from FDA		Jun2014 July2014
Conduct quantitative pilot study	Apr2015	
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	4Q2015	
Submit exploratory endpoint qualification dossier to FDA	1Q2016	

Content of Interest

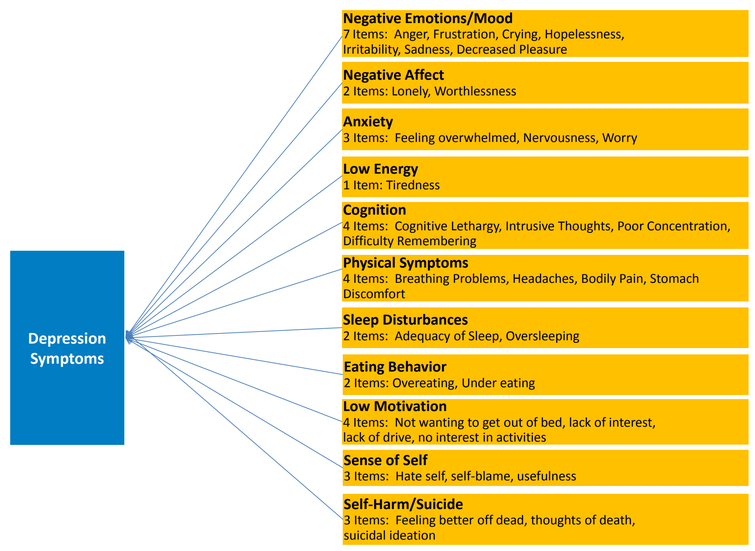
Endpoint Model for Treatment of Depression

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
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

- Cognitive interviews to evaluate equivalence of paper and Web-based versions of *SMDDS*
- Quantitative pilot study underway: Wave 1 data collection completed (n=300)
- One manuscript re-submitted to *The Patient*: *Patient-Centered Outcomes Research:* McCarrier et al. "Patient-Centered Research to Support the Development of the Symptoms of Major Depressive Disorder Scale (SMDDS): Initial Qualitative Research"
- One manuscript currently in development: "Systematic Review of Existing Patient-Reported Outcome Measures in Major Depressive Disorder"

Working Group Plans

Dissemination Plan

- It is anticipated that results from the quantitative pilot study will be submitted to the ISPOR 21st International Meeting

Quantitative Pilot Study

- Quantitative pilot study is currently underway. This will include two waves of data collection via a Web-based data entry portal.
  - The first wave of data collection has just been completed and data will be used to assess item function, determine scale structure, and inform revisions/refinements to the SMDDS.
  - Data from the second wave will be used to assess test-retest reliability and concurrent construct validity.
  - Cognitive interviews will be conducted between the first and second waves if changes are made to the SMDDS following the first wave.

Topics for Discussion

Ways in Which the Process Might Be Made More Efficient

- Encouraging new company representatives to access the readily available Depression WG document history on SharePoint and to work with C-Path and the co-chairs to come up to speed

Unique Issues and Resolutions

- The complexity of major depressive disorder requires addressing issues related to comorbidity with other psychiatric conditions, depressive subtypes, suicidal ideation, and behavioral concerns
  - For the quantitative component of the Content Validity Stage, the WG decided to use a Web-based data entry portal. This required a carefully considered approach to addressing safety issues, particularly ensuring adequate follow-up with subjects who express suicidal ideation

Working Group Participants

Company/Organization	Name
Eli Lilly & Company	Nicki Bush (Co-Chair)
Actavis, Inc., an affiliate of Forest Research Institute, Inc.	Maju Mathews, Abhilasha Ramasamy
Janssen	Carol Jamieson, Kristen Johnson
Pfizer, Inc	Lucy Abraham (Co-Chair), Jonathan Sporn
Roche/Genentech	Fiona McDougall
Shire Development Inc.	Linda Deal, Manisha Madhoo
Sunovion Pharmaceuticals, Inc.	Daisy Ng-Mak
Takeda Pharmaceuticals	Kumar Budur, Theresa Vera, Vanessa Perez
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, Talia Miller