Depression Working Group

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		Oct 2011
Background research (Literature Review and Expert Panel Meeting)		May 2012
Draft Instrument: Complete initial qualitative research and generate items (concept elicitation interviews, item generation, expert panel input, and initial round of cognitive interviews)		Aug 2013
Submit Qualitative Research Summary Briefing Document to FDA for review and feedback		Sep 2013
Received and responded to written comments from FDA		Nov 2013 Apr 2014
Received and responded to additional written comments from FDA		Jun 2014 Jul 2014
Conduct quantitative pilot study – Waves 1 and 2	W2-Sep 2015	W1-Apr 2015
Face-to-Face with FDA: instrument refinement and reduction		Jul 2015
Complete documentation of content validity and cross-sectional evaluation of other measurement properties	4Q2015	
Submit exploratory endpoint qualification dossier to FDA	1Q2016	

PRO Instrument Highlights

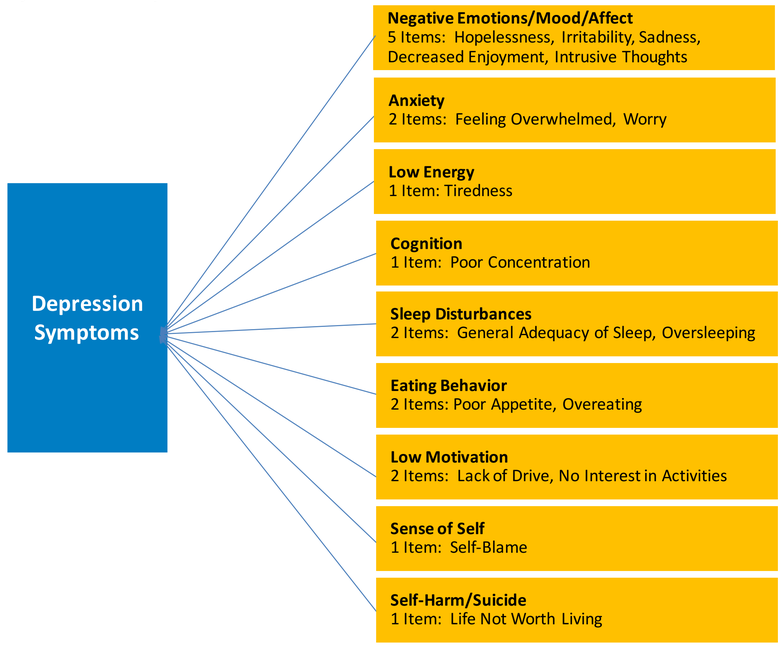
Endpoint Model for Treatment of Depression

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



Draft Instrument – *Symptoms of Major Depressive Disorder Scale (SMDDS)*

- *SMDDS* has 17 items addressing nine symptom domains
- *SMDDS* uses a 7-day recall period and a 5-point verbal rating scale
- PHT selected as the ePRO system provider
- Initial electronic data collection mode for the quantitative pilot study is a Web-based data entry portal

Working Group Plans

Information Dissemination Plan

- McCarrier KP, et al. Patient-centered research to support the development of the Symptoms of Major Depressive Disorder Scale (SMDDS): initial qualitative research. *The Patient: Patient-Centered Outcomes Research*. In press.
- Another manuscript currently in development titled "Systematic Review of Existing Patient-Reported Outcome Measures in Major Depressive Disorder"
- Quantitative pilot study results will be submitted for presentation at the 2016 International Society for Pharmacoeconomics and Outcomes Research 21st Annual Meeting

Quantitative Pilot Study

- Quantitative pilot study includes two waves of data collection via a Web-based data entry portal (Wave 1, n=300; Wave 2, n=200)
- Data from the Wave 1, completed in April 2015, was used to assess item function, determine scale structure, and inform revisions/refinements to the *SMDDS*.
- Wave 2, using the refined instrument, started in mid-August 2015. Data collected will be used to assess test-retest reliability and concurrent construct validity.

FDA Submission

- Plan to submit exploratory endpoint qualification dossier to FDA in first quarter of 2016

Unique Issues

- 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	Representatives
AbbVie	Xiaolan Ye
Allergan	Abhilasha Ramasamy
Eli Lilly and Company	Nicki Bush (Co-Chair)
Janssen	Carol Jamieson
Pfizer, Inc.	Lucy Abraham (Co-Chair), Jonathan Sporn
Roche/Genentech	Fiona McDougall
Sunovion Pharmaceuticals, Inc.	Daisy Ng-Mak
Takeda Pharmaceuticals	Lisa Mucha, Vanessa Perez
Nonmember Participant	Philip Ninan
Expert Panel Members	**Affiliation**
Michael Thase, MD	University of Pennsylvania
Madhukar Trivedi, MD	UT Southwestern
Linda Carpenter, MD	Brown University/Butler Hospital
Contract Research Organization	**Research Team**
Health Research Associates (HRA)	Mona Martin, Donald Bushnell, Kelly McCarrier, Talia Miller
ePRO System Provider	**Representative**
PHT/ERT	Sasha Hidalgo