Depression Working Group

Presented at the Eighth Annual PRO Consortium Workshop – Bethesda, MD – April 26-27, 2017

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 measure in major depressive disorder (MDD) treatment trials
- The WG concluded that there was no PRO instrument for use in MDD clinical trials developed in accordance with the FDA PRO Guidance

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
- Based on reviews of qualitative and PRO instrument-related literature, input from expert panelists, and findings from the concept elicitation interviews, the WG decided to develop a new instrument (i.e., the *Symptoms of Major Depressive Disorder Scale [SMDDS])*

Targeted Labeling Language

- Patients treated with [drug X] reported clinically significant reductions in severity of major depressive disorder compared with treatment [YY]. (*Based on group comparisons of means*)
- Compared with [YY], significantly more patients treated with [drug X] reported clinically significant reductions in severity of major depressive disorder. (*Based on group comparison using responder analysis)*
- Compared with [YY], patients treated with [drug X] reported significantly fewer days with depression symptoms. (*Based on group comparison of number of days to clinically meaningful response)*

Milestones

Milestone	Completed Date
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
Receive and respond to written comments from FDA	NOV 2013 APR 2014
Receive and respond to additional written comments from FDA	JUN 2014 JUL 2014
Complete quantitative pilot study	DEC 2015
Face-to-face meeting with FDA: instrument refinement and reduction	JUL 2015
Complete data analysis and quantitative pilot study report	APR 2016
Submit Qualification Briefing Package to FDA for exploratory use of *SMDDS*	1Q 2017

Highlights

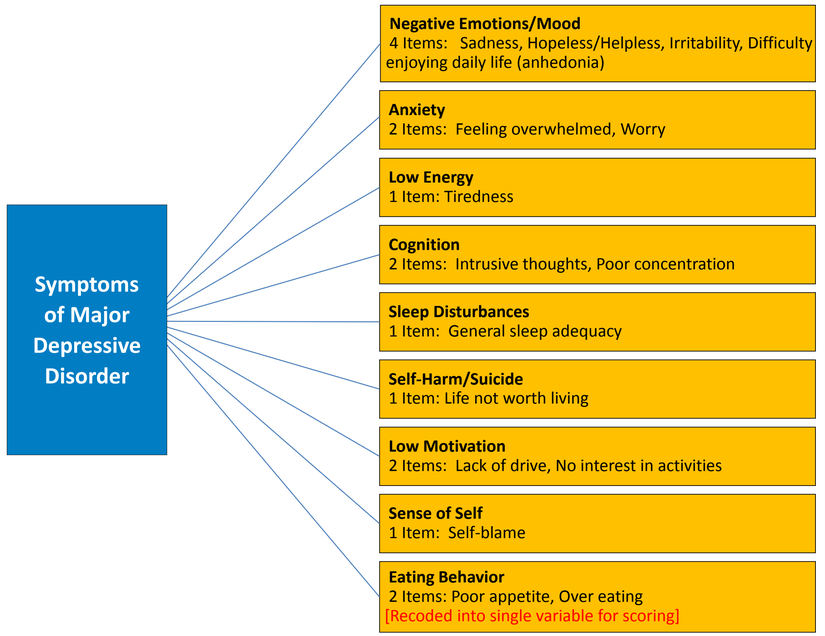
Example Endpoint Model for Treatment of Depression

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

Conceptual Framework



Measure – *Symptoms of Major Depressive Disorder Scale (SMDDS)*

Core Items: 16 items addressing nine symptom domains
Recall Period: 7-day
Response Options: 5-level verbal rating scale
Symptom Attribute: Severity was chosen based on patient description of major depressive disorder symptoms

Working Group Updates

Completed Activities

- Quantitative Pilot Study Report and quantitative data submitted to FDA in September 2016
- FDA feedback on Quantitative Pilot Study Report received in February 2017
- Qualification Briefing Package submitted to FDA in March 2017

Information Dissemination

- Manuscript currently in development titled "Systematic Review of Existing Patient-Reported Outcome Measures in Major Depressive Disorder"
- Workshop titled: A Multi-Stakeholder Collaborative Approach to Developing a Patient-Reported Outcome Measure for FDA Drug Development Tool Qualification: The PRO Consortium's Depression Working Group Experience" to be presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 22nd Annual International Meeting on May 24, 2017 in Boston, MA
- Manuscript on qualitative and quantitative development of the *SMDDS* to be developed following qualification for exploratory use

Unique Issues for the Working Group

- WG was requested by FDA to conduct additional analyses and provide additional information related to quantitative results, including:
  - Justification of scoring algorithm
  - Additional analyses needed to justify rule on missing item data
  - Request for IRT analysis of Wave 2 data
  - Request for justification of sum score (as opposed to IRT-based score)

Working Group Participants

Company/Organization	Representatives
AbbVie	Xiaolan Ye, MS, PhD
Allergan	TBD
Eli Lilly and Company	Elizabeth (Nicki) Bush, MHS (Co-Chair)
Janssen	Carol Jamieson, BSc
Pfizer, Inc.	Lucy Abraham, BSc, MSc, CPsychol (Co-Chair); Jonathan Sporn, MD
Roche/Genentech	Fiona McDougall, PhD, ClinPsyD
Sunovion Pharmaceuticals, Inc.	Daisy Ng-Mak, PhD
Takeda Pharmaceuticals	Lisa Mucha, PhD; Andrea Ireland, PhD
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, RN, MPA; Donald Bushnell, MA; Kelly McCarrier, PhD, MPH; Talia Miller
ePRO System Provider	**Representatives**
ERT (previously PHT)	Cheryl Van Walsh; Valdo Arnera, MD