Depression Working Group

Presented at the Fifth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2014

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 measure

Targeted Labeling Language (Examples)

- Patients treated with [*drug X]* 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 [*drug X]* 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 *[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
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	9/13/2013; 11/8/2013 received FDA feedback; 4/7/2014 WG responded
Quantitative component of the Content Validity Stage	4Q2014	
Psychometric Testing Stage	TBD	

Content of Interest

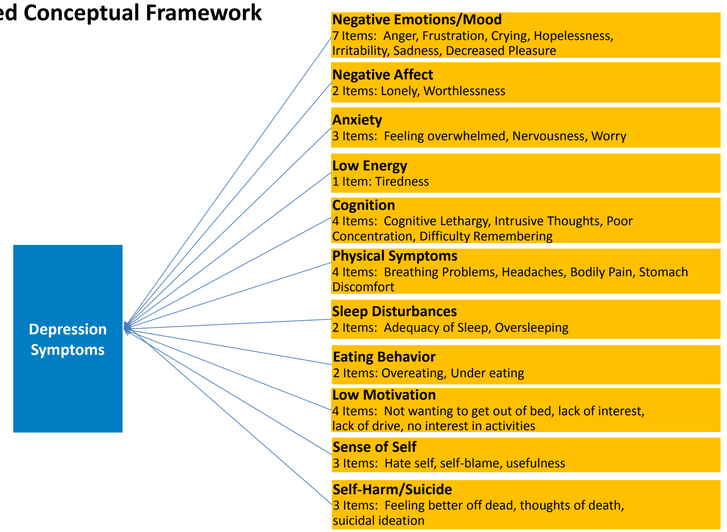
Endpoint Model for Treatment of Depression

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

- Lucy Abraham replaced Steve Blum as Co-Chair March 1, 2014
- Contract amendments for the quantitative component of the Content Validity Stage are in place and PHT is the ePRO system provider implementing the Web-based version of the SMDDS
- Qualitative Research Summary Briefing Document submitted to FDA on September 13, 2013
  - Positive feedback received from the FDA on November 8, 2013, including requests for clarification on subjects with generalized anxiety disorder (GAD) and the quantitative pilot study protocol
  - Based on additional FDA feedback, HRA and the WG modified the study design to include cognitive interviews comparing paper and Web-based SMDDS versions along with including a cross-sectional evaluation of the SMDDS in the target population.

Working Group Plans

Dissemination Plan

- 2013 information dissemination included 2 posters at ISPOR in May, a poster at NCDEU in May, a panel at DIA in June, and an oral presentation at ISOQOL in October
- Two manuscripts are currently under development regarding the instrument review and the qualitative research

Pilot Quantitative Study

- Conduct cognitive interviews to assess equivalence between the paper and Web-based versions of the SMDDS and usability of the Web-based data collection system
- Quantitative study will include two waves of data collected via a Web-based system. Data from the first wave 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.

Topics for Discussion

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
- For the quantitative component of the Content Validity Stage, the WG decided to use a Web-based instrument. This required a carefully considered approach to addressing safety issues, particularly ensuring adequate follow-up with subjects who may express suicidal ideation

Working Group Participants

Company/Organization	Name
AbbVie	TBD
Eli Lilly & Company	Susan Ball, Nicki Bush (Co-Chair)
Forest Research Institute	Maju Mathews, Abhilasha Ramasamy,
Janssen	Carol Jamieson, Kristen Johnson
Pfizer, Inc	Lucy Abraham (co-chair), Kasia Lobello
Roche	Fiona McDougall, Betsy Tschosik
Shire Development Inc.	Linda Deal, Manisha Madhoo
Sunovion Pharmaceuticals, Inc.	Daisy Ng-Mak
Takeda Pharmaceuticals	Kumar Budur, 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, Talia Miller