Cognition Working Group

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

Background

Rationale for Cognition Working Group (WG)

- PRO Consortium member representatives and FDA advisors identified mild levels of cognitive impairment due to Alzheimer's disease (MCI due to AD) as a priority area.
- This area lacks a PRO instrument that is fit for the purpose of measuring important patient-experienced aspects in the evaluation of treatment benefit in clinical trials.

Goal of the Cognition WG

- The Cognition Working Group is developing a patient-reported outcome measure to improve upon the current state of measurement of mild cognitive impairment due to Alzheimer's disease (MCI due to AD). The measure will capture the patient's perspective on specific aspects of patient functioning: complex activities of daily living (ADL) performance and interpersonal functioning and will contribute to the description of disease progression, and the measurement of treatment effects.

Draft Labeling Language

- Patients treated with X demonstrated [XX]% improvement on performance of Complex ADLs as compared to [XX]% improvement for patients treated with placebo.
- Patients treated with X demonstrated [XX]% improvement on Interpersonal Functioning as compared to [XX]% improvement for patients treated with placebo.
- After [X] months of treatment, the mean difference in the [XX] change scores for X treated patients compared to patients on placebo was [X]. X treatment was statistically significantly superior to placebo.
- Patients show less decline (or improvement) on Complex ADLs and Interpersonal Functioning over time when treated with X [XX]% as compared to placebo [XX%].

Milestones

Milestone	Expected Date	Completed Date
Scoping Stage		12/06/2010
Content Validity Stage		
Vendor selection and contracting		7/29/2010
Completion of background research (literature review and 1st expert panel)		9/30/2010
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)		06/03/2011
Refining initial instrument (cognitive interviewing, final expert panel)		9/10/2012
Quantitative analysis of the Content Validity Stage	4 Q 2013	
Content Validity Summary document submitted to FDA for interim review	1 Q 2014	
Psychometric Testing Stage	TBD	

Content of Interest

Endpoint Model for Treatment of MCI Due to AD

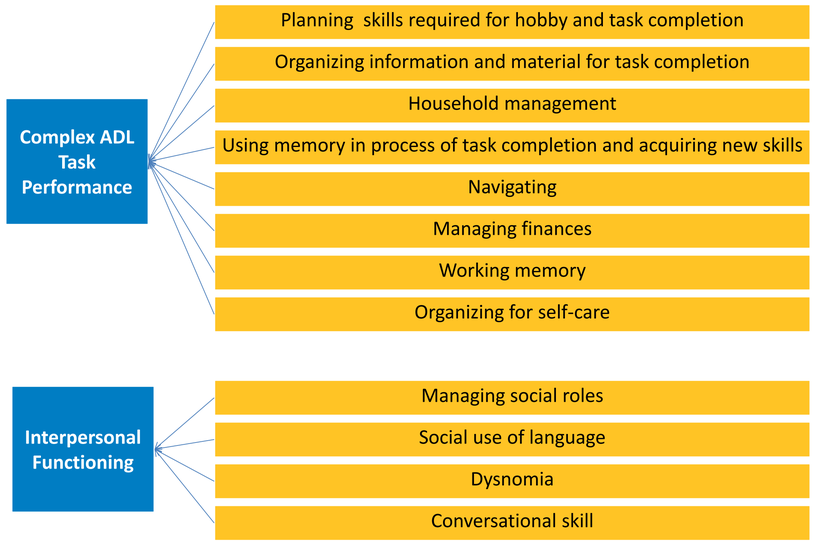
Endpoint Hierarchy	Endpoint Concept(s)	Clinical Outcome Assessment (COA)/Biomarker/Survival
Primary	**Cognition** • Cognitive test battery	**ClinRO and/or ObsRO***
	Function •Functioning in Complex Activities of Daily Living •Interpersonal functioning	**PRO**

*To be determined by each sponsor when designing their clinical trials

Target Population

- Patients 45 years and older
- Patients diagnosed with MCI due to AD

Hypothesized Conceptual Framework (Revised Based on Qualitative Research Results And Expert Panel Feedback)



Updates

- Completed an additional round of cognitive debriefing with patients on revised 26-item instrument
- Finalized instrument based on cognitive debriefing
- FDA Briefing Document for qualitative research is being finalized
- Adelphi Values has been selected as the vendor for the quantitative step in the Content Validity Stage and Psychometric Analysis Stage of instrument development

Working Group Plans

Upcoming presentations/publications

- Development of a patient-reported outcome (PRO) instrument to assess complex activities of daily living and interpersonal functioning in patients with mild cognitive impairment due to suspected Alzheimer's disease: the qualitative research phase. M Gordon, A Duhig, J Chandler, E Piault, L Frank, and W Lenderking on behalf of the Cognition WG. Poster presented at American Academy of Neurology meeting, March 21, 2013.
- Manuscript in-process based on AAN poster

Topics for Discussion

Concerns worth noting

- Progress has been slow on project and we had poor response to RFP for quantitative work

Unique issues for the working group and resolution

- WG members are identifying upcoming trials in their firms to implement the measure
- Current gaps include: Recall period for draft instrument & method(s) for determining adequacy of patient insight

Lessons learned

- Improve coordination of deliverables between WG members and vendor
- Pay attention to deliverables as received to insure deliverables are complete and accurate
- Define milestones in contracts based on expected deliverables

Working Group Participants

Company/Organization	Name
AbbVie	Amy Duhig (Co-Chair), Steven Hass
AstraZeneca AB	Daniel Eek
Boehringer Ingelheim Pharmaceuticals, Inc.	David Brill, Mark Gordon
Bristol-Myers Squibb	David Budd, Lucinda Orsini
Eisai Inc.	Lara Verdian
Janssen AI R&D, LLC	Loretto Lacey, Christopher Leibman, Gary Romano
Merck Sharp & Dohme Corp	Julie Chandler(Co-Chair), Yi Mo
Novartis Pharma AG	Ari Gnanasakthy, Jennifer Petrillo
Pfizer, Inc.	Joel Bobula, Katja Rudell
Roche	Todd Paporello, Elisabeth Piault-Louis, Diana Rofail, Glenn Morrison
Nonmember Participant	Lori Frank (PCORI)

Expert Panel Members	Affiliation
Paul Aisen, MD	University of California, San Diego, School of Medicine
Jeffrey Cummings, MD	Lou Ruvo Brain Institute, Las Vegas
Rachelle S. Doody, MD, PhD	Baylor College of Medicine
Steven H. Ferris, PhD	New York University School of Medicine
Douglas Galasko, MD	University of California, San Diego, School of Medicine
Serge Gauthier, MD, FRCPC	McGill Centre for Studies in Aging
Mary Sano, PhD	Mount Sinai School of Medicine
Bruno Vellas, MD	University of Toulouse
Gordon Wilcock, FRCP	University of Oxford, Nuffield Department of Medicine
Bengt Winblad, MD, PhD	Karolinska Institutet, Stockholm

Contract Research Organization	Research Team
UBC	Bill Lenderking, David Miller, Kellee Howard, Leah Kleinman