Cognition Working Group

Presented at the Third Annual PRO Consortium Workshop – Silver Spring, MD – April 4, 2012

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 seeks to develop patient-reported outcome measures that improve upon the current measurement of mild levels of cognitive impairment due to Alzheimer's disease (MCI due to AD). The measures 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 effect.

Targeted Labeling Language

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

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, identification of ePRO platform, translatability assessment)	3 Q 2012	
Quantitative analysis of the Content Validity Stage		TBD
Content Validity Summary document submitted to FDA for interim review		TBD
Psychometric Testing Stage	TBD	

Content of Interest

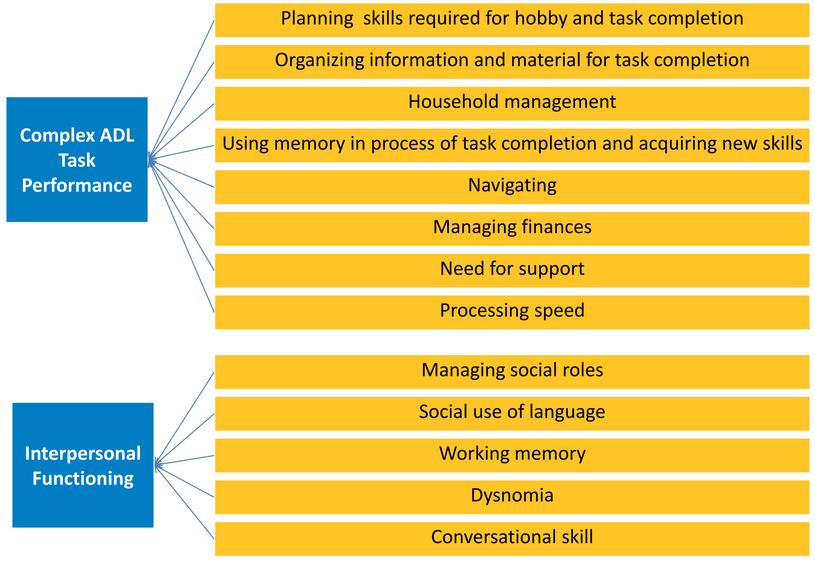
Endpoint Model for Treatment of MCI Due to AD

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

Target Population

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

Hypothesized Conceptual Framework (updated for Expert Panel January 2012)



Updates

- Completed cognitive debriefing with patients on a 29-item draft instrument (December/January 2012). The cognitive debriefing focused on documenting the comprehensibility of items, response options, and evaluation of selected items for possible deletion due to redundancy
- Held Expert Panel meeting in January 2012 to review the findings of the cognitive debriefing and further refine the instrument.
- Currently undergoing an additional round of cognitive debriefing with patients on revised instrument following recommendations from the Expert Panel meeting
- The next step is to develop an RFP for the quantitative step in the Content Validity Stage

Working Group Plans

Dissemination Plan

- Symposium submitted for presentation to Alzheimer's Association International Conference (AAIC): Measuring the Earliest Symptoms of Mild Cognitive Impairment
  - Development of a patient-reported outcome (PRO) instrument to assess mild cognitive impairment: the qualitative research phase: Mark Forrest Gordon, Chris Leibman, Amy Duhig, Lori Frank, Kellee Howard, and William Lenderking, on behalf of the Critical Path Institute's PRO Consortium Cognition Working Group

Topics for Discussion

Concerns worth noting

- Progress has been slow on the project
- Patient insight (i.e., the ability to self-report) remains a gap for the WG to address
- Selection criteria – how to define and recruit patients with MCI due to AD

Unique issues for the working group and resolution

- There are a number of upcoming trials (both inside and outside of industry) which could potentially assist with quantitative data collection
  - The WG will evaluate each opportunity to collaborate with investigators outside of industry and ensure that the risk/benefit is appropriate for these collaborations

Lessons learned

- Clinical expertise was extremely valuable for honing in on issues with the draft instrument

Working Group Participants

Company/Organization	Name
Abbott Laboratories	Amy Duhig (Co-Chair), Nicholas Greco, Steven Hass
AstraZeneca AB	Anna-Karin Berger, Daniel Eek
Boehringer Ingelheim Pharmaceuticals, Inc.	David Brill, Mark Gordon, Juergen Reess
Bristol-Myers Squibb	David Budd, Lucinda Orsini
Eisai Inc.	Lara Verdian, Veronika Logovinsky
Janssen AI R&D, LLC	Loretto Lacey, Christopher Leibman, Gary Romano
Merck Sharp & Dohme Corp	Julie Chandler(Co-Chair), Yi Mo
Norvartis Pharma AG	Ari Gnanasakthy, Jennifer Petrillo, Simu Thomas
Pfizer, Inc.	Joel Bobula, Katja Rudell, Holly Posner
Roche	Judith Dunn, Todd Paporello, 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 Institute

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