Follow-up on Clinical Meaningfulness in Alzheimer's Disease
Alzheimer's Experts Meeting
July 21, 2009

Objectives

I. Advance understanding of stakeholders' needs

- Does the current standard for defining clinical meaningfulness apply across all levels of severity of Alzheimer's disease? Or should clinical meaningfulness be defined separately for different severity levels? In particular, how should clinical meaningfulness be defined in MCI/EAD?
- What are the criteria/processes that regulators have for evaluating measures of clinical meaningfulness in MCI/EAD proposed by sponsors?

II. Data assessment

- What new data would be important for regulators to see from the field in Early AD/MCI?
- What data currently exists and can be applied?
- Are there potential alternatives to global or functional assessments for clinical meaningfulness in MCI/EAD?
    i. Under what circumstances might alteration in rate of cognitive decline by itself be considered a clinically meaningful outcome?
    ii. Is the only choice to demonstrate CM in MCI/EAD to conduct an 18-24m trial with N=thousands to detect a relatively small effect on global/functional compared to that shown in mild-moderate?
    iii. How can we enable optimal trial design for MCI/EAD: how do we (Agency/scientific community?) define what needs to be measured in terms of change in cognitive decline vs. placebo? Must CM be demonstrated? How can we define parameters to ensure that sponsors will invest in such trials?
- Do the experts/regulators believe that the EMEA JUL07 draft guidance on "delay of disability" has some usefulness in moving beyond symptomatics?

III. Speakers Charge

- An openness and readiness to presenting alternatives.
- An agreement from all stakeholders to continue working together on next steps.

IV. Next steps

- Assess need for guidance on issues discussed.
- Agreement to participate in consensus conference on outstanding issues.

Agenda

7:30 a.m. **Continental Breakfast**

8:00 a.m. **Introduction**

- Howard Fillit - Alzheimer's Drug Discovery Foundation on behalf of ACT-AD
- Robert Egge - Alzheimer's Association
- John Dwyer - LEAD

8:15 a.m.—9:15 a.m. **Determination of Clinical Meaningfulness in MCI/Early AD-Role of the Global**

- Jeff Cummings - UCLA
- Dave Knopman - Mayo Clinic
- Ken Rockwood - Dalhousie University
- Eric Siemers - Lilly

Discussion leader - John Morris

9:15 a.m.—10:15 a.m. **Minimally Acceptable Changes in Disease Course**

- Jeff Cummings -UCLA
- Russell Katz - FDA
- Ron Black - Wyeth

Discussion leader - Dave Knopman

10:15a.m.—11:15 a.m. **Framework for Maximizing the Utility of Criteria for Early AD/MCI Clinical Trials**

- Dave Knopman - Mayo Clinic
- John Morris - Washington University
- Dale Schenk - Elan

Discussion leader - Jeff Cummings

11:15 a.m.—12:00 p.m. **Discussion among all in attendance**

12:00 p.m.—12:30 p.m. **Summary and Next Steps**

- Dan Perry-ACT-AD