

NIA ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)

Michael W Weiner

Leon Thal

Ronald Petersen

Clifford Jack

William Jagust

Arthur Toga

John Trojanowski

Laurel Beckett

OVERVIEW OF THIS PRESENTATION

- Overview and Administrative Core: Weiner
- Clinical Core: Thal
- MRI Core: Jack
- PET Core: Jagust
- Biomarkers Core: Trojanowski
- Informatics Core: Toga
- Statistics Core: Beckett

Increasing Role of Imaging & Biomarkers in AD treatment trials and detection

- **Many studies have shown changes in the brain of normal aging and in AD**
- **Structural MRI shows shrinkage, esp of median temporal lobe and cortex**
- **FDG PET shows reduced metabolism**
- **AD Biomarkers can improve diagnosis and reflect disease progression**
- **Great potential for use in clinical trials and for early detection**

Role of imaging in treatment trials

- **Current trials using ADAS-cog etc have large sample size**
 - **Cognitive measures do not easily determine disease modifying effects of treatment**
- **PHARMA has high interest in use of imaging for treatment trials**
- **Current data from many labs, different methods, different subjects**

GOALS OF THE ADNI LONGITUDINAL MULTISITE OBSERVATIONAL STUDY

- **Develop “standards” for imaging**
- **Improve methods for clinical trials**
- **Determine the optimum methods for acquiring and processing images**
- **“Validate” imaging and biomarker data by correlating with neuropsych and behavioral data**
- **Provide a data base and biological samples for PHARMA**

OVERALL GOALS

Major goal is *collection of data and to establish a brain imaging and biomarker database*

- **Also development of improved methods for trials**
- **Clinical Core, Neuroimaging Core: public access**
- **Emphasis on MCI, with some AD and controls**
- **Processing of MRI, PET, and biomarkers**

ANTICIPATED FUNDING

- **\$12 million/yr, 5 years:**
- **Total funding \$ 60 million**
 - **\$40 Million provided by NIH**
 - **\$20 Million to be provided by industry**
 - **Some funding still to be obtained**
- **Cooperative agreement (UO1)**

STRUCTURE

- **Administrative Core: Weiner**
- **Clinical Core: Leon Thal, Ron Petersen, Marilyn Albert, Pierre Tariot, David Salmon**
 - **Based at ADCS at UCSD**
- **Neuroimaging Core**
 - **MRI: Cliff Jack, Norbert Schuff, Anders Dale, Nick Fox, Charles DeCarli, Matt Bernstein, Joel Felmlee**
 - **PET: Bill Jagust, Norm Foster, Eric Reiman, Bob Koeppe**
- **Informatics: Art Toga UCLA/LONI**
- **Biomarker Core: J.Q. Trojanowski, Les Shaw**
- **Statistics: Laurel Beckett**
- **45+ performance sites**

STUDY DESIGN

- **MCI (n= 400): 0, 6, 12, 18, 24, 36 months**
- **AD (n= 200): 0, 6, 12, 24 months**
- **Controls (n= 200): 0, 6, 12, 24, 36 months**
- **Clinical, MRI (1.5 T) at all time points**
- **FDG PET at all time points in 50%**
- **3 T MRI at all time points in 25%**
- **Blood and urine at all time points from all subjects, CSF from 20% of subjects less often**

IMAGING INFOMATICS

- Goal is rapid public access of *all raw and processed data*
- Art Toga at LONI will receive all QA'd MRI and PET data
- Images for processing downloaded from LONI, and results uploaded to LONI
- All image data will be available from LONI
- Clinical data base at ADCS/UCSD will be linked

STATISTICAL ANALYSIS

- **Laurel Beckett and Ron Thomas**
- **Specific aims, and hypotheses in application**
- **Statistical analysis plan needs further development**

INVOLVEMENT BY INDUSTRY IN THE APPLICATION

- **PHARMA and Imaging Companies will directly provide funds through the NIH Foundation. They will serve on the Steering Committee.**
- **Greater financial and scientific participation by industry is desirable!**
- **Specific mechanisms for industry involvement are being explored**

SITE REQUIREMENTS

- **45-50 sites have been selected**
- **Major requirement: demonstrated ability to recruit MCI subjects for trials**
- **Also need acceptable 1.5 T MRI**
- **Some sites will provide 3 T and PET**

TIME LINE

- **We have begun, Funds to be awarded Sept 04**
- **Oct 4 2004, Meeting of Steering and Advisory Committees in Toronto**
- **Preparatory Phase Oct –April**
- **Patient enrollment begins April-July 2005**
- **Enrollment ends July 2006. Completion 2009**

ANTICIPATED PROBLEMS

- **The study is very arduous with many procedures and many time points**
- **Recruitment**
- **Retention**
- **Getting started on time. Completion of study goals within the 5yr funding period**

CONCLUSION

- We expect funding in October 2004
- Considerable work is already underway
- Additional Pharmaceutical company participation is needed
- Links to a European initiative are being discussed