ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

M. Weiner, P. Aisen, R Petersen, C. Jack, W. Jagust, J Trojanowski, L. Shaw, A. Toga, L. Beckett, D. Harvey A. Gamst. R. Green.A Saykin, S. Potkin

Neil Buckholtz, David Lee, Pat Cole

Industry Scientific Advisory Board (ISAB)

And Site PIs, Study Coordinators and 822 subjects enrolled in 58 Sites in US and Canada

ADNI OVERVIEW

- Introductions and acknowledgements
- What have we accomplished
- What are the problems
- Planning for renewal (ADNI2)

FOUNDATION FOR THE National Institutes of Health

ADNI Industry Scientific Advisory Board

AstraZeneca UNITED KINGDOM
Bristol-Myers Squibb
Eisai
elan
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INNOGENETICS BIOTECHNOLOGY FOR HEALTHCARE
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Schering-Plough
SYNARC Start here, finish first.
Wyeth
alzheimer's association®
Alzheimer's Drug Discovery Foundation
INSTITUTE FOR THE STUDY OF AGING ISOA

MAJOR ACCOMPLISHMENTS OF ADNI

- Things are going as planned
- Full enrollment, low dropout
- Problems are relatively minor
- Huge amounts of data coming

ACCOMPLISHMENTS
Improved methods

- New improved methods for clinical trials have been developed and implemented
  - Greatly improved MRI
  - Multsite PET
  - Improved methods for CSF tau and abeta
- These methods are being used by several large trials conducted by ADCS and Pharma
- A network of sites is available for trials

WORLDWIDE ADNI

- ADNI has fostered similar projects worldwide
  - Australia: Colin Masters/Chris Rowe
  - Japan: Takeshi Iwatsubo
  - Europe: Giovanni Frisoni and Innomed etc
  - China: to come?
- This ultimately has huge value for international pharma

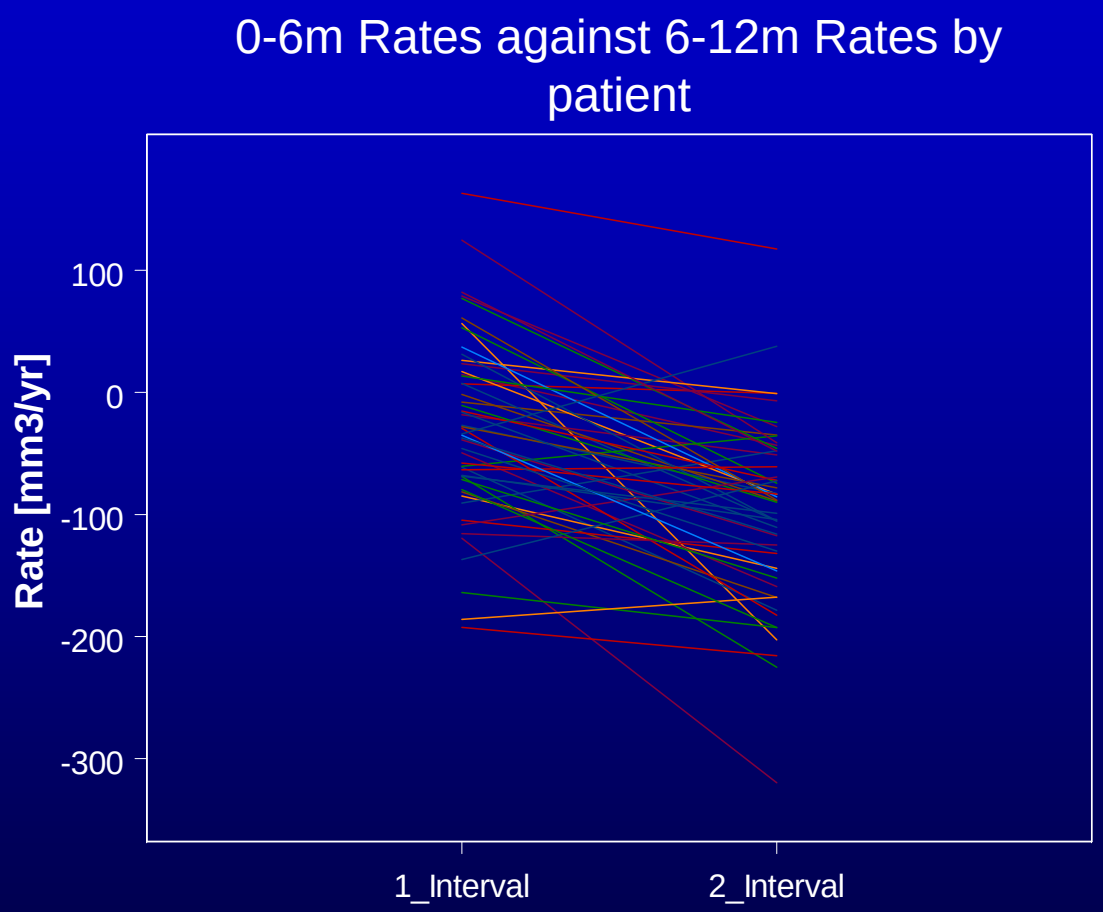
RESULTS

- **The initial impetus for ADNI was confusion concerning which imaging and biomarker measurements provided the "best rates of change", highest power to detect treatment effect**
- **The majority of today's presentations will concern results: Jack, Jagust, Trojanowski, Beckett**
  - **There is now a huge amount of data**
  - **Lots of results: abstracts and papers etc etc**
- **Today you will see a "early glimpse" Preliminary**

ALL RESULTS ARE VERY PRELIMINARY

- **We must emphasize**
  - **All results shown today are preliminary because**
    - **We only have 1 yr rate of change data on about half the subjects**
    - **Some of the data needs to be corrected**

Acceleration Of Atrophy Rates In AD



Acceleration:
34.3 ± 4.6 mm^3/year^2
$p < 0.0001$
Accounted for AD severity (MMSE)
No significant effect by ApoE

No significant acceleration in CONTROL or MCI

Effect Of ApoE On Atrophy Rates

Measures	NORMAL	MCI	AD	P[(2)]
V_0[(1)] (mm^3)	2017 ± 205	1811 ± 77	1654 ± 69	n.s.
Rate (mm^3/year)				
Apoe4 Carrier	-56.7 ± 13.3	-54.1 ± 11.6	-104.8 ± 13.3[(3)]	0.03
Non Carrier	-27.6 ± 12.9	-41.2 ± 12.8	- 62.6 ± 17.6	

- [(1)] V0 = baseline volume
- [(2)] Apoe4 effect, after accounting for diagnosis and cognitive impairment (MMSE) and random variations of baseline volumes and rates
- [(3)] p = 0.02 test by Maximum Likelihood
- Estimation ± standard error are listed

EXPECTED FINAL RESULT

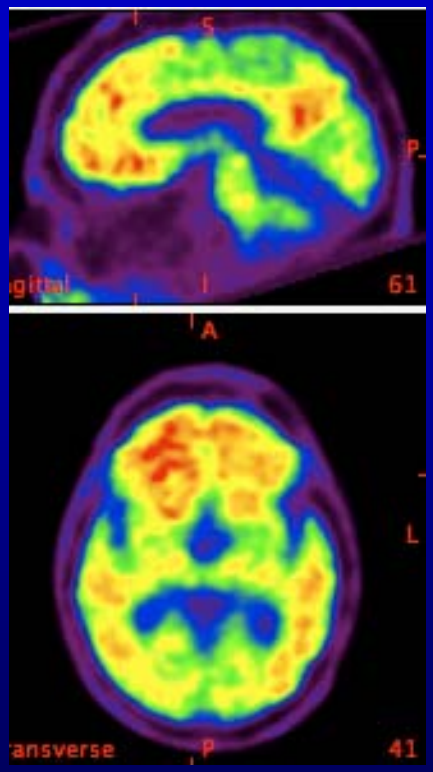
- **Established methods for AD clinical trials**
- **Will identify the best imaging and biomarker methods with high rates of change, small SD, and high power, which correlate with clinical measures.**
- **“surrogate measures” will be used in Phase 2 and 3 studies, and will be validated in the treatment setting!**
- **Surrogates may have “predictive power” and improve power of clinical measures**
- **Ultimately (a long way off), a ‘validated’ biomaker**

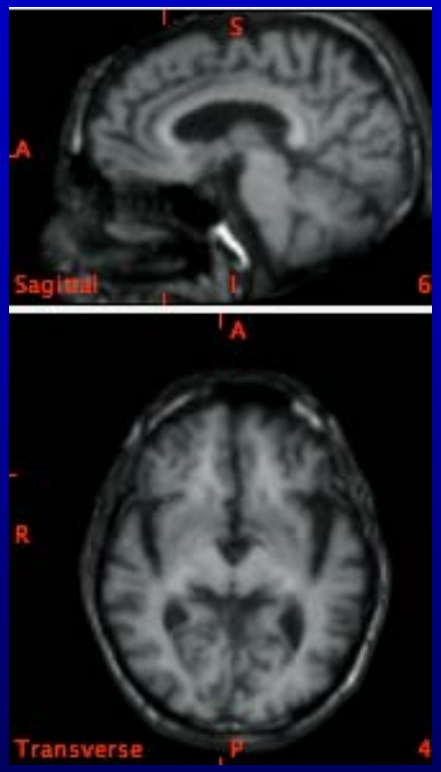
FUTURE DIRECTIONS
Renewal of ADNI

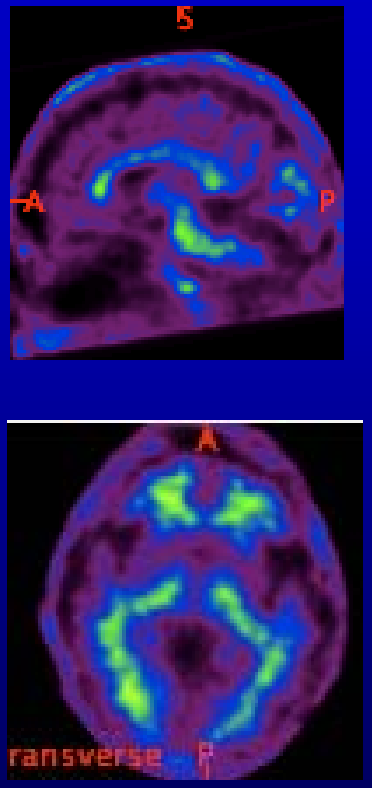
- **Continue to follow current normal &MCI enrolled, beyond 3 years**
- **Enroll MCI who are less impaired**
  - **fill the *"gap"* between MCI normal**
- **Possibly enroll a new AD cohort**
- **F 18 amyloid imaging: as seen in next slide**
- **3 T MRI: possibly functional MRI**
- **More biomarkers, species of abeta, proteomics**
- **Welcome suggestions**

[^{18}F]-AV1/ZK

Chris Rowe







Alzheimer's Disease

80 year old male

MMSE 26

Healthy Elderly Control

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FUTURE STEERING COMMITTEE MEETINGS

- ADNI will run through 2010
- Plan annual Spring meetings
- However ADNI data will be shown at many scientific conferences
  - And we may be planning “ADNI satellites” at forthcoming conferences (ideas welcome)

CONCLUSIONS
MAXIMIZING THE IMPACT
Value of ADNI to PHARMA

- **Industry is using ADNI methods and sites**
- **Many investigators will process and analyze ADNI data**
- **ADNI results may allow "use of prior information" in design and analysis of AD trials. Increasing statistical power**
- **Facilitates FDA recognition of biomarkers**
  - **Aids approval process**

MAXIMIZING IMPACT OF ADNI

- **ADNI will facilitate development of disease modifying therapy for**
  - **Treatment of AD**
  - **Prevention of AD**