
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)
ADNI Industry Scientific Advisory Board

• Nearly $25 million has been raised by the Foundation for NIH from 17 organizations (15 companies and 2 non-profits)

• Newest members of the Industry Scientific Advisory Board:
  – Johnson & Johnson
  – Schering-Plough
  – Synarc
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
  – Multisite 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

0-6m Rates against 6-12m Rates by patient

Acceleration:
34.3 ± 4.6 mm³/year²
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

- **(1) $V_0$** = 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**

<table>
<thead>
<tr>
<th>Measures</th>
<th>NORMAL</th>
<th>MCI</th>
<th>AD</th>
<th>$P^{(2)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_0^{(1)}$ (mm$^3$)</td>
<td>2017 ± 205</td>
<td>1811 ± 77</td>
<td>1654 ± 69</td>
<td>n.s.</td>
</tr>
<tr>
<td>Rate (mm$^3$/year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apoe4 Carrier</td>
<td>-56.7 ± 13.3</td>
<td>-54.1 ± 11.6</td>
<td>-104.8 ± 13.3$^{(3)}$</td>
<td>0.03</td>
</tr>
<tr>
<td>Non Carrier</td>
<td>-27.6 ± 12.9</td>
<td>-41.2 ± 12.8</td>
<td>-62.6 ± 17.6</td>
<td></td>
</tr>
</tbody>
</table>
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
Alzheimer’s Disease
80 year old male
MMSE 26

Healthy Elderly Control
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
• 3 T MRI: possibly functional MRI
• More biomarkers, species of abeta, proteomics
• Welcome suggestions
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