Alzheimer’s Disease Neuroimaging Initiative 3 (ADNI 3)

Michael W. Weiner
ADNI3 WILL (Probably) BE FUNDED
The “Problem” will be retention of ADNI 2 subjects
And recruitment of new subjects!
ACCOMPLISHMENTS OF ADNI

• Validation of “amyloid phenotyping”
• Over 1022 publications from ADNI
• Data widely used for design of AD clinical trials
  – Growing trials, problem for ADNI recruitment
ONGOING TRIALS COMPETING FOR SUBJECTS

- List provided by PPSB members
- This is not a thorough review of clinicaltrials.gov
- At least 14 major trials: CN, MCI, AD
**Prodromal TRIALS in 2016**
*(from Mike Egan)*

<table>
<thead>
<tr>
<th>Sponsor</th>
<th>Mode of Action/Drug</th>
<th>Phase</th>
<th>Status</th>
<th>Study Start-Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck</td>
<td>BACE Inhibitor MK-8931</td>
<td>Phase III</td>
<td>Recruiting (N=1,500)</td>
<td>Nov 2013- July 2019</td>
</tr>
<tr>
<td>Eli Lilly AstraZeneca</td>
<td>BACE Inhibitor AZD3293</td>
<td>Phase II/III</td>
<td>Recruiting (N = 2,200)</td>
<td>Sep 2014 – Aug 2019</td>
</tr>
<tr>
<td>Eli Lilly AstraZeneca</td>
<td>BACE Inhibitor AZD3293</td>
<td>Phase III</td>
<td>planned (N = &gt;1,500)</td>
<td></td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>solanezumab LY2599666</td>
<td>Phase III</td>
<td>planned (N = &gt;1,000)</td>
<td>Mid 2016– 2020 (projected)</td>
</tr>
<tr>
<td>Biogen</td>
<td>Aducanumab (BIIB037)</td>
<td>Phase III</td>
<td>Recruiting (N = 1350)</td>
<td>Aug 2015 – Feb 2020</td>
</tr>
<tr>
<td>Biogen</td>
<td>Aducanumab (BIIB037)</td>
<td>Phase III</td>
<td>Recruiting (N = 1350)</td>
<td>Sep 2015 – Feb 2020</td>
</tr>
<tr>
<td>Biogen Eisai Inc.</td>
<td>BACE Inhibitor E2609</td>
<td>Phase II</td>
<td>Recruiting (N = 700)</td>
<td>Nov 2014 – Jan 2018</td>
</tr>
<tr>
<td>AZTherapies</td>
<td>ALZT-OP1</td>
<td>Phase III</td>
<td>Recruiting (N = 600)</td>
<td>Sept 2015-March 2018</td>
</tr>
</tbody>
</table>
MORE TRIALS

- Eisai: BAN2401 – antibody prodromal and mild AD
- Eisai E-2609 - BACE inhibitor Prodromal AD
- Roche: Crenezumab Prodromal/Mild AD
- Lilly A4, and Janssen A5 (Early) cognitively normal
- TRACK-PAD: CN and Prodromal
- COMPETITION IS GOING MAKE ADNI ENROLLMENT DIFFICULT
ADNI 3 STUDY DESIGN

- Roll over of ADNI 2 subjects
- Enrollment of new ADNI 3 subjects
- Brain Health Registry helps recruitment
- Annual visits
- All subjects have baseline visit
- Addition of “financial capacity” instrument
- Amyloid PET and LP alternate years
- Frequent Tau PET and MRIs
- On-line cognitive assessments
- Continue to collect autopsy material
## ADNI3: Schedule of Events

### Rollover and New Subjects

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>12 month</th>
<th>24 month</th>
<th>36 month</th>
<th>48 month</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CN</strong></td>
<td>CV, MRI, Tau, AMY, LP</td>
<td>Phone Check</td>
<td>CV, MRI, Tau (+/-), AMY, LP</td>
<td>CV, MRI, Tau (+/-) OR Phone Check</td>
<td>CV, MRI, Tau, AMY, LP</td>
</tr>
<tr>
<td><strong>MCI</strong></td>
<td>CV, MRI, Tau, AMY, LP, FDG</td>
<td>CV, MRI</td>
<td>CV, MRI, Tau (+/-), AMY, LP</td>
<td>CV, MRI, Tau (+/-)</td>
<td>CV, MRI, Tau, AMY, LP</td>
</tr>
<tr>
<td><strong>AD</strong></td>
<td>CV, MRI, Tau, AMY, LP, FDG</td>
<td>CV, MRI, Tau</td>
<td>CV, MRI, Tau, AMY, LP</td>
<td>Phone Check (Neuropath only)</td>
<td>Phone Check (Neuropath only)</td>
</tr>
</tbody>
</table>

Rollovers continue with Florbetapir; New enrollees have Florbetaben Tau scans for CN and MCI depend on amyloid status and randomization:

- All CN, MCI, and AD have tau PET at beginning and end.
- 80% of amyloid+ CN and MCI have frequent tau scans.
- 80% of amyloid – CN and MCI only have Tau PET at beginning/end.

Randomization used, to avoid revealing amyloid status.
HIGHLIGHTS OF CORES

- CLINICAL: ATRI, BHR, Financial cap, Cogstate
- MRI: Connectome protocol
- PET: Tau, Amyloid (2 tracers), FDG
- BIOMARKER: Roche platform
- GENETICS: Systems Biology
- PATHOLOGY: Continued need for autopsies
- BIOSTAT: Clinical trial design
- INFORMATICS: User friendly access
THE BIG PROBLEMS

• Overall, the problem is recruitment/retention
• Importance of continuing ADNI2 rollovers
  – Past problem of high dropout rate ADNI1/2
  – Please encourage subjects to continue in ADNI
• Difficulty in enrolling new subjects
  – High subject burden
  – Competing clinical trials
• We are very welcome of suggestions