Alzheimer's Disease Neuroimaging Initiative 3 (ADNI 3)

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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)

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

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

	Baseline	12 month	24 month	36 month	48 month
CN	CV, MRI, Tau, AMY, LP	Phone Check	CV, MRI, Tau (+/-), AMY, LP	CV, MRI, Tau (+/-) OR Phone Check	CV, MRI, Tau, AMY, LP
MCI	CV, MRI, Tau, AMY, LP, FDG	CV, MRI	CV, MRI, Tau (+/-), AMY, LP	CV, MRI, Tau (+/-)	CV, MRI, Tau, AMY, LP
AD	CV, MRI, Tau, AMY, LP, FDG	CV, MRI, Tau	CV, MRI, Tau, AMY, LP	Phone Check (Neuropath only)	Phone Check (Neuropath only)

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