World Wide Alzheimer's Disease Neuroimaging Initiative
Teleconference Minutes
November 13 / 14
10:00 am Eastern/ 9:00 am Central/ 7:00 am Pacific

Attendees:

Ricardo Allegri	Heidi Jurgens
Sandra Black	Simon Lovestone
Neil Buckholtz	Richard Margolin
Giovanni Frisoni	Jose Luis Molinuevo
Jim Hendrix	Nina Silverberg
Takeshi Iwatsubo	Yoshi Tojo
Gustavo Jimenez-Maggiora	Mike Weiner

I. **Roll Call and Welcome** Jim Hendrix welcomed the group to the meeting and reviewed the agenda.

II. Progress Updates

a) NA-ADNI - Michael Weiner
Mike noted that significant updates to NA-ADNI were presented at AAIC in July (WW-ADNI Summary Notes from AAIC are available on the website).

Since AAIC there have been 2 main areas of progress: the legal issues around Paul Aisen's move from UCSD to USC and the submission of the ADNI-3 grant proposal.

The Clinical Core UCSD to USC Transition
ADNI has committed to working with Paul Aisen's group at USC since they are in the strongest position to provide the work needed for the remainder of ADNI2 and ADNI3 (if funded). The transition from UCSD to USC has not affected the functionality of ADNI but it has been a complicated and time-consuming process dealing with the legal and IP issues. UCSD recently released the materials/documentation that Paul's team left behind and have also agreed to move the ADNI website from UCSD to USC. UCSD is claiming ownership of the electronic data capture system (which functions as the "backbone" of data management for ADNI and other studies) even though it was created by Paul's team and paid for by ADNI. This issue is part of the on-going lawsuit. In the meantime, Paul's group has developed a new data capture system that will be used in ADNI3.

ADNI-3 Update
The ADNI-3 grant application has been submitted and NIH will be reviewed in Jan-Mar 2016. They are optimistic that it will get funded and start in August 2016. Mike shared that they are moving forward as if it will be funded: writing new protocols, submitting the IND for AV1451, updating consent, etc. so that everything will be in place and ready by August 2016.

There has been resolution to the technical issues regarding selection of the Tau PET ligand and the platform for CSF analysis. ADNI-3 will initially use the Avid/Lilly AV-1451 ligand. Lilly has agreed to make the tracer available for free while ADNI will need to pay for the distribution and the PET scans. There was some industry concern that Avid is making it difficult for other companies to get the ligand and are charging high prices to competitors for access. The ADNI3 team studied the issue carefully and it is clear that 1451 is the best Tau tracer currently available. However, as new tracers become available, they could be added to the ADNI3 study.

The selection of a platform for CSF analysis was taken on by the ADNI Private Partner Scientific Board (PPSB). The Biomarkers Core, led by Kaj Blennow, Les Shaw and John Tojanowski, evaluated new platforms but the PPSB organized a due diligence team led by Johan Luthman to evaluate all the options fairly. The cobas Elecsys assay system from Roche Diagnostics was selected. The system is fully automated with a very high throughput and very low variability. The ADNI leadership is considering re-running all available ADNI CSF samples in this system for consistency. A budget estimate for this project is in progress. It is proposed that all the samples would be run at once which will save time and reduce variance.

b) Canada ADNI – Sandra Black

Medical Imaging Trials NEtwork of Canada (MITNEC) C6 Project Group

Sandra provided an update on the MITNEC progress. This study aims to better understand the additive/interactive relationships of common pathologies (small vessel disease, periventricular white matter hyperintensities) and amyloid deposition, cognitive decline and dementia. Patients are being recruited from stoke prevention and memory clinics and ADNI subjects (NC, MCI and AD) will serve as control groups. There are recruitment sites in most major cities in Canada. Most of the sites are initiated and actively recruiting. The goal is to recruit 100 (of 150 total) participants by March 2016. Two Health Canada approved sites are now producing the florbetapir ligand – this is a significant because the lack of production sites had delayed the study.

Ontario Brain Institute: Ontario Neurodegenerative Research Initiative (ONDRI)

The ONDRI is a 3 year observational study of multiple neurodegenerative diseases across Ontario. The study will recruit 600 subjects with AD/MCI (150), ALS (90), FTD (60) PD (150), and VCI (150). The participants will undergo neuropsychological assessments, gait and ocular assessments, genomics and neuroimaging at baseline and every year with a telephone assessment every 6 month.

Canadian Consortium for Neurodegeneration in Aging (CCNA)

The CCNA is an ambitious project that plans to recruit 1600 participants for a 3-year study that will look at wide variety of issues in 3 main themes of prevention, treatment and quality of life.

c) European ADNI - Giovanni Frisoni

Giovanni provided on update on the progress of PharmaCog WP5/E-ADNI. There are clinical sites in France, Italy, Spain, Greece, Germany and Netherlands.

Enrollment and follow-ups (baseline to 36 months) are going well and exceeding the minimum patients expected.

Baseline levels of AB42 (CSF ELISA) were initially going to be used to stratify the MCI patients into positive, intermediate and negative groups. Looking at AB42 alone was not sufficient to identify meaningful patient populations, but when looking at AB42/p-Tau ratio a tri-model distribution emerges.

When looking at changes in global cognition (ADAS-Cog) and hippocampal volume at the 12-month time point, the AB42/p-Tau ratio was superior in stratifying the MCI patients classified at baseline as positive, intermediate or negative based upon identified cutoffs.

Giovanni shared a list of recent and submitted publications; there is also a series of papers in preparation that will be a special issue in a peer-reviewed journal. The theme is "The IMI PharmaCog WP5/European ADNI study: status and progression of prodromal AD as revealed by a matrix of clinical, neuropsychological, and biological markers" -- there will be 22 papers in total broken down by introduction, cross-sectional and longitudinal studies.

d) EPAD – Simon Lovestone

EPAD is a public-private consortium which aims to develop the infrastructure to quickly and efficiently enable proof of concept trials for the development of treatments for the prevention of AD and dementia. The EPAD "funnel" aims to accelerate patient access and trial enrollment by creating an EPAD Registry from Parent Cohorts. The EPAD Registry will then feed into the EPAD Cohort which is the readiness cohort for the EPAD PoC Trial.

Simon provided an update on EPAD progress. Selection of research participants and engagement with parent cohorts is ongoing. Participants in the EPAD Registry will go into the EPAD Longitudinal Cohort Study (LCS) which is the gateway into the EPAD Project for research participants. The LCS population must be fit for purpose and this is done by looking for data that defines the most suitable participants from the parent cohorts.

The EPAD LPS protocol is ADNI-like and includes cognitive assessments at 6 and 12 months, EPAD Neuropsychological Evaluation (ENE), neuroimaging, CSF and other biofluid samples for genomics and biomarkers and clinical/other risk factors. The ENE now includes new cognitive tests some of which are exploratory and/or digital. Neuroimaging includes structural and functional MRI, PET amyloid imaging is to be confirmed in IMI2.

They expect the first research participants to be recruited into EPAD LCS in April 2016 and then will quickly scale up from there as they already have participants pre-identified.

e) **Argentina ADNI** - Ricardo Allegri
Ricardo provided an update on Arg-ADNI; they are nearing the end of evaluation of the 30 month time point and have retained 51 of the 60 subjects initially enrolled. They are also planning the evaluation of the 48 month time point which will begin in April 2016 and will include complete assessments: clinical/cognitive, blood, CSF, MRI, FDG-PET, amyloid PET and newly added Tau PET with AV1451.

f) **Japanese ADNI -** Takeshi Iwatsubo
Takeshi provided an update on the progress of J-ADNI1 which includes data from 537 subjects and over 3000 clinical/cognitive records, ~2500 MRI scans, ~1500 FDG-PET scans, ~600 PiB scans and 330 CSF samples. The false allegations have been cleared up and the database publication is being prepared. The plan is to release all data in January 2016 via the NBDS database for sharing worldwide.

J-ADNI2 which focuses on preclinical AD (150 preclinical AD, 100 early MCI, 100 late MCI) is being halted and re-started as "AMED preclinical AD study" as of November 2015. The budget for AMED preclinical (J-ADNI2) is ~$2M USD total public funding from AMED/MHLW which is only ~40% of that required. The J-ISAB/PPSB budget is currently frozen. There continues to be broad support from all stakeholders for the study in Japan and future data sharing.

The establishment of an A4 site at the University of Tokyo is currently under discussion with Dr. Sperling, ATRI and Lilly.

g) **Other ADNI Efforts – (Korea and China)**
Representatives from Korea ADNI and China ADNI were not able to join the call, but they sent along brief updates which Jim shared with the group.

Korea-ADNI (K-ADNI):
After delays in setting up the infrastructure and subject recruitment, registration has begun. There are still some issues with image transfer and logistics that are being worked out. 10+ sites are undergoing "site feasibility check-ups" to be included in the clinical site pool – this expansion should expedite the recruitment process for baseline subjects.

China ADNI:
Since AAIC in July 2015 there has been the addition of one more site bringing the total to 11 sites in 7 cities. The number of subjects recruited and maintained continues to grow and is now up to 102 total. The C-ADNI National Meeting was held in Beijing in October 2015 and several topics where discussed including standardization of trial recruitment/exclusion criteria, encouragement for site were recruitment is strong, possible treatment scheme for Chinese Traditional Medicine trials for late stage of ADNI and a large scale epidemiology study about prevention/risk factors for AD in China. The supply for amyloid tracer has been resolved and the PET Core will start amyloid PET imaging.

III. New Business – All

There was discussion and interest in finding ways to increase outreach and engagement of the global community (AD field, science community, public) to inform in more “real-time” the efforts, progress and outcomes of WW-ADNI. This would not be data sharing per se but more information on updates, differences in protocols, new progress, awareness initiatives, etc. that could be shared at different levels depending on the audience (e.g., WW-ADNI, GAP family, others). One important factor is the need for increased participation in clinical trials and the PR effort needed to help accomplish this.

Jim put forward that a sub-committee could be formed to begin clarifying the aims and goals of this effort; others who are interested can join organically and the plan will be to have something to share with the larger WW-ADNI membership at AAIC 2016 in Toronto.

Jim also noted that instead of a full day of WW-ADNI at AAIC 2016, there are plans to have a half-day devoted to WW-ADNI and a half-day devoted to the PAD’s (i.e. Europe, Trk (US), Canada, Japan) for the Toronto meeting.

The next meeting will be scheduled for the spring of 2016.