

Questions and Answers from ADAD Family Webinar on 11/22/15

Tau and Tau scanning

Q. What is Tau?

A. Tau is a protein that is found in the nerve cells and stabilizes the structure within the nerve cells that the cells need to divide, carry substances and use for support. If this protein becomes abnormal, it will form twisted fibers (tangles) inside of the nerve cells and destroy them.

Q. What is Tau imaging?

A. Tau imaging is a fairly new form of PET imaging that identifies abnormal tau tangles in the brain. We are able to have scans from cognitively normal to advanced stages of Alzheimer's disease. When cognition is normal, there is little Tau present, and when there are symptoms, we can see more tangles. It is well established that increased symptoms correlate with increased Tau seen with the PET imaging. But we are still trying to identify the earliest time that TAU scans can detect abnormal Tau levels.

Some centers have begun Tau imaging. We are hoping for 2 to 3 scans per person.

Q. Do we know any more about the relationship between Tau and beta Amyloid?

A. This has been studied extensively. There are molecular mechanisms that we know about but we do not know the direct link between Tau and beta amyloid. We think that amyloid changes occur before abnormal tau but the order of events is unclear. Tau PET will definitely help in this understanding as well as how tau levels change over time. Understanding is crucial to developing drug therapies and families have helped in this research.

Q. Is Tau scanning more accurate than beta Amyloid scanning?

A. It shows something completely different from beta Amyloid scanning but we think it is about as accurate in detecting abnormal tau as the amyloid PET scans.

Q. Why is a Lumbar Puncture still vital if we have added a Tau Scan?

A. This is a critical question, as CSF (cerebral spinal fluid) offers key information. The CSF fluid has led to the discovery of the amount of soluble Tau that increases just prior to the age of onset but appears to be decreasing shortly after. We do not know why this is happening. A second key importance of the CSF is in that the DIAN study, Tau increases when Amyloid beta plaques are present. CSF may hold the key to soluble Tau and the amyloid relationship. Once collected, we can use this in the future when new ways to analyze CSF are created not just for amyloid and tau. The CSF is a fantastic contribution. Please still continue to contribute. We share aliquots to look for new biomarkers all over the world. This is such an important part of our research.

New study procedures in DIAN observational study

Q. Obtaining skin samples were mentioned, when will they start?

A. Currently skin biopsies are happening at some DIAN sites and most DIAN sites will be doing skin biopsies by 2016.

Extension of the DIAN-TU trial

Q. If we are in the DIAN-TU now, will we be in it for 4 years?

A. There is an updated amendment for the 4 year study and not all centers have finished their IRB submissions as of yet. What will happen is that some people will continue until all people have 4 years of being in the trial. This actually means that for some people that started first, say 18-24 months before the last person entered the trial, they would actually continue in the trial until the last person enrolled reaches 4 years. So, they would be in the trial for 5 ½ to 6 years. The alternate is to have everyone stop when they reach 4 years of being in the trial. The advantage of the former is that we will have more power in the trial to detect a treatment benefit and the disadvantage is that it is more of a time commitment for participants.

Q. Is there a plan for an open label extension?

A. Our work at this point indicates that the best opportunity to see if a treatment is working is to continue everyone in the study until the last person has reached 4 years on the treatment they were randomized to at the time they entered the trial. If the drug is successful, **there may be an open label extension where everyone is on active drug.** However, the final analysis will be performed after everyone enrolled has completed 4 years.

We continue to explore options for an open extension but at this time it is not likely to occur in the current trial.

Q. Dr. Bateman asked, "How do you feel about staying in the study for 4 years plus?"

A. Replies included: "I agree"; "I will do whatever is needed for the research, what's best for science"; "I will stay in the TU"; "I will stay in the study"; "I would like the participant to be given a choice"; "If I wasn't allowed to continue, I would be upset."

Q. What are the future drugs and how many are there?

A. We are working with our Pharma partners and hope to announce a new drug(s) in 2016.

We had tremendous success with DIAN-TU reaching enrollment. This was so important because ADAD is so rare, we estimate only around 10,000 have it. The biggest risk to the trials is the low number of participants. Our success has helped to encourage more participation. However, some potential participants could not get in on time. We hope another stage of enrollment will begin in 2016.

Q. What is the geographical diversity of DIAN-TU?

A. DIAN-TU is in the US, Canada, Europe and Australia. Sites in South America and Asia have recently joined the DIAN observational study and we expect they will join the DIAN-TU in the near future.

Outreach to family members

Q. Why is it important for general outreach and outreach to family members who are not yet participating?

A. The faster the enrollment in the trial, the faster the trial can be completed. This allows us to determine if a treatment is working faster.

Q. Has anyone sent letters or e-mails to reach out to family members?

A. Caller: "Yes, I have done that. I have sent letters to my family and to other families I have met with early-onset AD".

Q. Dr. Bateman, "What has anyone else done that reached out to their family?"

A. Caller: "I used my video from the Family Conference and posted it on Facebook. I received an amazing and supportive reaction from everyone. When I posted it on Facebook, It was viewed 9,000 times.

A. Caller, "I try and get the message out as much as I can. I give people Ellen's number or the registry web site link".

Q. What is a good way to reach out to family members?

A. Share the registry telephone number 1-844-342-6397 and the DIAN Expanded Registry website: www.dianexr.org

If you have a media item, we would like to post it on the registry website, if you do not mind sharing.

ADAD Family Conference

Q. Will there be another ADAD Family conference?

A. We are planning to have a family conference for ADAD at the AAIC (Alzheimer's Association International Conference) in Toronto, Canada, on Saturday, July 23, 2016. Currently, there are no funds. We hope to be able to fund the conference but want you to prepare. If you do not have a passport, you will need one to go to Canada. So please plan ahead. The DIAN-TU will not be able to pay or reimburse for the cost of a passport.

Q. For the fundraising, how much do we need?

A. Last year, the participant day was paid for by a donor and through support from the Alzheimer's Association. We expect the cost to be \$175,000.00 to \$200,000.00. If we could raise half of that, we feel we could get the whole meeting covered.

Q. For fundraising in the UK, can donations to DIAN be consider charitable gifts?

A. Non-profit organizations for fundraising are needed as a mechanism to handle the funds. We do not know of one at this time.

If there are any specific questions that you would like answered, please do not hesitate to contact us at 1-844-342-6397, dianexr@wustl.edu or by visiting www.dianexr.org.