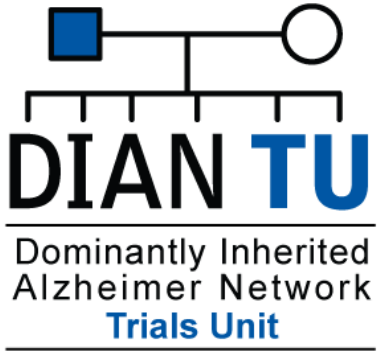

DIAN TU Treatment Trials
An Update
Sunday August 25, 2013

4:00 to 6:00 PM CDT

Presented by Randall Bateman MD

DIAN Trials Unit Director

DIAN Clinical Core Leader

Question and Answer Session

Agenda
DIAN-TU

DIAN TU
Dominantly Inherited Alzheimer Network
Trials Unit

Introductions

DIAN Therapeutic Trials

Questions and Answers

From DIAN participants

Inclusion/Exclusion Criteria

- 15 years before parental age of onset to 10 years after parental age of onset
- Participants include individuals without impairment or with possible very mild symptoms (memory loss), or mild dementia
- 18 years of age or older.

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Inclusion/Exclusion Criteria

- devices for birth control (IUD, etc.) and other implanted medical devices (defibrillators, etc.) may not be compatible with the MRI scans.
- This is a website about MRI scanning where you can check the compatibility of implanted devices with a MRI.

http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_mr

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Inclusion/Exclusion Criteria

- This is a web site that explains the details of PET scanning.

http://www.radiologyinfo.org/en/info.cfm?pg=pet

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Inclusion/Exclusion Criteria

- Stage of Disease
  - Normal
  - Mildly Symptomatic
- Mutation Status
  - Not required to be known
  - If you know you are negative you are not eligible.

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Genetic Counseling and Testing

- Enrolled Treatment Trial Study participants who indicate they wish to know their mutation status will be referred to a genetic counselor.

- The cost of the genetic counseling and testing will be paid for by the study. This service is provided by the study, and is optional. If you choose to have the genetic testing performed and the results indicate you are a carrier of an autosomal dominant mutation, we ask that you do not share these results with the study team. If the mutation result is negative you are not eligible for the DIAN-TU trial.

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Placebo

- Placebo contains no active medication but looks like and is administered the same as the active drug.
- FDA standard for clinical trials
- Intravenous or sub cutaneous injection of placebo.
- In this trial 75% of mutation carriers will receive active drug and 25% will receive placebo
- All mutation negative participants will receive placebo.

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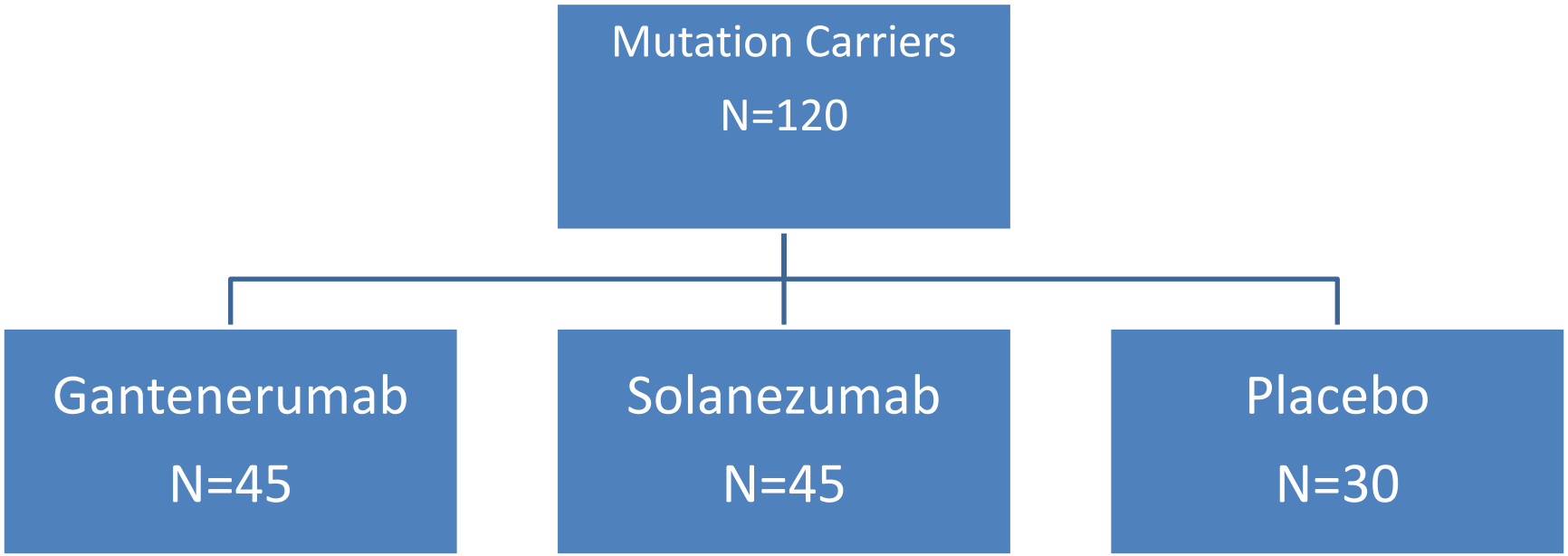
Randomization

Approximately 210 enrolled
to a goal of 120 mutation carriers



Study Drugs

Solanezumab and Gantenerumab

- Monoclonal antibodies that bind to beta-amyloid.
- Passive immunization.
- Modify early changes in the brain caused by beta-amyloid.

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Side Effects

- Solanezumab given by intravenous infusion for 30 minutes you are observed for 2 hours after to watch for side effects.

i. The trial Monitors for side effects and maintains dosing of the drug and safety visits.

ii. Rare side effects:
    - Increased Water Content of the Brain tissue
    - Small Bleeds in the Brain Tissue (micro-hemorrhage). These side effects are monitored by Brain MRIs every 3 months.

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Side Effects

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- Gantenerumab is given subcutaneously, just under the skin on the belly.

i. The trial Monitors for side effects and maintains dosing of the drug and safety visits.

ii. Rare side effects:
    - Increased Water Content of the Brain tissue
    - Small Bleeds in the Brain Tissue (micro-hemorrhage). These side effects are monitored by Brain MRIs every 3 months.

Study Visits

- At Home Screening Visit
- Initial Baseline Visit, screening and Complete Assessment
- Once a month at your home or near where you live for drug administration and check up
- Every 3 Month MRI near where you live
- Annual Visit at the DIAN-TU site for all tests

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Study Visits

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What happens / What you need to do	Study Visit Number													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Timing (weeks)		0	4	8	12	16	20	24	28	32	36	40	44	48
Your study doctor will check that you are suitable to take part in the study	X	X												
Your study doctor will ask questions about other medicines you are taking, about your Alzheimer's disease and your medical history	X	X	X	X	X	X	X	X	X		X	X		X
Your study doctor will perform a physical and/or neurological examination		X												
An ECG (recording of your heart activity) will be performed		X			X			X						
Your blood pressure, pulse rate, body temperature & breathing will be measured		X	X	X	X	X	X	X	X	X	X	X	X	X
Blood and/or urine samples will be collected	X	X	X		X			X						
Pregnancy Test	X	X	X	X	X	X	X	X	X	X	X	X	X	X
You will receive Study Drug on these days		X	X	X	X	X	X	X	X	X	X	X	X	X
You will stay on site for 2 hours after start of infusion		X	X											
A MRI brain scan will be performed		X												
Lumbar Puncture/PET Scans will be done		X												
Memory and Thinking Assessments will be done	X	X						X						
Study staff will ask you how you are feeling, and about any other medicines that you are taking		X	X	X	X	X	X	X	X	X	X	X	X	X
Study staff will ask you about your mood and risk for suicide	X	X			X			X			X			

Baseline Visit

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At the baseline visit, the screening process will determine eligibility, and biomarker studies assessed, including:

- **A screening EKG**
  - to look for any cardiac (heart) abnormalities.
- **MRI**
  - which looks at the structure of the brain.
- **Three PET scans**
  - scheduled over the entire visit. Each PET scan uses a small amount of a radioactive tracer to observe either the energy use of the brain or the presence of amyloid plaques.
- **A lumbar puncture**
  - for collection of cerebrospinal fluid.

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Baseline Visit continued:

- **A clinical evaluation with a study clinician**
  - to assess for changes in memory and thinking, judgment, personality and mood. The clinical exam will include a physical and neurologic exam.
- **Paper-pencil and computerized testing**
  - to assess your memory and thinking abilities.
- **Blood sampling**
  - to determine if there are certain markers in the blood (and if so how much) that might indicate the presence of disease.

Baseline Visit continued

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- **Blood sampling for genetic testing**.
  - Your blood will be sent to a study approved lab using a unique ID number to test for the reported family mutation. You will not receive the results of this testing. If, during your study participation, you wish to learn your mutation status, the study team will refer you to a certified genetic counselor.

Baseline Visit Schedule

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<table>
<tr><th>Day 1</th><th>Day 2</th><th>Day 3</th><th>Day 4</th></tr>
<tr><td></td><td></td><td rowspan="2">7:00
Fasting and CSF, blood collection (2.5 hours)
*Late Breakfast by 8:00 (To begin fasting after breakfast.)
9:30 AV 45</td><td rowspan="5">Departure home.</td></tr>
<tr><td>07:30
Informed consent discussion
1 hours
Urine pregnancy test if indicated</td><td>08:00 Cognitive assessment Psychometrics
(2.5 hours)
10:00 begin fasting</td></tr>
<tr><td>09:00 MRI 30 minutes</td><td>10:30 Sign drug specific ICF</td></tr>
<tr><td>11:15 Lunch</td><td rowspan="2">1:00 PET PIB
(1 hour)</td><td>1:00
Lunch
1:30 Blood samples and Drug Administration</td></tr>
<tr><td>12:00 Clinical Assessment
(2 – 3 Hours)</td><td>2:00-4:00
Study Drug observation</td></tr>
<tr><td></td><td>2:30 PET FDG
(1 hours)</td><td></td></tr>
</table>

FAQs

- **Weekend Treatments?**

  Yes, weekend and evening treatments are possible.

- **How long is the Trial?**

  The first part of the trial is two years. Depending on the success of the drugs it may last longer.

- **Do you keep taking your regular medication?**

  Yes.

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FAQs

- **When will trials begin?**

  The Washington University site began recruitment December of 2012.

- **Do I participate at my DIAN Site?**

  Yes, preferably.

- **Can participants taking medications for memory impairment (Namenda®, Aricept®, Razadyne®, Excelon®) remain on their medications during trial participation?**

  Yes, but we ask that the dose stays the same. You would discuss this with the study nurse.

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FAQ's

- **Who decides whether participants get the active drug or placebo?**

  A computer system randomly assigns participants to active drug or placebo. The assignment to drug or placebo is "blinded" which means neither the participant nor any member of the study team will know whether the individual is receiving the study medication or placebo. All mutation negative participants will be assigned to placebo for safety purposes and so that mutation status is not revealed to the participant or the study team.

FAQ's

- **If you have side effects from a drug, does mean that you are mutation positive?**

  No. Even people on placebo may have side-effects. A side effect is likely to be mild and may not be different from everyday type discomforts such as headache, fatigue and nausea. All side effects that you experience will be documented.

  The trial will evaluate the biomarkers for changes to determine if there is a response to the study medication.

FAQ's

Continued..

The trial will evaluate the biomarkers for changes to determine if there is a response to the study medication.

The study staff will do everything possible to keep study staff, and you blinded as to your mutation status, but it is possible that participation in the study could result in your leaning your mutation status. For example if you have a side-effect that is associated with the active drug.

DIAN EXPANDED REGISTRY

- SOURCE OF INFORMATION
  - IN THE NEWS
- FREQUENTLY ASKED QUESTIONS
- POSTS OF PAST WEBINARS
- REGISTER FOR DIAN TU
  - www.dianxr.org
  - 1-800-747-2979

FAQ's

- *You are encouraged to contact the DIAN Expanded Registry nurse coordinator at:* www.DIANXR.org or 1-800-747-2979 *to discuss questions related to your participation.*
- *You can find more information on the DIAN TU trial at:* http://clinicaltrials.gov/ct2/show/NCT01760005 . *The trials are beginning at various DIAN performance or partner sites.*

FAQ's

Information regarding approved DIAN trial sites will be available on each of the provided webpages. The DIAN-TU anticipates that there will be approximately 12 sites in the US with additional international sites in Canada, Europe, Australia and likely other countries.

This information has been posted on the www.DIANXR.org web page and has been sent to you via email.