DIAN TU
Dominantly Inherited Alzheimer Network
Trials Unit

ADAD Family Webinar
DIAN-TU Treatment Trial UPDATE
Sunday, November 22nd, 2015

4:00 - 6:00 PM CST / 10:00 PM – 12:00 AM GMT

Presented by Randall Bateman, MD

Charles F. and Joanne Knight Distinguished Professor of Neurology

Washington University in St. Louis, School of Medicine

Director, Dominantly Inherited Alzheimer's Network-Trials Unit (DIAN-TU)

DIAN
Dominantly Inherited Alzheimer Network

Knight ADRC
Alzheimer's Disease Research Center
WASHINGTON UNIVERSITY ST. LOUIS

Washington University in St. Louis
School of Medicine

Agenda

- ADAD Family Conference
- Study updates
  - DIAN Expanded Registry
  - DIAN Observational Study
  - DIAN-TU Trial
- Discussion

If you have a question during the webinar please go to the chat tab on the right hand side of your screen and type in your question or email it to: dianexr@wustl.edu

ADAD Family Conference

July 18th, 2015, Washington, D.C.

144 attendees

- 98 ADAD individuals and families (many DIAN and DIAN-TU participants)
- 18 Researchers
- 8 Pharma representatives
- 20 others (Alzheimer's Association representatives and donors, NIH, FDA, EMA, media, philanthropic and foundation representatives)

ADAD Family Conference

July 18th, 2015, Washington, D.C.

Conference evaluation results (65% completion rate)

- 95% thought the conference was "excellent"
- 99% found the information presented to be "very useful".
  - 100% were "extremely" and "quite satisfied" with legal/financial, genetic counseling (legal/financial and support sessions were ranked as most helpful)
  - 94% were "extremely" and "quite satisfied" with the research, pharma, regulatory presentations and discussions
- 100% were interested in attending a future ADAD Family Conference

"This was an intense conference. Very emotional and very informative. Great networking. Gives me hope that we are getting close to finding a cure."

- Conference participant

Website link to public presentations:

http://alzresearch.wustl.edu/dotnetprotect/diantu/2015-dc/

Username: **family** Password: **familyconference2015**

To request password for family presentations, please send request to: dianexr@wustl.edu

Next ADAD Family Conference

Tentatively planned for:
July 2016 AAIC, Toronto CANADA

- **Suggested agenda items** (from participants):
  - Research/regulator/pharma updates
  - Basic information on amyloid, biomarkers, etc.
  - Legal/financial information
  - Longer support sessions
  - More networking opportunities
  - Compassionate use/right to try experimental drug therapies
  - ***Please send suggestions to*** *dianexr@wustl.edu*
- **Fundraising efforts**

Join the DIAN Expanded Registry at www.dianexr.org to receive updates about the ADAD Family Conference and research announcements!!!

DIAN Expanded Registry (EXR)

www.dianexr.org

844-DIAN-EXR (844-342-6397)

- Registry of individuals and families with and at risk for autosomal dominant Alzheimer's disease (AD). Includes AD researchers, physicians and other professionals.
- Provides information on current and future research opportunities focused on autosomal dominant AD. Primary referral source for the DIAN-TU Trial.
- Additional benefits:
  - Source of information on autosomal dominant AD
  - Media coverage about DIAN
  - DIAN-TU Trial brochure and FAQ
  - Archived webinars
  - Exploratory Genetic Testing
- EXR staff contacts registrants to collect more information about their family's experience with Alzheimer's disease. All collected information is stored on a secured server at Washington University, School of Medicine, in accordance with privacy protection protocols.

DIAN-EXR Metrics

- **Total registrants: 1020**
  - Individual & Family Registrants: 866
  - 251 have a known ADAD mutation in family
  - Researchers & Professionals: 154
- **Number of individuals referred to Trial sites: 215***
  - 148 DIAN Obs participants who are also DIAN-EXR registrants
  - 67 DIAN-EXR registrants only

    **Note: individuals with or at risk for an approved ADAD mutation are referred to the trial, but may not be eligible per other trial criteria, e.g. cognitive (CDR) status, health issues*
- **Exploratory Genetic Testing**
  - 57 symptomatic individuals (probands) tested with 30 positive for ADAD
- **Site Expansion**
  - More than 40 sites actively being considered for DIAN-TU site with ADAD participants identified
  - More than 3500 potential participants

DIAN & DIAN-TU Eligible Participants - Site Expansion

Additional Participants identified who are eligible and highly interested in research studies

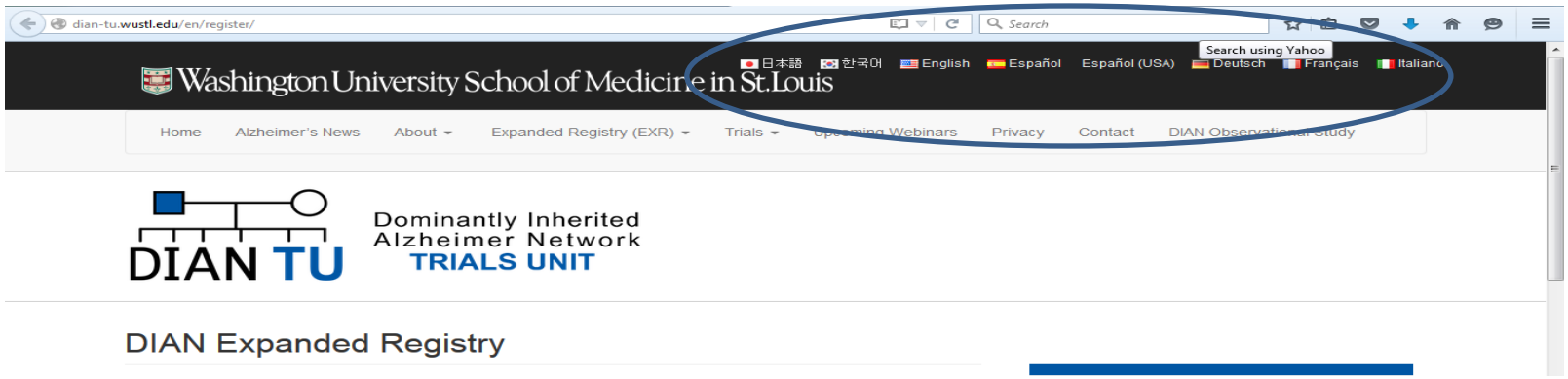
- More than 40 sites with ADAD patients identified
- More than 3500 potential participants

DIAN & DIAN-TU Site Expansion:
Additional Participants for Recruitment

DIAN & DIAN-TU	Country	Families	Subjects
Current Sites	Australia	24	67
	Argentina	6	39
	Canada	29	239
	Germany	12	49
	France	111	539
	Puerto Rico	76	1513
	Spain	16	36
	United Kingdom	7	12
	United States	99	232
Total		**380**	**2726**
Potential Expansion Sites	Bulgaria	12	28
	China	>100	>100
	Denmark/Sweden	13	58
	Germany	5	37
	Italy	80	373
	Netherlands	17	49
	Poland	1	9
	Russia	7	18
	Switzerland	2	6
	Korea	7	52
	Japan	19	52
	United States	96	150
Total		**359**	**932**
GRAND TOTAL		**739**	**3658**

DIAN Expanded Registry - Outreach

- Expand family pedigrees
- Engage non-participating family members
- Exploratory testing to find new, eligible families
- Town-hall meetings for sites/countries (e.g. Puerto Rico)
- Increased engagement with genetic counselors and genetic testing labs (Athena Diagnostics, Prevention Genetics, Fulgent Diagnostics)
- Informational videos to enhance website
- Website translation and better promotion of DIAN-EXR (sites, tweets, etc.)



Resources

Websites:

- DIAN Observational **http://www.dian-info.org**
- DIAN Expanded Registry **http://www.dianexr.org**
- DIAN-TU **http://www.dian-tu.org**

Contact Information:

- **DIAN-EXR email: dianexr@wustl.edu**
- DIAN Expanded Registry Coordinator: **844-DIAN-EXR (844-342-6397)**
- DIAN Global Coordinator: **314-286-2643**

Dominantly Inherited Alzheimer Network (DIAN) Observational Study*

The DIAN Obs. Study is a multi-center, international, observational, longitudinal study of individuals with or at risk for autosomal dominant AD.

- **Aims**:
  - Better understand the progression of biological, clinical and cognitive changes in Alzheimer's disease
    - Facilitate drug development
    - Inform on timing of treatment
  - **<u>Design and perform DIAN with future treatment trials, per NIH request</u>**
- The DIAN has currently enrolled more than **430 participants**

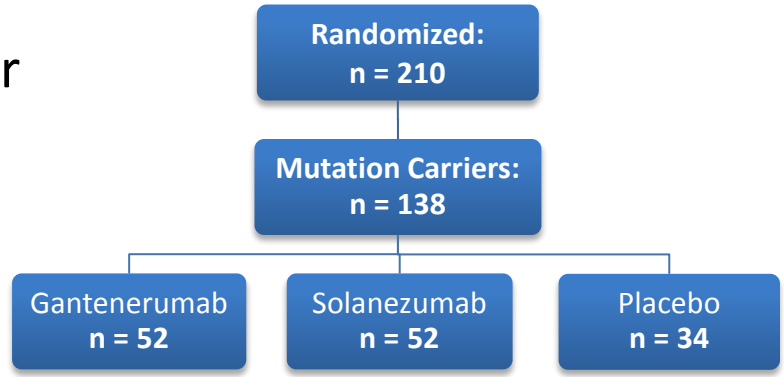
UF1 AG032438, RJ Bateman, PI; the German Center for Neurodegenerative Diseases (DZNE) completely supports German DIAN sites.

DIAN Obs. Study updates

- Enrollment will target participants younger than parental age at onset (AAO), emphasizing those **greater than 15 years younger than parental AAO**
- Change in visit frequency to in-person **assessments every other year**.
- Planned **modification of the computerized cognitive battery** to eliminate burdensome or duplicative measures and add a Cogstate-based test battery.
- Sub-studies:
  - Skin sample collection for fibroblast
  - **Tau imaging**

DIAN-TU-001 Trial

- Placebo controlled, **double-blinded**, cognitive outcome trial with biomarker interim analysis
- **3-arm trial:**
  - gantenerumab
  - solanezumab
  - pooled placebo (gant placebo + sola placebo)



- ~210* enrolled to reach 138 mutation carriers (52 per active drug arm, 34 pooled placebo) **Estimated 72 non-carriers (placebo)*
- Drug treatment duration = **4 years** (2 years for biomarker endpoint with an additional 2 years for cognitive endpoint)

DIAN-TU-001 Trial Status

- **First stage of enrollment reaching milestone in November 2015!**
  - 99% retention
  - ~100% completion of all assessments
- **DIAN-TU NexGen Grant** – submitted Oct 2nd (Feedback by March, 2016)
  - 2 new drugs
  - High dose
  - Home-based cognitive testing
  - More frequent analysis for earlier read-out

Discussion Points

1) What will happen after 4 years of treatment?
   - Continue until all participants have reached 4 years (active or placebo) or stop everyone at 4 years
   - Active transition/open label after 4 years

2) Importance of general outreach & outreach to family members who are not yet participating
   - Impacts getting a readout on the drug faster (the faster the enrollment, the faster the readout)

3) Recent question from a trial participant:
   - Why is an LP still vital if we've added a Tau scan?

4) Feedback regarding ADAD Family conference

If you would like to ask a question or comment go to the chat tab at the right hand side of your screen or email your question to dianexr@wustl.edu

THANK YOU!!!

QUESTIONS?

Participant perspective

If you have a question please go to the chat tab on the left hand side of your screen and type in your question or email it to: dianexr@wustl.edu

DIAN Observational Study

Principal Investigator
RJ Bateman

Coordinating Center Cores

Admin – RJ Bateman
Clinical – JC Morris
Biomarkers – AM Fagan
Biostatistics – C Xiong
Genetics – AM Goate
Imaging – T Benzinger
Informatics – D Marcus
Neuropathology – NJ Cairns

Performance Sites

United States: Washington Univ, Butler Hosp/Brown Univ • Columbia Univ • Indiana Univ • UCSD • U of Pittsburgh • Mayo Clinic-Jacksonville • MGH/BWH

Europe: Institute of Neurology-Univ College London • Ludwig-Maximilians-Universität München • University of Tübingen

Australia: Prince of Wales Medical Research Institutes-Sydney • Mental Health Research Institute-Melbourne • Edith Cowan Univ-Perth

DIAN-TU Administrative and Clinical Operations Team

Randall Bateman – Director and PI

Stephanie Belyew, Virginia Buckles, Matt Carril, David Clifford, Mary Downey-Jones, Cynthia Duggan, Kaisheng Fan, Kathy Fanning, Angela Fuqua, Ron Hawley, Amanda Houchin, Michelle Jorke, Denise Levitch, Jacki Mallmann, Tayona Mayhew, Eric McDade, Susan Mills, John Morris, Angela Oliver, Katrina Paumier, Anna Santacruz, Jessi Smith, Joy Snider, Annette Stiebel, Peter Wang, Glenn Wideman, Ellen Ziegemeier

DIAN-TU Cores

Administrative: Randall Bateman and team
Biomarkers: Anne Fagan and team
Biostatistics: Chengjie Xiong and team
Genetics: Alison Goate, Carlos Cruchaga and team
Imaging: Tammie Benzinger and team
Cognition: Jason Hassenstab and team
Informatics: Dan Marcus and team

We gratefully acknowledge the DIAN and DIAN-TU participants and family members, DIAN Team, DIAN Steering Committee, Knight ADRC, Alzheimer's Association, ADAD Forum, NIH U01AG042791, NIH R01AG046179, DIAN-TU Pharma Consortium, GHR, Anonymous Foundation, Pharma Partners (Eli Lilly, Hoffman-LaRoche, Avid Radiopharmaceuticals, CogState), and Regulatory Representatives.

DIAN-TU Collaborators

Project Arm Leaders: Steve Salloway, Martin Farlow, Martin Rossor
Consultants : Berry Consultants, Univ. of Rochester – Cornelia Kamp
DIAN-TU Therapy Evaluation Committee: Paul Aisen, Randall Bateman, Dave Clifford, David Cribbs, Bart De Strooper, Kelly Dineen, David Holtzman, Jeffrey Kelly, William Klunk, Cynthia Lemere, Eric McDade, Susan Mills, John Morris, James Myles, Laurie Ryan, Raymond Tait, Robert Vassar
DSMB Members: Gary Cutter, Steve Greenberg, Karl Kieburtz, Scott Kim, David Knopman, Allan Levey, Dave Clifford, Randall Bateman, Kristine Yaffe
ADCS: Ron Thomas and Paul Aisen
University of Michigan: Robert Koeppe
Mayo Clinic: Clifford Jack

DIAN-TU Trial Sites

United States

Columbia University, *Lawrence Honig*
University of Puerto Rico, *Ivonne Jiménez-Velázquez*
Indiana University, *Jared Brosch*
University of Pittsburgh, *Sarah Berman*
Washington University, *Joy Snider*
University of Alabama, *Erik Roberson*
Butler Hospital, *Ghulam Surti*
Emory University, *James Lah*
Yale University, *Christopher Van Dyck*
UCSD, *Doug Galasko*
University of Washington, Seattle, *Suman Jayadev*

Canada

McGill University, *Serge Gauthier*
UBC Hospital, *Robin Hsiung*
Sunnybrook Health Sci Centre, *Mario Masellis*

Italy *(activation pending)*

IRCCS Centro San Giovanni di Dio Fatebenefratelli, *Giovanni Frisoni*
Azienda Ospedaliera Universitaria Careggi, *Sandro Sorbi*

United Kingdom

The National Hospital for Neurology & Neurosurgery, *Catherine Mummery*

Australia

Neuroscience Research Australia, *William Brooks*
The McCusker Foundation, *Roger Clarnette*
Mental Health Research Institute, *Colin Masters*

France

Hopital Roger Salengro, *Florence Pasquier*
Hopital Neurologique Pierre Wertheimer, *Maité Formaglio*
CHU de Rouen, *Didier Hannequin*
CHU de Toulouse, *Jérémie Pariente*
Groupe Hospitalier Pitie, *Bruno Dubois*

Spain

Hospital Clinic I Provincial de Barcelona, *Raquel Sánchez Valle*

Be A Part of The Solution!

Dominantly Inherited Alzheimer's disease Drug Trials

- Does your family have a mutation on one of the three known genes that causes Alzheimer's Disease (AD)?

- OR –

- Does your family have 3 generations of AD that starts younger than 60 years of age?

We are registering this specific group of people for drug trials. You might qualify if:

1. **You are over 18 years old and have a parent with Dominantly Inherited AD.**
2. **You are interested in participating in a drug study to test a drug that may slow down or prevent memory loss.**

The drug is provided free of charge and all expenses will be paid.
Risks will be discussed as part of the informed consent process.

Register at www.dianexr.org
or 844-DIAN-EXR (342-6397)

DIAN
Dominantly Inherited Alzheimer Network