DIAN TU
Dominantly Inherited Alzheimer Network
Trials Unit

DIAD Family Webinar

Sunday, May 22nd, 2016

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

Presented by:

Randall Bateman, MD, Director, DIAN-TU and DIAN Observational Study

Eric McDade, DO Assistant Director, DIAN-TU

Jason Hassenstab, Ph.D. Leader, Cognition Core, 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

- 2016 DIAD Family Conference
- Updates
  - DIAN Expanded Registry
  - DIAN Observational Study
  - DIAN-TU Trial
  - NextGen grant/other funding
- Discussion
  - Home-based cognitive testing
  - Maximal dose
  - Primary prevention

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

2015 DIAD Family Conference

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

"You should be proud of what you have pulled off. I am stunned at what is being done in this area. It is cutting-edge, and it is the right thing to do"

Janet Woodcock

Director, Center for Drug Evaluation and Research (CDER)

US Food and Drug Administration (FDA)

Visit http://dian-tu.wustl.edu/en/home/ to view the DIAD 2015 Family Conference Highlights video

2016 DIAD Family Conference

Too Young To Forget

July 23rd, 2016 AAIC, Toronto CANADA

Agenda Overview

- Family Presentations
- AD Research Updates (DIAN, DIAN-TU, field)
- Advocacy and Public Policy
- Panel Discussion
  - Advocacy and Pharma
  - Drug Re-purposing for AD
- Non-pharmacological & Pharmacological Approaches and Modifiable Risk Factors
- Caregiving and Long-Term Care
- Legal and Financial Matters
- Ethical Issues in Risk Disclosure
- Support Sessions

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

2016 DIAD Family Conference Funding

- Alzheimer Association award, co-host with 5 years of funding

  Dr. Maria Carrillo "*It is our belief that regular DIAD family conferences will benefit not only the family participants but also the broader global research community, Alzheimer's advocacy and regulatory agencies and industry representatives seeking patient input*"
- Generous donation from Charles F. and Joanne Knight for attendee travel
- DIAD family fundraising: Contributions to-date **$1955** (ebay sales, paint parties, private donations)

Future Conference Funding

- **NIH Grant** submitted in April, 2016 for 4 years of funding (2017-2020)
- **Alzheimer Association award**, 5 years of funding (2016-2020)
- **Independent fundraising ideas**

  - ❑ ebay sales of specialty items
  - ❑ Fundraising parties
  - ❑ Game nights
  - ❑ Private donations
  - ❑ Film screenings
  - ❑ Auctions
  - ❑ Celebrity donors
  - ❑ Foundation awards opportunities
  - ❑ Corporate sponsorship, micro grants

- Interest in forming subcommittees for fundraising 2017 conference in London: Need to begin this year

Future DIAD Family Conferences

- 2017: ***DIAD and Sporadic AD***, London, England, July 15th, 2017
- 2018: ***Tools and Technologies***, Chicago, IL, July 22nd, 2018
- 2019: ***Genetics***, location and date TBD
- 2020: ***AD Prevention Trials***, location and date TBD

DIAN Expanded Registry (EXR)

www.dianexr.org

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

- Provides information on current and future research opportunities focused on dominantly inherited AD (DIAD).
- Primary referral source for the DIAN-TU Trial
- Two-way communication mechanism: Rapid outreach to families; vehicle for families to contact with questions
- Additional benefits:
  - Source of information on dominantly inherited AD
  - Media coverage about DIAN and DIAN-TU
  - Archived webinars
  - Exploratory Genetic Counseling and Testing (GCT) Program
  - Surveys to formally collect information from registrants on topics important to DIAN and to DIAN-TU trial design
    - New survey distributed in May to DIAD families: 48 completed to date

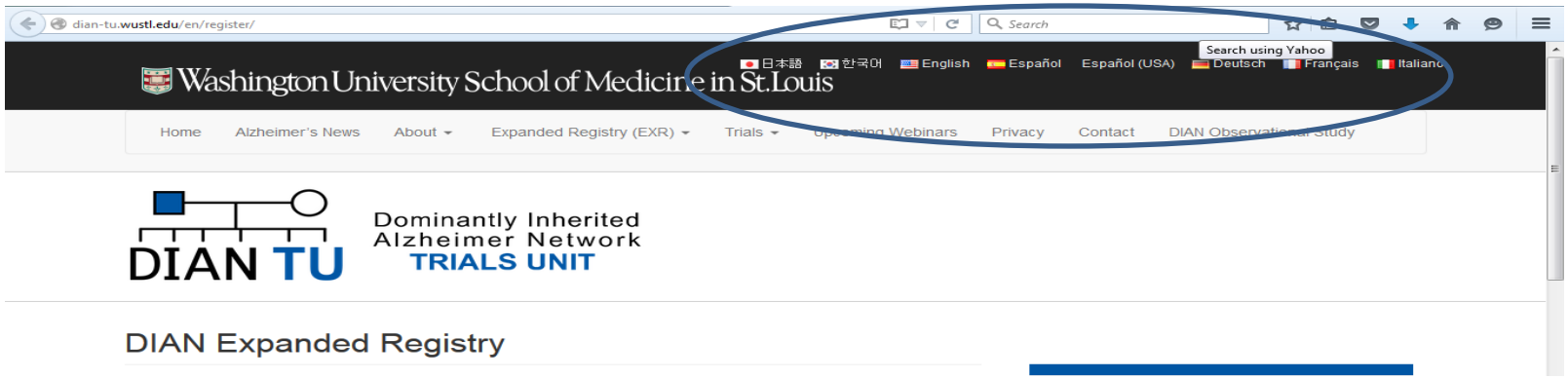
DIAN EXR Current Metrics

- **Total registrants: 1133**
  - Individual & Family Registrants: 964
  - 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**
  - 62 symptomatic individuals (probands) tested with 33 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 Expanded Registry – Outreach Goals

- 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.)



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**

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: **1-844-DIAN-EXR (1-844-342-6397)**
- 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.

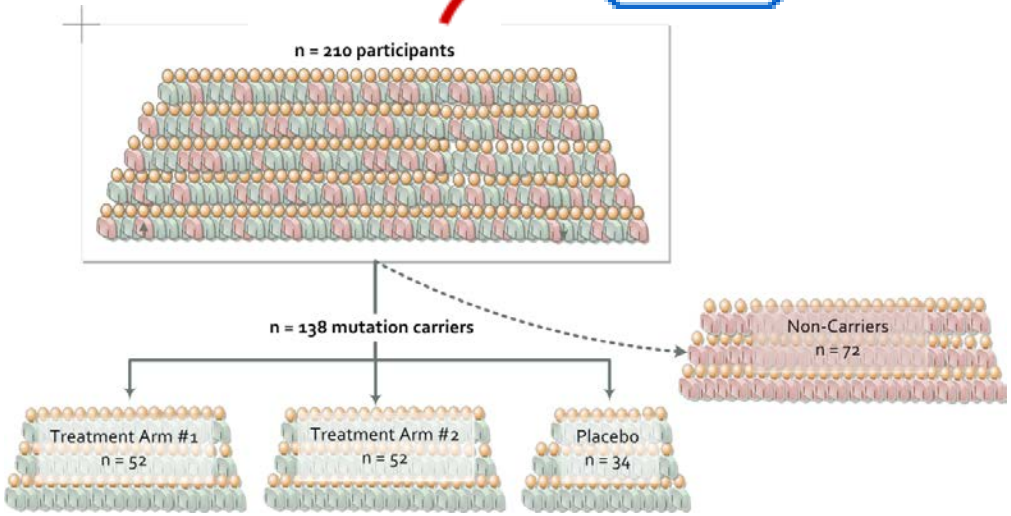
- The DIAN has currently enrolled more than **445 participants**
- 10 DIAN-related presentations at 2015 AAIC
- 20 journal publications in 2015

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

DIAN Obs Impact on DIAN-TU Therapeutic Trials

- **Trial development**: the participation of individuals and families in the DIAN Obs study has provided, and will continue to provide, crucial data used to design and develop DIAN-TU current and future trials.
- **Novel mutations**: continued participation in DIAN Obs is extremely important, especially in those cases where mutations found in families are not well known. Continued research on these mutations provides much-needed data as future trials commence.

DIAN-TU-001 Trial



- Placebo controlled, **double-blinded**, cognitive outcome trial with biomarker interim analysis

Three-arm trial:

Gantenerumab, Solanezumab, Pooled 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

- **Enrollment for first two drug arms complete**
- **DIAN-TU NexGen**
  - Alzheimer's Association funding received for start-up
  - NIA grant pending approval
  - Trial design
    - Maximal dose
    - Home-based cognitive testing
    - More frequent analysis for earlier read-out

Discussion Points

1. Home-based cognitive testing
2. Maximal dose
3. Primary Prevention

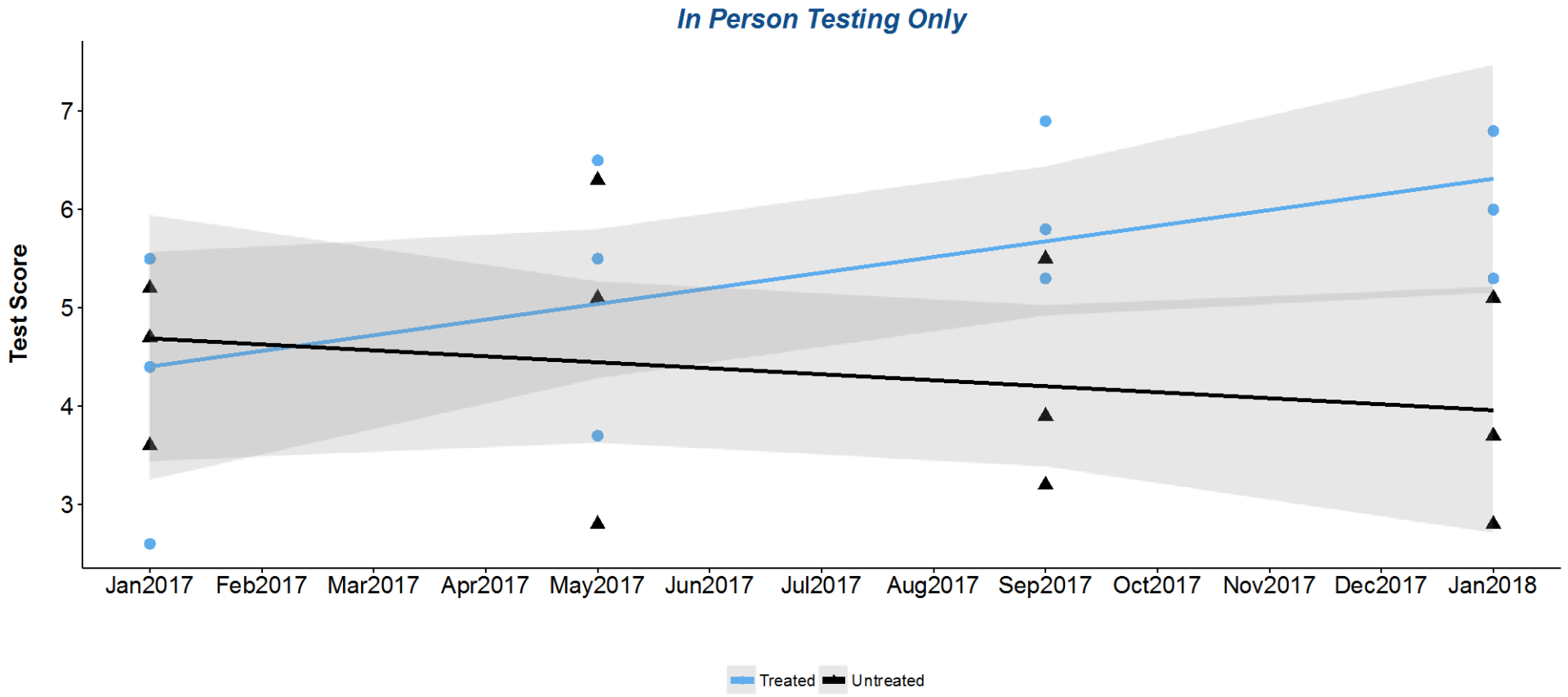
If you would like to ask a question or comment go to the chat tab at the right hand side of your screen or email your question to dianexr@wustl.edu

Home-Based Cognitive Testing

- Cognitive testing gives us good information, but there is a margin of error.
  - Test performance is impacted by fatigue, anxiety, boredom, minor illnesses, etc.
- More frequent cognitive testing is necessary.
  - Easier said than done!
    - Work Schedules/Costs/Inconvenience
    - But…we can come to you.
  - During the monthly visit from nurse, we will ask participants to complete 4 tests on the iPad.
    - tests will be familiar, same tests already completed at sites.
    - Requires about 12-15 minutes total.

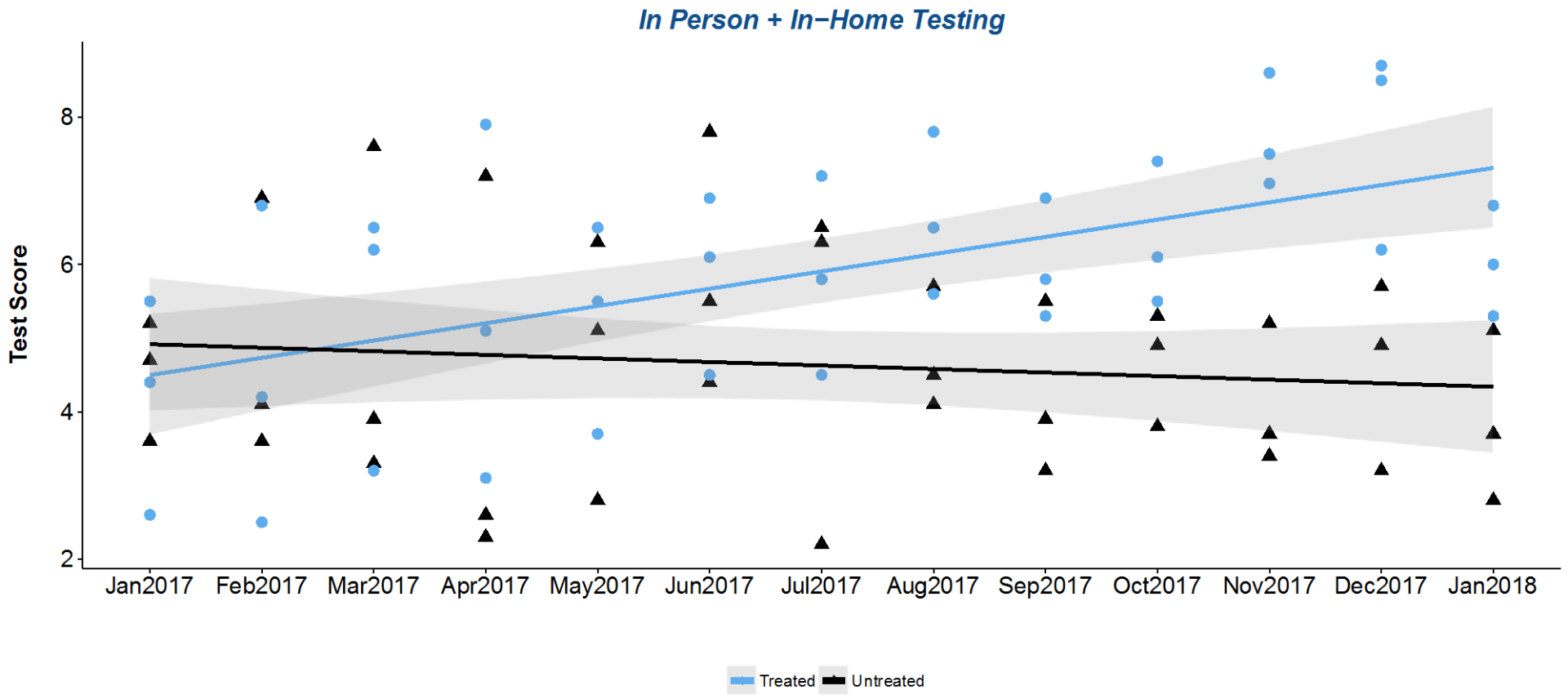
Home-based Cognitive Testing

- Why more testing? Consider a hypothetical example:
  - A “drug” that improves memory is administered to six participants, 3 receive the active drug, 3 receive placebo. Memory is tested 4 times in one year. Although there is likely a benefit, the margin of error is too great and the drug fails.



Home-based Cognitive Testing

- Why more testing? Consider a hypothetical example:
  - If we increase the frequency of testing, we have “power” to see an effect. The benefit of the drug is identical, but this time the drug is deemed successful and moves on towards becoming an approved treatment.



Maximal Dose

- What is maximal dose and why is it important?
- Safety concerns
- How is max dose determined?

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 • USC • U of Pittsburgh • Mayo Clinic-Jacksonville • MGH/BWH

South America: Fundación para la Lucha contra las Enfermedades Neurológicas de la Infancia (FLENI) Instituto de Investigaciones Neurológicas Raúl Correa

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

Asia: Osaka City Univeristy

DIAN-TU Administrative and Clinical Operations Team

Randall Bateman – Director and PI

Stephanie Belyew, Virginia Buckles, Matt Carril, David Clifford, Mary Downey-Jones, 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, Shannon Sweeney, Guoqiao Wang, Ellen Ziegemeier

DIAN-TU Cores

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

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DIAN-TU Collaborators

Project Arm Leaders: Steve Salloway, Martin Farlow, Martin Rossor
Consultants : Berry Consultants, Univ. of Rochester – Cornelia Kamp, Cardinal Health Regulatory Sciences, Granzer Regulatory Consulting
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*