

# DIAD Family Webinar

## Sunday, October 30, 2016

4:00 - 6:00 PM CST / 9:00 PM – 11:00 PM GMT

**Presented by:**

**Eric McDade, DO**

Director, DIAN Expanded Registry

Associate Director, DIAN-TU



# Agenda

- ❖ **Recap of 2016 DIAD Family Conferences in Toronto and Germany**
- ❖ **Plans for 2017 DIAD Family Conference in London**
- ❖ **Next Steps for the DIAN-TU**
- ❖ **What is “Clinically-Meaningful” in the DIAN-TU studies?**
- ❖ **Use of the DIAN Expanded Registry for surveys to research participants**

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](mailto:dianexr@wustl.edu)

# Recap of DIAD Family Conference

*Too Young To Forget*

July 23<sup>rd</sup>, 2016 AAIC, Toronto CANADA

## **Attendees: 222**

- 117 Family members from 8 countries (Argentina, Australia, Canada, England, Ireland, Scotland, United States and Wales)
- 75 Researchers/professionals
- 30 Alzheimer Association donors

## **Evaluation Results (n= 42 family member/friend)**

- Information useful: 71% extremely; 10% moderately
- Technicality of presentations: 79% appropriate
- Satisfaction with family presentations: 86% extremely
- Overall satisfaction with conference: 71% extremely
- Conference attendees: 52% were new attendees in 2016
- Plan to attend 2017 Conference in London: 88%

# Recap of DIAD Family Conference

*Too Young To Forget*

**July 23<sup>rd</sup>, 2016 AAIC, Toronto CANADA**

## **Evaluation Results continued (n= 42 family member/friend)**

Top 3 most helpful sessions:

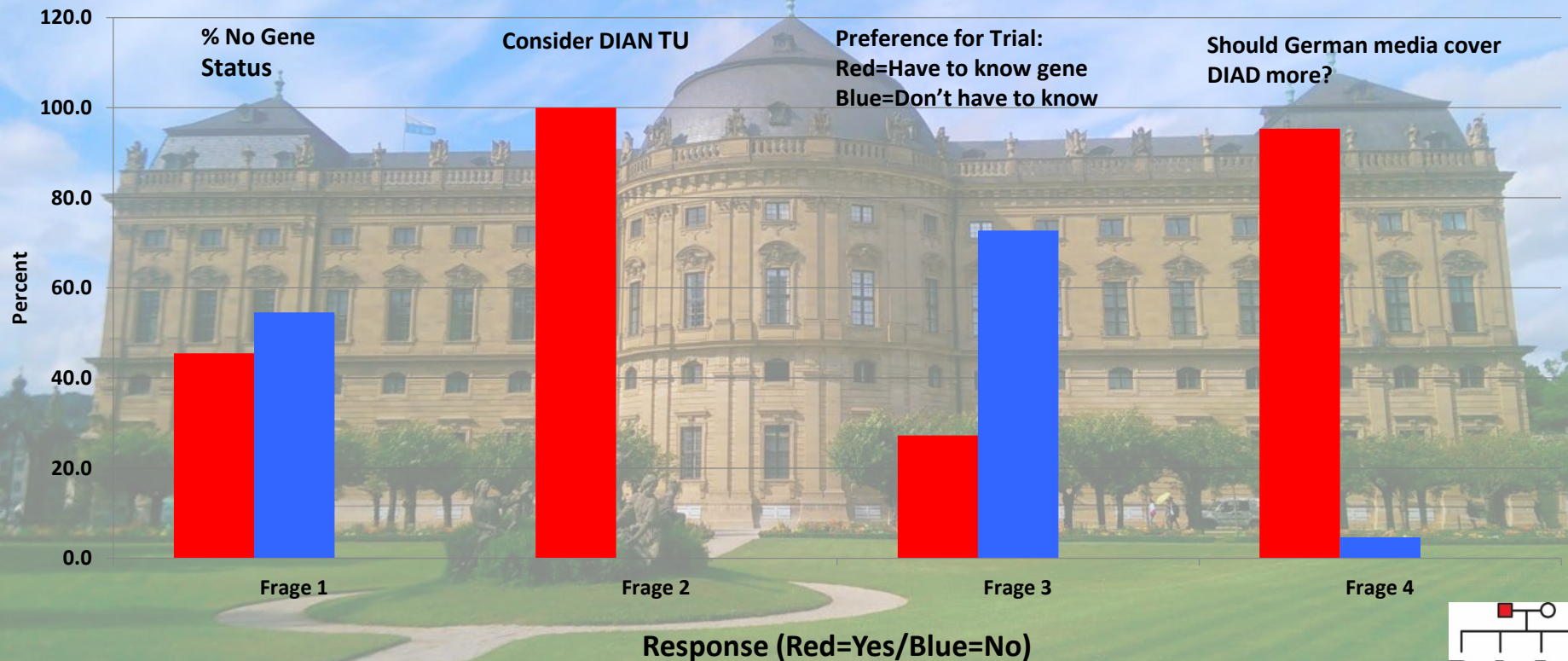
- 1) Drug development and approval (joint pharma presentation and drug re-purposing)
- 2) Emerging research (Non-pharmacological approaches)
- 3) Alzheimer's overview (State of AD research and DIAN/DIAN-TU updates)

Suggestions for future conferences:

- Panel discussion with family members about learning own genetic status
- More time for Questions/Answers sessions
- More time for one-on-one interactions with researchers
- How to talk to children and other family members about participation in research
- Break up the day into different segments to avoid “death by PowerPoint”

# German DIAD Family Meeting 2016

- ~20 Researchers and Professionals (BfArM, Roche, German Alz. Society, Media (Alzforum, Frankfurter Allgemeine Zeitung)
- >60 family members
- Survey Results (n=20)



# DIAD Family Conference Funding

- NIH Grant: 4 years of funding (2017-2020)

*“This meeting was deemed highly significant with potential to address future needs in the community and this application was met with a high level of enthusiasm.”*

- **Alzheimer’s Association: 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

**Discussion point:** Which strategy do you feel was most successful?

# 2017 DIAD Family Conference

## July 15<sup>th</sup> London, England

**Theme:** DIAD/Sporadic AD Comparison: the critical role of discoveries in DIAD for informing the rest of the field.

### Objectives:

1. Provide a forum for interactive dialogue about research, trial design, drug development and other concerns raised by basic and clinical researchers, DIAD families, regulatory agencies, pharmaceutical representatives and nonprofit organizations.
2. Unite DIAD scientists, encourage AD researcher development and summarize the state of research on DIAD
3. Inform and support families with and at risk of developing DIAD to encourage engagement

### Discussion Points:

- Travel expense coverage options
- Fundraising activities:
  - planning calls will start in November
  - Subcommittees

# Dominantly Inherited Alzheimer Network (DIAN) Observational Study\*

The DIAN 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**
- **Site expansion in Argentina, Japan and Korea**
- Over 20 DIAN-related presentations at 2016 AAIC
- 20 journal publications in 2015

*\*UF1 AG032438, RJ Bateman, PI; the German Center for Neurodegenerative Diseases (DZNE) completely supports German DIAN sites; Government Agency for Scientific Research from Argentina (Agencia- Mincyt - CONICET); Japan's Health and Labour Sciences Research Grant (Research and Development Project on Dementia); National Grants from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (since 2013)*



# DIAN related publications

- DIAN related publications significantly benefit the scientific and clinical field
- Critical to trial development
- It is possible that research findings could identify information that would imply genetic status (non-individual data)

# DIAN-TU-001 Trial Status

- **Current Drug Arms**

- Enrollment for first two drug arms complete
- Timing of biomarker interim analyses

- **DIAN-TU NexGen**

- Alzheimer's Association funding received for start-up
- NIA funding received for start-up (grant resubmission pending review)
- Potential enrollment starting early-mid 2017

# DIAN-TU Trial Data

Test Measure		Assessments per participant	Quantity	Compliance Rate
<b>Clinical Measures</b>	CDR, CDR-SB, MMSE, FAQ, GDS, NPIQ	5	≈1000	<b>100%</b>
<b>Cognitive Measures</b>	CogState, Pencil / Paper	5-10	≈ 1000-2000	<b>99%</b>
<b>Fluid Biomarkers</b>	Plasma, Serum, CSF	4	≈ 800	<b>99%</b>
<b>Imaging Biomarkers</b>	PiB, AV-45, FDG	4	≈ 800	<b>99%</b>

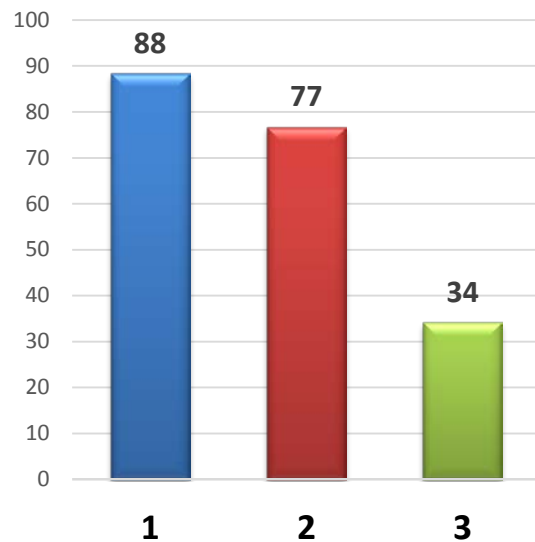
Imaging Modality / Tracer	Baseline	Year 1	Year 2	Year 4	Total # Scans
<b>AV-1451</b>	30	107	141	141	419

# How do we establish a clinically-meaningful result for all participants in the DIAN-TU studies?

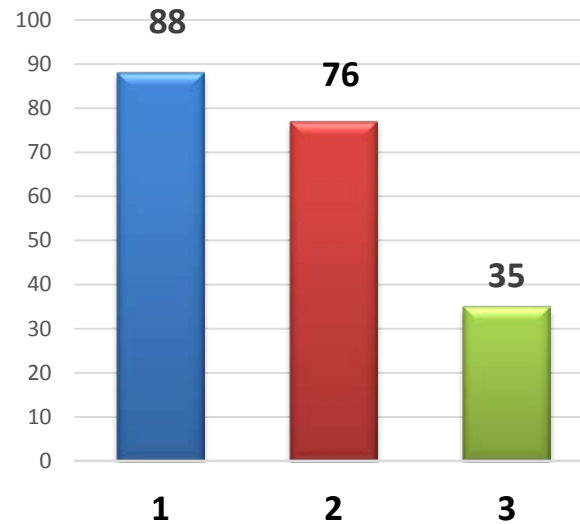
- What effect is meaningful when you don't have any symptoms of a disease
- How do you measure improvements?
- Many different ways to ask this
  - Surveys
  - New tests
    - In person tests
    - At home /computer based tests

# Response to questions of risk based on treatment delay in symptoms

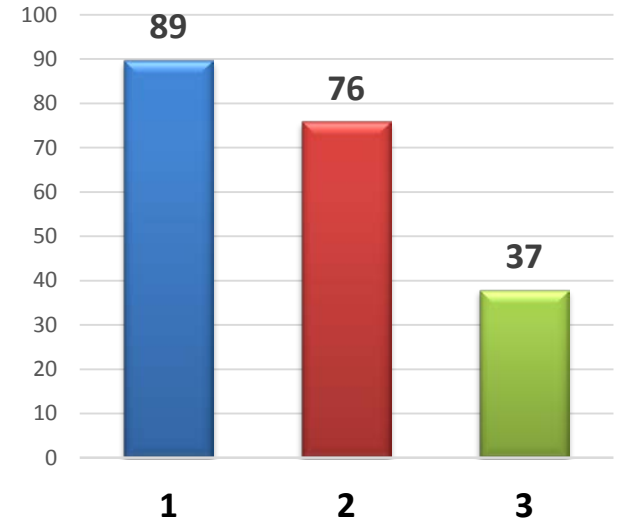
Percent willing to take medication for a 6 month delay in symptoms



Percent willing to take medication for a 1 year delay in symptoms



Percent willing to take medication for a 5 year delay in symptoms



# DIAN-TU Primary Prevention Trial

- Primary prevention vs. secondary Prevention
- Will require entering trial at an even earlier time than in the current trial
- May require longer duration in trial

# Preliminary survey responses relating to Primary Prevention

- > 90 % of respondents indicated that they would be willing to stay in a clinical trial for over 5 years
- Majority agreed that participants younger than 15 years before the anticipated age of onset should be included
- What do the callers think of children younger than 18 participating in research (NOT CLINICAL TRIALS)?

# DIAN Expanded Registry outreach efforts

- 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.)
- Surveys to participants
- Potential future computer or phone based cognitive testing



# Additional resources

## Websites:

- **JOIN** the DIAN Expanded Registry at [www.dianexr.org](http://www.dianexr.org)
- DIAN-TU [www.dian-tu.org](http://www.dian-tu.org)
- DIAN Observational [www.dian-info.org](http://www.dian-info.org)

## Contact Information:

- **DIAN EXR email:** [dianexr@wustl.edu](mailto:dianexr@wustl.edu)
- DIAN Expanded Registry Coordinator:  
**1-844-DIAN-EXR (1-844-342-6397)**
- DIAN Global Coordinator: (314) 747-1940

**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](mailto: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 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*

# DIAN-TU Administrative and Clinical Operations Team

*Randall Bateman – Director and PI, Eric McDade – Associate Director*

*Stephanie Belyew, Virginia Buckles, David Clifford, Mary Downey-Jones, Kathy Fanning, Amanda Fulbright, Angela Fuqua, Kurtis Hanks, Ron Hawley, Dottie Heller, Michelle Jorke, Denise Levitch, Jacki Mallmann, Tayona Mayhew, Susan Mills, John Morris, Katrina Paumier, Anna Santacruz, Jessi Smith, Annette Stiebel, Shannon Sweeney, Guoqiao Wang, Linda Watkins-Imhof, 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

*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

**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, Scott Kim, David Knopman, Allan Levey, Kristine Yaffe

**ADCS:** Ron Thomas and Paul Aisen

**University of Michigan:** Robert Koeppe

**Mayo Clinic:** Clifford Jack