A newsletter distributed by The Dominantly Inherited Alzheimer Network Expanded Registry (DIAN EXR), Washington University School of Medicine Department of Neurology



# DIAN EXR Newsletter

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#### Contact the Editor

If you have an idea for a story or have questions about the information in this newsletter, please contact the editor:

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### A New Era

On July 15, 2023, families from across Europe congregated for the 2023 European Regional DIAD Family Conference: A New Era. A total of 93 at-risk family members and caregivers from across 8 countries gathered with 96 researchers in Amsterdam, Netherlands. Presentations and panels discussed amyloidmodifying therapies, genetically targeted drug technologies, and DIAN-TU trial updates. After the formal presentations and a garden lunch, family members selected practical sessions focusing on a range of topics, including preserving brain health, caregiving, life planning with a positive genetic status, fertility, grief, and talking to children about DIAD.

In reflecting on the conference, family members shared that the experience helped remind them that they are not alone, and that together, their efforts in research participation and advocacy are working toward progress. Researchers in attendance shared the power in hearing families' stories, stating that such personal contact boosts professional motivation and also helps them to be better informed about the disease's impact on families. At family conferences, learning takes place in all directions, working to slow disease.



Pictured: the DIAN Expanded Registry administrative team (Brooke Kinsaul, Jamie Bartzel, and Ellen Ziegemeier) at the Rosarium in Amsterdam at the conclusion of the 2023 European Regional DIAD Family Conference

To access video footage from this conference, visit <u>https://dian.wustl.edu/for-</u> <u>families/family-conferences/2023-regional-</u> <u>diad-family-conference-a-new-era/</u>

### DIAN-TU at Alzheimer's Association International Conference

July of 2023 brought together a global community of Alzheimer's researchers, clinicians, and care providers in Amsterdam, Netherlands, for the annual <u>Alzheimer's</u> <u>Association International Conference (AAIC)</u>. Among the researchers convening was DIAN-TU Clinical Research Fellow Dr. Haiyan Liu (*pictured at right*), who co-chaired a session on novel fluid biomarkers and shared her work demonstrating involvement of ubiquitin modifiers and proteasome components in DIAD pathology.

Reflecting on her experience at AAIC, Dr. Liu shared, "The opportunity to present at AAIC allowed me to showcase our efforts to a wider audience and gather invaluable insights from respected colleagues in our domain. I was genuinely inspired by the range of research subjects and the depth of the conversations. This whole experience has further solidified my passion for our field and has given me renewed motivation to continue my work."



## Update on the DIAN-TU-001 Gantenerumab Open Label Extension

This announcement excerpt is regarding the Knight Family DIAN-TU Open Label Extension (OLE) Study with gantenerumab (made by Roche and Genentech) [<u>Clinicaltrials.gov #NCT01760005</u>]. Based on the results of the completed Roche Phase 3 GRADUATE studies of gantenerumab in sporadic AD in late 2022, it was decided to determine if dominantly inherited Alzheimer's disease (DIAD) participants in the DIAN-TU-001 OLE study were benefiting from gantenerumab high-dose treatment. The DIAN-TU and Roche performed an interim efficacy analysis of the DIAN-TU-001 OLE to:

- 1. determine if gantenerumab OLE treatment and/or long-term treatment results in clinical benefit and determine the extent of amyloid removal compared to the double-blind period.
- 2. determine the potential effects of gantenerumab on clinical and cognitive measures to support decisionmaking regarding next steps for the DIAN-TU-001 OLE.

The primary outcome did not show pre-specified threshold changes in outcomes between the gantenerumab treated and controls. One of the subgroups did meet the pre-specified threshold. Based on these findings, and the status of gantenerumab development plan, Roche and the DIAN-TU have decided to discontinue the DIAN-TU-001 gantenerumab OLE. Other measures are being analyzed and will be communicated in scientific meetings and publications.

The Knight Family DIAN-TU and Roche recognize and truly appreciate the commitment of our participants and their families. The DIAN-TU understands the uncertainty and concerns with stopping treatment, and we are actively working to identify treatment continuation and trial options for the DIAN-TU-001 OLE participants with expected announcements in the next few months.

... In late 2022, when it was learned that the GRADUATE studies of gantenerumab, in patients with sporadic AD, were negative, it was decided that an interim efficacy analysis of the DIAN-TU-001 OLE should be performed to see if the higher doses of gantenerumab used in the OLE were providing a benefit to patients with DIAD. ... DIAN-TU researchers will continue to analyze data according to the DIAN-TU-001 OLE Statistical Analysis Plan to further understand the outcomes of the study. A more detailed presentation of the study results will be presented to stakeholders in the coming months.

We thank the DIAN-TU participants and their families, site investigators and coordinators, Pharma Collaborators, our funders (the NIA/NIH, Alzheimer's Association, GHR Foundation, and other organizations), regulators, the DIAN-TU Study Team ... and many others for their continued support of the DIAN-TU trials. We remain committed to our participants ... whose contributions have provided key insights into the progression and treatment of AD, led to the identification of stage dependent changes with amyloid removal, and helped in the development of potential surrogate biomarkers.

Read the full DIAN-TU announcement at <u>https://dian.wustl.edu/our-research/clinical-trial/research-updates/</u>.

### **DIAN-TU-001 OLE Participant Conversations**

Prior to public statements about analysis findings, participants in the DIAN-TU-001 Open Label Extension (OLE) with gantenerumab met with trial leadership via webinar to discuss trial findings and subsequent decision-making processes. Principal investigator and program director Dr. Randall Bateman and co-director Dr. Eric McDade provided a recap of the secondary prevention trial and OLE history and summarized interim data analysis findings.

Some participants in the OLE have contributed up to a decade of trial data. "There is no other group of people in the world like you," stated Dr. Bateman, addressing trial participants directly. These individuals are unique in both the length they have contributed to the study—longer than anyone in any other trial of Alzheimer's disease—as well as their dedication to this rigorous process, with a 99% completion rate of scans, lumbar punctures, and cognitive tests.

Drs. Bateman and McDade emphasized the entire DIAN-TU team's immense gratitude for our participants. After an individual stated their dedication to any action that would change the future for those facing DIAD, Dr. Bateman responded that this is "a beautiful and powerful sentiment ... by your deeds, by those actions, you make all this possible."

Every clinical trial is a team effort. While research questions posed by investigators guide a trial's direction, the journey is impossible without the efforts of dedicated participants. And these participants are supported by caring family members, friends, and even one another. Together, we progress in our knowledge of DIAD—and our fight against it.



Pictured: Dr. Randall Bateman addresses DIAN-TU-001 Open Label Extension participant questions during a live webinar on the topic of interim efficacy analysis findings

## Resources and Support for DIAD Families

#### Rare Dementia Support (RDS) United Kingdom

RDS is a UK-based collaborative service led by the UCL Dementia Research Centre and partners, offering specialist support, advice, information and community for individuals with, at risk of, or supporting someone with a rare dementia diagnosis, including dominantly inherited familial AD. Meeting annually in London since 2010, the RDS familial AD support group also offers opportunities for individuals to connect online.

You can learn more about RDS by visiting <u>www.raredementiasupport.org</u>, view webinars and educational resources on the <u>RDS YouTube channel</u> and join the RDS community by <u>signing up here</u> to become a member.

#### Youngtimers

Youngtimers is led by and for individuals at risk for DIAD and their supporters, and offers virtual support groups and workshops in multiple languages. To join a virtual support group, visit <u>https://www.youngtimers.org/supportgroup</u>. Current groups include English-speaking gatherings for caregivers, at-risk, and symptomatic individuals, as well as a Spanish-language group.

Youngtimers is also hosting a three-part mental health workshop series in October 2023. Learn more and register at <u>https://www.eventbrite.com/e/fall-workshop-series-pt-1-of-3-facing-the-truths-and-feeling-the-feelings-tickets-669016906577</u>.

#### **Rare Dementia Support Canada**

RDS Canada provides a free information and support service for people living with, or affected by, a diagnosis of rarer or young onset dementia, including DIAD. The RDSC also provides educational resources for supporters and practitioners. Learn more and connect with support at <u>https://raredementiasupport.ca/</u>.

### Save the date for an international DIAD gathering!

Sunday, November 19, 2023 11:00 am PST (GMT-8)/2:00 pm EST (GMT-5)/7:00 pm GMT

Would you like to connect with other people facing DIAD? This community stretches across the globe; you are not alone! Join this international community for a 90-minute gathering to share stories and connect. Rare Dementia Support and Youngtimers are bringing together individuals from the US, Canada, and UK (and beyond) impacted by DIAD. This collaboration aims to support individuals who are symptomatic, asymptomatic (confirmed positive genetic status), at-risk (confirmed mutation in the family but genetic status unknown), and/or supporting or caregiving for someone with DIAD as well as bereaved. The virtual gathering will begin as one collective community and then separate into smaller breakout rooms to share stories with others in similar situations.

To receive registration information for this event, connect with any of the three groups above: Rare Dementia Support UK, Youngtimers, or Rare Dementia Support Canada.

## MyDIAN Sleep Study

Have you seen the new questionnaire available in the MyDIAN portal in the Linkt app? When was the last time you logged in? If you don't have notifications enabled, you could be missing research participation opportunities and timely announcements from the Expanded Registry and Dominantly Inherited Alzheimer Network team.

The Lifestyle Factors study just launched a new survey about sleep habits to learn more about how sleep duration, quality, and disturbances may impact the age of onset and progression of Dominantly Inherited Alzheimer's Disease. You can help contribute by spending a few minutes answering some brief multiple choice questions. This is just the latest in a series of questionnaires about environmental influences - such as diet, exercise, and education - available for the Lifestyle Factors study.

If you haven't opened MyDIAN recently or if you've never downloaded the app, now is the time to check it out! The EXR has been sending email invitations to join MyDIAN over the last several months, so look back in your inbox to see if you missed the link to join. If you haven't received an email from us about it, or if you need the invite resent to you, reach out to the EXR to ask at <u>dianexr@wustl.edu</u>. We would love to help you get connected!

Brooke Kinsaul



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## **Recent DIAN Publications**

## Cerebrospinal fluid proteomics define the natural history of autosomal dominant Alzheimer's disease

https://doi.org/10.1038/s41591-023-02476-4

## Large multi-ethnic genetic analyses of amyloid imaging identify new genes for Alzheimer disease

https://doi.org/10.1186/s40478-023-01563-4

## Positron emission tomography and magnetic resonance imaging methods and datasets within the Dominantly Inherited Alzheimer Network (DIAN)

https://doi.org/10.1038/s41593-023-01359-8

### Tau accumulation in autosomal dominant Alzheimer's disease: a longitudinal [18F]flortaucipir study https://doi.org/10.1186/s13195-023-01234-5

## Proteomics of brain, CSF, and plasma identifies molecular signatures for distinguishing sporadic and genetic Alzheimer's disease

https://doi.org/10.1126/scitranslmed.abq5923

The DIAN data are increasingly published in scientific reports to enable investigators worldwide to learn of our progress and to advance scientific understanding of Alzheimer's disease. Because of this, there is a small but possible risk that a DIAN participant reading or hearing of these scientific reports might guess, correctly or incorrectly, information about themselves. This includes guessing one's own or a family member's mutation status. We at DIAN take every step to minimize this risk, including ensuring that all DIAN data in journal articles, scientific meetings, press coverage, etc., lack identifying information for any participant, but it is possible than even such de-identified data may reveal a pattern of symptoms or a relationship with other medical disorders that could suggest that a particular person is mutation positive. You can avoid reading these scholarly articles or listening to presentations related to the DIAN study to decrease this risk.

## Alzheimer's in the News

First Alzheimer's drug to slow disease, Leqembi, gets full FDA approval <a href="https://www.cbsnews.com/news/first-alzheimers-drug-slow-disease-leqembi-gets-full-fda-approval/">https://www.cbsnews.com/news/first-alzheimers-drug-slow-disease-leqembi-gets-full-fda-approval/</a>

In "Show Me the Science," Washington University researchers discuss Leqembi FDA Approval <u>https://medicine.wustl.edu/news/podcast-newly-approved-drug-may-slow-progression-of-alzheimers/</u>

Tau-based biomarker tracks Alzheimer's progression https://medicine.wustl.edu/news/tau-based-biomarker-tracks-alzheimers-progression/

When Gut Bacteria May Be an Early Sign of Alzheimer's Disease https://time.com/6287229/gut-alzheimers-connection-microbiome-bacteria/

Study defines disparities in memory care <u>https://medicine.wustl.edu/news/study-defines-disparities-in-memory-care/</u>

#### Cognitive function in Down syndrome-associated Alzheimer's focus of grant

https://medicine.wustl.edu/news/cognitive-function-in-down-syndrome-associated-alzheimers-focus-of-grant/



Pictured: Brain scans of an Alzheimer's patient taken over the course of years show growing areas of yellow, indicating the presence of the Alzheimer's protein amyloid beta and reflecting its spread through the brain over time

Image credit: Brian Gordon

## Extend an Invitation to Join the EXR!

Do you know someone who is genetically at risk for DIAD, is supporting a family member or friend affected by DIAD, or works with patients who are affected by DIAD? Invite them to join the DIAN Expanded Registry!

## It's easy to send an invitation: just <u>download our flyer</u>. You can then email or print the flyer to share it with someone who would benefit from the Registry.

Once someone joins the Expanded Registry, we follow up within 1-2 business days to discuss research opportunities if the registrant qualifies. In addition, once an individual has joined the Registry, they receive additional information and resources from us every 1-3 months.

Copy and paste this link to access our flyer: <u>https://dian.wustl.edu/wp-</u> <u>content/uploads/2023/08/DIAN-EXR-Flyer-2023-Color-English.pdf</u>

The DIAN website is a great place to learn more about our research and find additional information. Please visit our <u>News page</u> for articles related to DIAN and Alzheimer's disease. Family members share their stories on the <u>Family</u> <u>Voices page</u>. If you are interested in research opportunities, please contact the DIAN Expanded Registry at <u>dianexr@wustl.edu</u>. If you are not part of the registry and would like to be, please visit <u>dian.wustl.edu</u> to register.





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