DOI: 10.1002/alz.041129

DRUG DEVELOPMENT

PODIUM PRESENTATIONS

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Results of the DIAN-TU prevention trial of solanezumab and gantenerumab in dominantly inherited AD

Overview of dominantly inherited AD and top-line DIAN-TU results of solanezumab and gantenerumab

Randall J Bateman[1] | Andrew J. Aschenbrenner[1] | Tammie L.S. Benzinger[1] | David Clifford[1] | Kelley Coalier[2] | Carlos Cruchaga[3] | Anne M. Fagan[4] | Martin R. Farlow[5] | Alison M. Goate[6] | Brian A. Gordon[7] | Jason Hassenstab[1] | Clifford R. Jack Jr.[8] | Robert A. Koeppe[9] | Eric McDade[7] | Susan Mills[1] | John C. Morris[7] | Stephen P. Salloway[10] | Anna Santacruz[1] | Peter J. Snyder[11] | Guoqiao Wang[1] | Chengjie Xiong[1] | B. Joy Snider[2] | Catherine J. Mummery[12] | Ghulam M. Surti[13] | Didier Hannequin[14] | David Wallon[14] | Sarah Berman[15] | James J. Lah[16] | Ivonne Z. Jiménez-Velazquez[17] | Erik D. Roberson[18] | Christopher H. Dyck[19] | Lawrence S. Honig[20] | Raquel Sanchez-Valle[21] | William S. Brooks[22] | Serge Gauthier[23] | Colin L. Masters[24] | Doug R. Galasko[25] | Jared R. Brosch[26] | Ging-Yuek Robin Hsiung[27] | Suman Jayadev[28] | Maïté Formaglio[29] | Mario Masellis[30] | Roger Clarnette[31] | Jeremie Pariente[32] | Bruno Dubois[33] | Florence Pasquier[34] | Scott W. Andersen[35] | Karen C. Holdridge[35] | Mark A. Mintun[35] | John R. Sims[35] | Roy Yaari[35] | Monika Baudler[36] | Paul Delmar[37] | Rachelle Doody[38] | Paulo Fontoura[36] | Geoffrey A. Kerchner[38] | DIAN-TU Study Team

[1] Washington University in St. Louis School of Medicine, St. Louis, MO, USA

[2] Washington University, Saint Louis, MO, USA

[3] Hope Center for Neurological Disorders, Washington University School of Medicine, St. Louis, MO, USA

[4] Washington University School of Medicine, St. Louis, MO, USA

[5] Department of Neurology, Indiana University School of Medicine, Indianapolis, IN, USA

[6] Ronald M. Loeb Center for Alzheimer's Disease, New York, NY, USA

[7] Knight Alzheimer Disease Research Center, St. Louis, MO, USA

[8] Mayo Clinic, Rochester, MN, USA

[9] University of Michigan, Ann Arbor, MI, USA

[10] Alpert Medical School of Brown University, Providence, RI, USA

[11] University of Rhode Island, Kingston, RI, USA

[12] University College London, London, United Kingdom

[13] Butler Hospital, Providence, RI, USA

[14] CNR-MAJ/Rouen University Hospital, Rouen, France

[15] University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[16] Emory University School of Medicine, Atlanta, GA, USA

[17] University of Puerto Rico, School of Medicine, San Juan, Puerto Rico
[18] University of Alabama at Birmingham, Birmingham, AL, USA
[19] Yale School of Medicine, New Haven, CT, USA
[20] Columbia University Medical Center, New York, NY, USA
[21] Universitat de Barcelona, Barcelona, Spain
[22] University of New South Wales, Kensington, NSW, Australia
[23] McGill University Research Centre for Studies in Aging, Montreal, QC, Canada
[24] The Florey Institute of Neuroscience and Mental Health, Melbourne, VIC, Australia
[25] University of California, San Diego, San Diego, CA, USA
[26] Indiana Alzheimer's Disease Center, Indianapolis, IN, USA
[27] Vancouver Coastal Health Research Institute, Vancouver, BC, Canada
[28] University of Washington, Seattle, WA, USA
[29] Hopital Neurologique Pierre Wertheimer, Lyon, France
[30] Hurvitz Brain Sciences Program, Sunnybrook Research Institute, Toronto, ON, Canada
[31] University of Western Australia, Perth, Australia
[32] Department of Neurology, CMRR and INSERM U825, Toulouse, France
[33] Institute of Memory and Alzheimer's Disease (IM2A), Department of Neurology, Pitié-Salpêtrière Hospital, AP-HP, l'Hôpital, Paris, France
[34] CHRU Lille, Lille, France
[35] Eli Lilly and Company, Indianapolis, IN, USA
[36] Roche/Genentech Product Development, Neuroscience, Basel, Switzerland
[37] F. Hoffmann-La Roche Ltd, Basel, Switzerland
[38] Roche Pharma Research and Early Development, Basel, Switzerland

Correspondence
Randall J Bateman, Washington University in St. Louis School of Medicine, St. Louis, MO, USA.
Email: batemanr@wustl.edu

Abstract

Background: Alzheimer's disease (AD) prevention trials aim to intervene prior to significant neuronal loss, brain damage, and symptom onset to delay or slow cognitive decline. In dominantly inherited AD (DIAD), mutation carriers develop symptomatic AD at predictable ages with near 100% penetrance. In 2012, the Dominantly Inherited Alzheimer Network Trials Unit Adaptive Prevention Trial (DIAN-TU APT) platform launched a double-blind, randomized, placebo-controlled, parallel group trial of two anti-amyloid-beta monoclonal antibodies with two different antigenic targets, gantenerumab and solanezumab (NCT01760005). The DIAN-TU scientific development, implementation of the first AD prevention trial, trial challenges and opportunities, including dose escalation, and top-line results will be presented.

Method: DIAN was established in 2008 in response to a call from the National Institute of Aging to establish a network to study DIAD and enable future clinical trials. Successive breakthroughs in understanding disease processes enabled the launch of the DIAN-TU adaptive prevention trial, a global adaptive platform trial supporting testing multiple drugs in parallel. The DIAN-TU partners include patients and families at risk for DIAD, global academic researchers, the NIH, Alzheimer's Association, philanthropic supporters, the DIAN-TU Pharma Consortium, and pharmaceutical companies with drugs being tested. Important milestones include developing a platform to enable a comprehensive efficient treatment trial for this rare population, adding tau PET as part of AMP AD, adapting dosing mid-trial and extending the original biomarker trial to

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

continue randomized dosing to test a cognitive endpoint until the last patient reaches 4 years, developing a disease progression statistical model and inclusion of DIAN observational data to increase the power to determine drug effects.

Result: The primary and key secondary outcomes of the DIAN-TU trial will be presented for each therapy in the context of targeting amyloid-beta at pre-clinical and clinically symptomatic stages of disease.

Conclusion: These results inform about AD hypotheses, timing of treatment and the prospect of slowing, or preventing AD in DIAD and sporadic AD.