

## **Investigational drugs chosen for major Alzheimer's prevention trial**

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Leading scientists have selected the first drugs to be evaluated in a worldwide clinical study to determine whether they can prevent Alzheimer's disease.

The pioneering trial, expected to start by early 2013, initially will test three <u>promising drugs</u>, each designed to target Alzheimer's in different ways.

In people with inherited <u>mutations</u> that cause early-onset Alzheimer's, the study will seek to identify whether the drugs can improve Alzheimer's disease <u>biomarkers</u> and effectively prevent the loss of cognitive function.

"This trial is the result of a groundbreaking collaboration between academic institutions, pharmaceutical companies and patient advocacy groups, with key support from regulatory groups," says principal investigator Randall Bateman, MD, the Charles F. and Joanne Knight Distinguished Professor in Neurology at Washington University School of Medicine in St. Louis. "We are excited that this diverse portfolio of drugs and approaches will accelerate the discovery of an effective treatment for Alzheimer's."

The trial will be conducted by the Dominantly Inherited Alzheimer's Network Trials Unit (DIAN TU) at Washington University School of Medicine in St. Louis. The trials unit is supported by the DIAN, an NIHfunded collaboration of world-leading Alzheimer's research centers; the



Alzheimer's Association; and the DIAN Pharma Consortium, composed of 10 <u>pharmaceutical companies</u> that have been advising DIAN researchers on the planning of the trial.

Alzheimer's researchers have selected the investigational drugs from more than a dozen nominations submitted by the DIAN Pharma Consortium. Each drug has a unique approach to counter the <u>toxic</u> <u>effects</u> of amyloid beta, the main ingredient of <u>brain plaques</u> found in Alzheimer's patients. Each also has passed earlier <u>clinical trials</u> that evaluated safety and effectiveness of the drugs and whether they engaged their targets in patients.

The investigational drugs are:

\*Gantenerumab, an antibody made by Roche that binds to all forms of aggregated amyloid beta and helps remove them from the brain. Gantenerumab is currently in an international phase II/III trial known as SCarlet RoAD, started in 2010, that will test the drug's ability to stop Alzheimer's prior to dementia.

\*Solanezumab, a monoclonal antibody in phase III clinical trials. Discovered and developed by Eli Lilly and Company, it binds to soluble forms of amyloid beta after they are produced, allowing amyloid beta to be cleared before it clumps together to form plaques.

Also selected for potential inclusion in the trial is a beta-secretase (BACE) inhibitor, a small molecule in Phase II clinical trials that was also discovered and developed by Lilly. BACE is theorized to work by reducing the amount of amyloid beta proteins produced, slowing the accumulation of plaques.

Roche and Lilly have agreed to make the treatments available at no cost to the investigators. The two companies also will provide supporting



grants for each drug to help make the trial possible. The new trial also is supported by a \$4.2 million grant from the Alzheimer's Association. The researchers have applied for support through the National Institutes of Health; the National Institute on Aging is currently reviewing the grant application.

"Trying to prevent Alzheimer's symptoms from ever occurring is a new strategy," says John C. Morris, MD, principal investigator of DIAN and the Harvey A. and Doris Friedman Distinguished Professor of Neurology at the School of Medicine. "We are most appreciative of the support this approach has received."

The trial will involve 160 people who have inherited mutations that mean they are almost certain to develop Alzheimer's at a young age, typically in their 30s, 40s or 50s. The trial also will monitor the health of 80 DIAN participants who did not inherit the Alzheimer's mutations.

"This is a very exciting moment in Alzheimer's disease research, and it gives me renewed hope for a future without Alzheimer's," says DIAN participant Brent Whitney. "I hope my grandchildren someday learn of this condition in history books, like I learned about polio."

Participants with inherited forms of Alzheimer's will be randomly assigned to receive one of three investigational drugs (75 percent chance) or a placebo (25 percent chance). Those without mutations also will receive a placebo.

"Normally in clinical trials there is a 50/50 chance of receiving the active <u>drug</u> or a placebo, but the efficient design of testing three drugs will allow us to significantly boost the number of participants who receive active treatments," Bateman says.

All of the experimental group's subjects will be within 10 to 15 years of



the anticipated age when symptoms of cognitive decline and dementia are expected to appear. Earlier DIAN studies have shown that at this point in their lives, people who have Alzheimer's mutations are likely to have biological indicators that show the disease is beginning in the brain, including evidence of brain plaques and changes in the blood and cerebrospinal fluid.

Scientists will monitor these indicators of early Alzheimer's to see whether the new treatments slow or stop the disease process. The first part of the trial is planned to last for two years. It will be expanded and extended if one or more of the drugs are effective in slowing or stopping indicators of presymptomatic Alzheimer's disease.

"Roche is honored that gantenerumab was selected by DIAN to be a part of this groundbreaking Alzheimer's disease study," says Luca Santarelli, head of Roche Neurosciences. "This clinical test supports Roche's commitment to provide earlier treatment options to those at risk for this devastating disease."

"We are pleased that Lilly was chosen to contribute solanezumab, and potentially our beta-secretase inhibitor, for use in this pioneering Alzheimer's disease study," said Jan Lundberg, PhD, executive vice president, science and technology, and president, Lilly Research Laboratories. "We look forward to collaborating with the DIAN TU investigators, along with the other public and private partners, to better understand if early treatment with these investigational medicines can influence this terrible disease."

More information: <a href="http://www.dianxr.org/">www.dianxr.org/</a>

Provided by Washington University School of Medicine



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