TREATMENT

Rethinking the Road to Treatment

Carleen Pine Adams

"We're hopeful that by intervening early we can stop the disease before it progresses and causes dementia."

-DR. RANDALL BATEMAN

Alzheimer's researchers have spent decades developing medications to attack amyloid plaques in the brain — a hallmark of the disease. Randall Bateman, M.D., a neurology professor at Washington University in St. Louis, is not surprised that experimental anti-amyloid drugs have yet to show a significant cognitive benefit in clinical trials — nor is he discouraged.

"Trials to date have predominantly focused on people who have already developed memory loss, confusion and difficulties communicating, but we now know Alzheimer's pathology is present up to 20 years before symptoms emerge," he says. "You have to wonder whether those earlier cases were simply instances of 'too little, too late.'"

Dr. Bateman is leading the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), one of several Alzheimer's Association-supported studies that are testing anti-amyloid drugs earlier in the disease process. DIAN-TU gives experimental therapies to individuals who carry genes that guarantee they will develop Alzheimer's but who do not yet exhibit symptoms.

"We're hopeful that by intervening early we can stop the disease before it progresses and causes dementia," Bateman says. His team believes a drug that works for people with an inherited form of Alzheimer's could also work for individuals with the more common older-onset form because the disease appears to progress in a similar way no matter how or when it starts.

Supported from its earliest days by Alzheimer's Association donors, who continue to fund expansions and enhancements of the study, DIAN-TU features an innovative trial design: Researchers are testing experimental medications in different groups of volunteers simultaneously rather than sequentially — and will use the same infrastructure to test new drugs until one or more medications prove to be effective.

Two anti-amyloid drugs have been under study since 2013, and a third was added to the trial in 2017 as part of the DIAN-TU Next Generation (NexGen) study. A fourth treatment was recently selected for investigation. The DIAN-TU High-Dose Escalation Study, also started in 2017, increased the amount of one of the trial's original anti-amyloid drugs, Solanezumab,

Dr. Randall Bateman, Jim Weddle and Dr. Maria Carrillo

after a separate study showed it could be given safely in doses up to four times higher than what was previously used in DIAN-TU.

Financial services firm Edward Jones has joined forces with the Association to help advance DIAN-TU. "We want to help end this disease as quickly as possible because it threatens our clients' financial well-being and quality of life," says Managing Partner Jim Weddle. "Research supported through the Alzheimer's Association has the ability to turn opportunities into true progress."

TARGETING OTHER DISEASE PATHWAYS

Alzheimer's is a complex disease that likely has a variety of causes. Neuroinflammation, a response of the body's immune system, is one pathway of growing interest for dementia researchers. Too little inflammation may allow amyloid plaques to form unchecked, while too much may kill vital neurons. In partnership with the Part the Cloud movement, the Association is currently funding four clinical trials testing existing drugs — including one already approved by the Food and Drug Administration (FDA) for another condition — to see if they have a beneficial impact on neuroinflammation in people with mild-to-moderate cognitive impairment. Scientists are especially interested in studying medications already approved by the FDA since they have passed rigorous safety testing and may potentially be fast-tracked for use.

Another promising avenue of Alzheimer's research is combination therapy — the simultaneous use of two or more drugs, known as drug "cocktails." Through the Alzheimer's Combination Therapy Opportunities (ACTO), a special grant program, the Alzheimer's Association and Alzheimer's Drug Discovery Foundation jointly provided $1.85 million to support a clinical trial of an investigational therapy that combines two existing drugs to target two distinct Alzheimer's disease processes.

"A combination of drugs has made an unbelievable difference in the lives of individuals with HIV, and we are hopeful that the same approach can slow down the progression of Alzheimer's," says Carleen Pine Adams, president of the Pine Family Foundation, which invested in ACTO.

As the world's largest nonprofit funder of Alzheimer's research, the Alzheimer's Association is committed to supporting the most innovative science available. "With clinical trials improving in design and more novel therapeutics being tested," says Keith Fargo, Ph.D., Alzheimer's Association director of Scientific Programs and Outreach, "we're confident we will eventually be able to successfully treat this disease."