

## **CTAD Highlights November 20, 2014**

Over 700 Alzheimer's disease researchers from around the world converged on Philadelphia today as the 7<sup>th</sup> annual Clinical Trials in Alzheimer's Disease (CTAD) began. Rachele Doody, M.D., Ph.D., from Baylor College of Medicine in Houston, Texas, kicked off the conference with an overview of where the field stands with respect to developing new treatments for the progressive neurodegenerative disease, which currently affects some 35 million people worldwide.

Dr. Doody cited numerous potential strategies for treating dementia, including drugs and nutraceuticals that target risk factors, neurotransmitter-based therapies, neuroprotective or regenerative drugs, and drugs that modify proteins thought to be involved in AD pathogenesis. Moreover, she urged investigators to reject the distinction between symptomatic and disease-modifying drugs and instead focus on developing drugs that provide a clinical benefit. Such drugs, she said, will most likely modify the disease even if that is not the intended goal.

### **Collaborations for Alzheimer's Prevention**

An umbrella group called the Collaboration for Alzheimer's Prevention (CAP) was created in 2012 to coordinate efforts from three – now four -- prevention initiatives: the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU), the Alzheimer's Prevention Initiative (API), the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) study, and the newest member, the TOMMORROW Study. CTAD provided another opportunity for the CAP members to share progress from each of their studies with the Alzheimer's community.

The goal of CAP is to harmonize biomarker, clinical, and cognitive measures to maximize their utility for the entire field, said Randall Bateman, M.D., director of the DIAN-TU and a neurologist at the Washington University School of Medicine. While each trial focuses on a different population and tests a different compound, the investigators hope that by sharing expertise and data, converging on common outcome measures, standardized sample and data collection, and developing common participant recruitment and retention strategies, they will collectively answer critical questions in AD prevention. For example, while the studies have created different cognitive composite measures, through their work with CAP they converged on a similar set of cognitive domains to be tested, so that results can be compared across trials. In addition, thanks to support from the Alzheimer's Association and the Accelerating Medicines Partnership (AMP), a public-private partnership between the NIH and ten industry partners, tau imaging will now be included in all of these prevention trials.

Each of these studies faces tremendous hurdles in terms of recruiting, screening, enrolling, evaluating, and retaining large numbers of subjects over a long period of time and across dozens of trial sites. "It doesn't take a village to do one of these trials, it takes a confederacy," said Pierre Tariot, M.D., director of the API.

Reisa Sperling, M.D., director of the A4 study went even further. “I think it’s actually going to take a globe to defeat this disease.”

It will also take new tools, novel trial designs, new analytical methods, and other shared resources, all of which were topics of discussion at CTAD. For example, Jessica Langbaum, Ph.D., of the Banner Alzheimer's Institute in Phoenix, Arizona described the evolution of the Alzheimer's Prevention Registry. Launched in May 2012 to accelerate enrollment in coming prevention trials including Banner's API trial, the registry is intended to be a shared resource for the scientific community as well as an awareness-raising tool for the general population. Now, after a series of refinements, including an interactive U.S. map that lists study opportunities, the registry has enrolled over 45,000 individuals toward their eventual goal of 250,000 enrollees. An interactive world map is planned, as well as a researcher portal that will allow tracking recruitment success for various projects.

### **New investigational compounds**

Discovery and development of new drugs to treat dementia is indeed proceeding across diverse mechanisms, as mentioned earlier by Dr. Doody. Some of the highlights from today's sessions include:

- R. Scott Turner, M.D., Ph.D., a neurologist at Georgetown University described a study to examine the effects of resveratrol on CSF biomarkers. The safety and tolerability trial enrolled 120 patients with mild-to-moderate AD. Patients were given placebo or escalating doses of resveratrol over 52 weeks. The drug was well tolerated and appeared to penetrate the blood-brain barrier to get into the central nervous system. No significant differences were seen in the primary outcome measures, but there were some signs that it may have stabilized deposition of amyloid in the brain and, similar to other anti-amyloid strategies, there was an increase in brain shrinkage, although the mechanisms involved in this are not clear. While the trial lacked a good clinical readout, Dr. Turner suggested that further study is warranted.
- Shifu Xiao, M.D., Ph.D., from the Shanghai Jiaotong University School of Medicine, presented the results of a phase II clinical trial of GV-971 in mild-to-moderate AD. GV-971 is a compound extracted from seaweed that appears to prevent the aggregation and deposition of amyloid beta. Patients were randomized to placebo, low dose, or high dose of the drug. Cognitive, behavioral, and functional improvement was seen only in those receiving the high dose of the drug. The drug is now being tested in a phase III study in China.
- Alireza Atri, M.D., from the Massachusetts General Hospital described an ongoing phase III program of a drug called idalopiridine, which blocks receptors that bind the neurotransmitter serotonin in the brain. In animal studies the drug appeared to reverse cognitive deficits; and in a completed phase II study, it improved cognition in patients with moderate AD who were

also being treated with donepezil. Interestingly, the drug also appeared to decrease anxiety, which is a significant and disturbing problem for patients with AD and their caregivers.