Study Shows *G. biloba* Does Not Prevent Dementia

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Ginkgo biloba does not prevent onset of dementia in general or of Alzheimer's disease in particular, according to data from a large, randomized clinical trial.

Basic and observational research has suggested the herbal product should be a promising therapy, but "no adequately designed and powered clinical trial has evaluated the [herb's] safety and effectiveness in the primary prevention of dementia," said Dr. Steven T. DeKosky of the University of Pittsburgh and his associates in the Ginkgo Evaluation of Memory study.

The National Center for Complementary and Alternative Medicine and the National Institute on Aging, Bethesda, Md., sponsored the study of 3,069 community-dwelling subjects aged 75 and older. They were randomly assigned to receive *G. biloba* or placebo twice daily and followed for a median of 6 years to track development of dementia (JAMA 2008;300:2253-62).

The *G. biloba* was a standard formulation used in many of the branded products sold in the United States and was administered at the highest, most commonly used dosage. An expert panel assessed the subjects' cognitive status, focusing on therapy adherence and subject retention, given their advanced age and concomitant morbidity.

A total of 523 subjects developed dementia, including 16% in the placebo group and 18% in the active treatment group, a nonsignificant difference. The rate of total dementia was not significantly different between subjects receiving ginkgo (3.3 cases per 100 person-years) and those receiving placebo (2.9 cases per 100 person-years), neither was the rate of Alzheimer's disease at 3 cases per 100 person-years and 2.6 cases per 100 person-years, respectively.

The findings remained consistent across subgroups of patients categorized by age, sex, and the presence or absence of mild cognitive impairment at baseline. Mortality and the adverse event profiles were similar between the groups, with similar incidence of coronary heart disease events, stroke, and bleeding events.

Because the delay from initial brain changes to clinical dementia is known to be long, it may take many years to manifest an effect of *G. biloba*, positive or negative, the authors wrote, and they are planning further analysis of brain function and pathology by group using MRIs.

Dr. DeKosky reported receiving grants or research support from Elan Corp., Myriad Genetics Inc., Neurochem Inc., and GlaxoSmithKline, and serving on the advisory boards of or consulting for several additional pharmaceutical companies. ■

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portion of which are antiamyloids. But she agreed that these compounds grab the lion's share of attention. "The amyloid story gets articulated over and over again because a lot of people in academia feel most comfortable with a story that's already been told. But there's no a priori reason that any one of these approaches should work better than another."

In fact, researchers might be looking at antiamyloids through the wrong end of the lens, said Dr. Marwan Sabbagh, chief medical and scientific officer of Sun Health Research Institute, Sun City, Ariz. Rather than a one-step cure, the compounds may be best used in primary prevention. "The problem is, we may be approaching it too late," he said in an interview. "By the time you clinically manifest dementia, it might be too late for the drugs to help, even if they clear the plaques."

Using antiamyloids to remove the protein before it aggregates might interrupt the pathologic cascade that Dr. Hardy envisioned, decreasing the excitotoxicity, the tangles, and the inflammation that kill neurons.

"The ideal future for an amyloid-based approach would probably be a combination of immunotherapy to break up existing plaques, and secretase inhibitors to prevent the formation of additional plaques," said Dr. Sabbagh, who is an investigator on the phase III bapineuzimab trial. Putting this to practical use will require some big advancements in early detection—probably imaging techniques—that can identify patients with a small plaque burden and little or no cognitive impairment. "The question is: Will we be able to advance the field enough to use them in that manner?" ■