

Donepezil May Have Short-Term Benefit For Mild Cognitive Impairment

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People with mild cognitive impairment (MCI) taking the drug donepezil were at reduced risk of progressing to Alzheimer's disease (AD) for the first 18 months of a 3-year study when compared with their counterparts on placebo, according to a presentation of preliminary data from a recently completed clinical trial held under the auspices of the national Alzheimer's Disease Cooperative Study, which is directed by the University of California, San Diego (UCSD) School of Medicine.

Supported by the National Institute on Aging (NIA), part of the National Institutes of Health, the study showed that the reduced risk of progressing from MCI to a diagnosis of AD among participants on donepezil disappeared after 18 months, and by the end of the study, the probability of progressing to AD was the same in the two groups.

Presented at the Alzheimer Association's 9th International Conference on Research on Alzheimer's Disease and Related Disorders (ICAD) in Philadelphia on July 18, 2004, the study compared donepezil, vitamin E, or placebo in participants with MCI to see whether the drugs might delay or prevent progression to AD. Over the course of the study, among people who did progress to AD, the MCI participants on donepezil averaged 661 days until a diagnosis of AD, a second group on vitamin E averaged 540 days from MCI to AD, and those on placebo averaged 484 days to AD. The study investigators reported a statistically significant effect when donepezil was compared to placebo, but said there was no apparent benefit from vitamin E.

The study's principal investigator was Ronald Petersen, M.D., Ph.D., of the Mayo Clinic, Rochester MN; Leon Thal, M.D., UCSD professor of neuroscience, heads the nationwide Alzheimer's Disease Cooperative Study.

The NIA and the scientists conducting the study emphasized that further analyses will be needed to assess the practical, clinical implications of the new data; the study is very complex, and the effects appear time limited.

"We will subject the data to considerable scrutiny over the next few months for additional information on whether and, if so, when the drug could benefit people with MCI," said Neil Buckholtz, Ph.D., Chief of the NIA's Dementias of Aging Branch. "Today's presentation of a possible but limited effect of donepezil is encouraging. But we are hoping that further clinical studies in MCI patients will result in more significant progress in delaying a diagnosis of Alzheimer's disease."

Besides primary support from the NIA, additional funding for the study was provided by Pfizer, Inc., and Eisai Inc. Pfizer and Eisai additionally contributed the donepezil study medication, and vitamin E was given by DSM Nutritional Products, Inc.

People with this form of MCI have notable memory loss and are at higher risk of developing AD than those of similar age and health in the general population. During the study, patients with MCI were given donepezil, vitamin E, or a placebo. Donepezil was selected because of its current approval as a drug for treating patients already diagnosed with AD. The antioxidant vitamin E has been linked in animal research to a reduction in cognitive decline and in some population studies to reduced risk of AD.

In addition to being tested for AD, the participants were assessed in specific areas of cognitive function, including orientation, language, and attention, and in everyday function, such as activities of daily living. These secondary analyses suggest that decline among the group on donepezil occurred at a slower rate on tests of global cognition, memory, and language than the other participants during the first half of the study but progressed at the same rate thereafter.

"Certainly, we need to continue our analyses," said the study's principal investigator Petersen. "But these are the first reported data to show some kind of positive treatment effect on progression from MCI to AD, suggesting that it may be possible to design better trials to intervene at an earlier stage in the disease process and slow the progression to AD."

The Memory Impairment Study was conducted nationwide at 69 sites. It involved 769 participants with MCI, who were followed for 3 years and tested for AD at 6-month intervals during their 36 months in the study. The average age of the participants was 73.

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