

Lipid-Lowering May Improve Cognition in A-Fib

BY BRUCE JANCIN
Denver Bureau

VIENNA — Potent cholesterol-lowering therapy appears to reverse neurocognitive decline in normolipidemic elderly patients with atrial fibrillation, Dr. Elke Wezenberg said at the annual congress of the European Society of Cardiology.

If this new finding from the small pilot SPACE (Silent Brain Infarction and Cognitive Decline Prevention in Atrial Fibrillation

by Cholesterol Lowering in the Elderly) trial is confirmed in a planned larger, more definitive study, then the use of lipid-lowering medications would be warranted in all patients with atrial fibrillation (AF), regardless of their cholesterol level, added Dr. Wezenberg, a psychiatrist at Radboud University Nijmegen (the Netherlands).

She attributed the positive cognitive effects of the SPACE regimen of 40 mg of atorvastatin/10 mg of ezetimibe daily to the drugs' anti-inflammatory action. Par-

ticipants had relatively high baseline C-reactive protein (CRP) levels indicative of extensive systemic inflammation. Their CRP levels decreased significantly during 1 year of lipid lowering, and the decline correlated inversely with the observed improvement in cognitive function.

SPACE was a double-blind, placebo-controlled prospective study involving 31 patients, mean age 74, with an average 14-year history of AF. All were on warfarin and adequately anticoagulated, with an in-

ternational normalized ratio of 2.0-3.0. At baseline and again after 1 year, participants were evaluated for depression using the Montgomery-Asberg Depression Rating Scale (MADRS), by MRI for white matter lesions, and by an extensive neuropsychological test battery for memory, language, executive function, and speed of information processing.

At baseline, participants were free of clinically significant depressive symptoms, had no signs of impairment on the Mini-Mental State Examination, and were asymptomatic in terms of activities of daily living. But nearly all showed baseline mild neurocognitive impairment, with greater than expected difficulties on specific neurocognitive tests, especially those

Lipid-lowering therapy resulted in significant improvement in speed of information processing, memory, and executive function.

concerned with speed of information processing, memory, executive function, and psychomotor speed. At 1 year, the placebo group showed continued decline in these domains. In contrast, the AF patients on lipid-lowering

therapy showed significant improvement over baseline in speed of information processing, memory, and executive function as assessed by switching tests. The active treatment arm also showed a nonsignificant trend for a reduction in white matter lesions, believed to be of vascular origin.

An estimated 2.2 million Americans have AF, making it the most common cardiac arrhythmia by far. Its prevalence climbs with age, reaching roughly 8% in patients aged 80 or older.

It is well established that AF is a risk factor for ischemic strokes, silent brain infarcts, and dementia, even when patients are adequately anticoagulated. The rationale for SPACE comes from prior studies showing that inflammatory markers are increased in patients who have AF, white matter lesions, and/or cognitive impairment—and lipid-lowering drugs are known to decrease inflammation.

The SPACE findings are at odds with the 5,804-patient randomized Pravastatin in Elderly Individuals at Risk of Vascular Disease (PROSPER) study, in which 3 years of pravastatin didn't slow cognitive decline (Lancet 2002;360:1623-30).

In an interview, Dr. Wezenberg said she thought the main explanation for the disparate results is that PROSPER involved a heterogeneous population with a far lower risk for stroke and microinfarcts than a population made up of individuals with AF. Moreover, the degree of lipid lowering achieved with pravastatin was considerably less than with the SPACE regimen. And as the PROSPER investigators noted, pravastatin is a hydrophilic statin that doesn't efficiently cross the blood-brain barrier.

The SPACE study was funded by the departments of psychiatry and cardiology at Radboud University Nijmegen. ■

Experience the Revolution of cancer information.



The world's leading medical publisher introduces a professional website for trusted oncology information.

- Search and download recent articles from over 100 Elsevier cancer related journals
- Daily summaries of articles from leading society journals like JCO, JNCI, CA, Blood, JAMA and NEJM
- Professional drug monographs, interactions, chemotherapy regimens and patient handouts
- Videos, blogs, forums and much more
- Guided by an esteemed Advisory Board that includes four past presidents of ASCO

World class resources. All in one place.

Register today at www.oncologystat.com

