Donepezil Makes Difference in Severe Alzheimer's

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Patients with severe Alzheimer’s disease showed improved cognition and function when treated with donepezil in a 24-week, placebo-controlled trial, Dr. Sandra Black and her associates reported in a paper published in the annual meeting of the American Geriatrics Society.

The results are consistent with a Swedish nursing home study in a similar, institutionalized population (Lancel 2006;367:1266-70), suggesting that even patients with severe disease can benefit from treatment with donepezil.

The researchers suggest that this stage of disease can show measurable benefits of treatment with donepezil,” Dr. Black, professor of medicine and head of neurology at Brookdale Health Sciences Centre, University of Toronto, said in an interview. “They give a new evidence-based option for treatment, which gives hope for a better quality of life in the final phase of this devastating disease.”

Currently, donepezil (Aricept) is approved to moderate Alzheimer’s disease. In February 2006, the U.S. Food and Drug Administration accepted a supplemental new drug application for donepezil in severe Alzheimer’s disease.

Doses of 5 mg and 10 mg of donepezil are typically administered once daily, although the higher 10-mg dose did not provide significantly greater clinical benefit in previous clinical trials.

In their study, Dr. Black and her colleagues randomized 343 patients with severe Alzheimer’s disease to an initial dose of donepezil of 5 mg/day for 6 weeks and then 10 mg/day of donepezil (176 patients) or placebo (167 patients) for 24 weeks. Participants were not allowed to receive concomitant donepezil or any other anticholinesterase medication.

Among the patients treated with donepezil, 28% improved and 34% worsened, compared with 23% and 48% of placebo patients, respectively. The primary end point was change from baseline in Severe Impairment Battery (SIB) total score and Clinical Interview-Based Impression of Change–Plus (CIBI-Plus) scores at 24 weeks.

The primary analysis was based on the intent-to-treat population using a last observation carried forward analysis at 24 weeks. The intent-to-treat population consisted of all patients who were randomized, received at least one dose of either donepezil or placebo, and had a baseline and at least one postbaseline efficacy value.

Categories in the CIBI-plus analysis were collapsed (1.5=improved; 4= no change; and 5= worsened) because the distribution of values was sparse in categories 1, 2, and 7.

Donepezil was significantly superior to placebo on the SIB score at week 24 in the intent-to-treat population (mean difference 5.3), and at weeks 8, 16, and 24 in 127 of the 167 placebo patients who completed the study, Dr. Black reported.

The collapsed category CIBI-plus analysis significantly favored donepezil at week 24 in the intent-to-treat population and in patients who completed the study. Among donepezil-treated patients, 28% improved and 34% worsened, compared with 23%, 29%, and 48% of placebo patients, respectively.

Most reported adverse events were mild to moderate (74%), the most common of which was nausea (4% for Aricept and 2% for the placebo).