Atorvastatin for the Treatment of Mild to Moderate Alzheimer Disease

Preliminary Results

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Background  Laboratory evidence of cholesterol-induced production of amyloid β as a putative neurotoxin precipitating Alzheimer disease, along with epidemiological evidence, suggests that cholesterol-lowering statin drugs may favorably influence the progression of the disorder.

Objective  To determine if treatment with atorvastatin calcium affects the cognitive and/or behavioral decline in patients with mild to moderate Alzheimer disease.

Design  Pilot intention-to-treat, proof-of-concept, double-blind, placebo-controlled, randomized (1:1) trial with a 1-year exposure to once-daily atorvastatin calcium (80 mg; two 40-mg tablets) or placebo using last observation carried forward analysis of covariance as the primary method of statistical assessment.

Participants  Individuals with mild to moderate Alzheimer disease (Mini-Mental State Examination score of 12-28) were recruited. Of the 98 participants providing informed consent, 71 were eligible for randomization, 67 were randomized, and 63 subjects completed the 3-month visit and were considered evaluable.

Main Outcome Measures  The primary outcome measures were change in Alzheimer's Disease Assessment Scale–cognitive subscale and the Clinical Global Impression of Change Scale scores. The secondary outcome measures included scores on the Mini-Mental State Examination, Geriatric Depression Scale, the Neuropsychiatric Inventory Scale, and the Alzheimer’s Disease Cooperative Study–Activities of Daily Living Inventory. The tertiary outcome measures included total cholesterol, low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol levels.
**Results**  Atorvastatin reduced circulating cholesterol levels and produced a positive signal on each of the clinical outcome measures compared with placebo. This beneficial effect reached significance for the Geriatric Depression Scale and the Alzheimer's Disease Assessment Scale–cognitive subscale at 6 months and was significant at the level of a trend for the Alzheimer's Disease Assessment Scale–cognitive subscale, Clinical Global Impression of Change Scale, and Neuropsychiatric Inventory Scale at 12 months assessed by analysis of covariance with last observation carried forward.

**Conclusion**  Atorvastatin treatment may be of some clinical benefit and could be established as an effective therapy for Alzheimer disease if the current findings are substantiated by a much larger multicenter trial.

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