Solanezumab Fails to Halt Cognitive Decline Due to Alzheimer's Disease

Trial participants with Alzheimer's disease who received 400 mg of solanezumab every 4 weeks did not experience any significant halt in cognitive decline.

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August 14, 2019 – People with Alzheimer's disease experiencing mild dementia who received solanezumab intravenously every 4 weeks for 76 weeks had no significant difference in cognitive decline compared with those who received a placebo during this study.

Lawrence S. Honig, MD, PhD, with the Department of Neurology and Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Medical Center, New York, and colleagues reported their findings in the January 25, 2018, issue of the *New England Journal of Medicine.*

Alzheimer's disease is characterized by the accumulation of amyloid beta (Aβ) plaques and neurofibrillary tangles in the brain. The Aβ hypothesis suggests that an overproduction of or decreased clearance of Aβ in the brain early in the disease process causes deleterious effects in cognition and function.

Solanezumab, a humanized monoclonal antibody, binds to the Aβ peptide to increase its clearance from the brain. In two prior studies of the antibody, no significant reduction in cognitive decline or function was found in patients with more severe Alzheimer's disease. Findings in these two trials did indicate in secondary analyses that patients with mild Alzheimer's disease treated with solanezumab had a 34% cognitive and functional decline compared with 18% of those who received a placebo.

A cohort of 2129 people, 55 to 90 years of age, with mild Alzheimer's disease were recruited for the double-blind study. Patients were screened for amyloid-related disease by Aβ1-42 measurements in cerebrospinal fluid or by use of florbetapir positron-emission tomography. Cognitive and functional decline was compared at 80 weeks between patients receiving intravenous infusions of either placebo or 400-mg solanezumab every 4 weeks for 76 weeks.

The primary outcome was change in Alzheimer's Disease Assessment Scale 14-item cognitive subscale score (ADAS-cog14; range from 0 to 90 with higher scores indicating greater cognitive impairment), The mean ±SD baseline ADAS-cog14 in the solanezumab group was 28.9±8.3 and 29.7±8.5 in the placebo group (P = .02). Compared with baseline scores at study start at 80 weeks, there was no significant change between the two groups (between-group difference, -.80; P=.10).

Adverse effect rates were not significantly different between the placebo group and the group receiving solanezumab (83.5% for the placebo group; 84.5% for the solanezumab group). The group receiving solanezumab reported 4 event categories significantly more often. These were dysuria, nasal congestion, vitamin D deficiency, and spinal osteoarthritis.

"In patients with mild Alzheimer's disease, the results of the trial showed no benefit of solanezumab on the primary outcome of cognitive decline and did not reproduce the secondary analyses of the prior studies," concluded Dr. Honig.

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