Solanezumab Does Not Affect Cognitive Decline in Patients With Mild Alzheimer's Disease

Patients with mild dementia due to Alzheimer's disease taking solanezumab showed no difference in cognitive decline compared with those taking placebo.

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April 9, 2020 – The change from baseline to week 80 in the score of the 14-item cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-cog14) in patients taking solanezumab did not differ significantly from patients taking placebo.

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 published the results of the EXPEDITION3 trial in the January 25, 2018, issue of the *New England Journal of Medicine*.

Solanezumab is a humanized immunoglobulin G1 monoclonal antibody that was designed to increase clearance from the brain of soluble amyloid beta (Aβ) in order to prevent the formation of Aβ plaques, one of the neuropathological hallmarks of Alzheimer's disease. Secondary analyses from two completed clinical trials involving patients with mild-to-moderate Alzheimer's disease (EXPEDITION and EXPEDITION2) found patients with mild disease taking solanezumab had less cognitive decline by approximately 34% compared to those taking placebo. The primary outcome in EXPEDITION and EXPEDITION2 was negative - solanezumab did not significantly reduce cognitive or functional decline in patients with mild-to-moderate Alzheimer's disease.

EXPEDITION3 enrolled only patients who had mild Alzheimer's disease, defined as a Mini–Mental State Examination (MMSE) score of 20 to 26, and was intended to further investigate the secondary analyses from the previous two trials.

The double-blind, randomized trial enrolled 2129 patients with mild Alzheimer's disease and biomarker evidence of amyloid-related disease. Patients received intravenous infusions of either 400-mg solanezumab or placebo every 4 weeks for 76 weeks. Results showed no significant between-group difference at week 80 in the change in ADAS-cog14 score from baseline (change, 6.65 in the solanezumab group and 7.44 in the placebo group; difference, −0.80; $P = .10$).

Due to the failure of the primary outcome to reach significance in the prespecified hierarchical analysis, the secondary outcomes were considered to be descriptive and were reported without significance testing.

A total of 891 of 1054 patients (84.5%) in the solanezumab group and 890 of 1067 (83.4%) in the placebo group experienced at least one adverse event. Vitamin D deficiency, nasal congestion, spinal osteoarthritis, and dysuria occurred more frequently in the solanezumab group while gait disturbance and somnolence occurred more frequently in the placebo group.

“In patients with mild Alzheimer’s disease, the results of the EXPEDITION3 trial showed no benefit of solanezumab on the primary outcome of cognitive decline,” study authors concluded. “Further trials with solanezumab with different doses and timing may require examination.”

Trial funding and oversight was provided by Eli Lilly.

New England Journal of Medicine. Published January 25, 2018.