Solanezumab Does Not Affect Cognitive Decline in Alzheimer Disease Patients

Mild Alzheimer disease patients treated with solanezumab do not show any statistically significant difference in cognitive decline than those treated with placebo.

Kashif Piracha, MD

February 5, 2022 – Patients with mild Alzheimer disease did not develop a slower cognitive decline when treated with solanezumab than those who were treated with placebo, a phase 3 study showed.

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 disease continues to be an important cause of morbidity and mortality in people 65 years or older. According to the Alzheimer's Association, an estimated 6.2 million Americans are living with Alzheimer disease in 2021.This estimate is projected to increase to 12.7 million Americans by 2050. This disease is characterized by the deposition of extracellular amyloid-beta (Aβ) plaques and intracellular neurofibrillary tangles in the brain. These pathologic substances subsequently lead to synaptic and neuronal losses resulting in cognitive decline.

Two completed phase 3 clinical trials (EXPEDITION and EXPEDITION 2) previously failed to show a significantly reduced rate of cognitive decline in mild Alzheimer disease patients treated with solanezumab. However, in prespecified pooled secondary analyses, these patients had less cognitive decline by approximately 34% and less functional decline by approximately 18% than those patients who received placebo. The current trial was conducted to further investigate the secondary efficacy analyses from the earlier two trials.

This international trial involved participants 55 to 90 years of age. These participants met the diagnostic criteria for mild Alzheimer disease based upon a Mini-Mental State Examination score of 20 to 26. They also showed amyloid deposition either by florbetapir positron-emission tomography or Aβ1-42 measurements in cerebrospinal fluid. They were then randomly assigned to receive either 400 mg of IV solanezumab or placebo every 4 weeks for 76 weeks. A change from baseline to week 80 in the score on the 14-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog14) was set as the primary outcome measure.

Participants who received solanezumab had a mean change from baseline in the ADAS-cog14 score of 6.65, while those who received placebo registered a mean change from baseline of 7.44 on the same scale. There was no statistically significant between-group difference at week 80 (difference, -0.80; 95% confidence interval [CI], -1.73 to 0.14; p=0.10). Thus, solanezumab failed to show a clinically significant benefit as compared with placebo in the rate of cognitive decline of patients with mild Alzheimer disease.

The major adverse effect noted was cerebral edema or effusion lesions on magnetic resonance imaging. This occurred with one patient in the solanezumab group and two patients in the placebo group.

The study was supported by Eli Lilly.

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