Solanezumab Treatment for Alzheimers Does Not Slow Cognitive Decline

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July 9, 2019—A trial of solanezumab to reduce cognitive decline in patients with Alzheimer's disease was unsuccessful, according to the results of a phase 3 clinical study.

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

Alzheimer's disease neuropathology is characterized by extracellular amyloid beta (Aβ) plaques, and one theory posits that overproduction or reduced clearance of Aβ leads to early development of the disease. Therefore, treatments that slow the production of Aβ or increase its clearance from the brain may slow the progression of the disease. Solanezumab, a monoclonal antibody that binds to the Aβ peptide, was designed to increase its clearance from the brain.

The current study included 2129 patients with mild Alzheimer's disease, defined as a score of 20 to 26 on a Mini-Mental Status Examination (MMSE) and biomarker evidence of Aβ deposition in the brain. Patients were randomly assigned to receive either a 400-mg dose of solanezumab or placebo intravenously every 4 weeks for 76 weeks. Treatment response was based on the change from baseline to 80 weeks on various Alzheimer's disease and dementia assessment scales.

The primary outcome measure was the cognitive subscale of the Alzheimer's Disease Assessment Scale, or ADAS-cog14. This scale ranges from 0 to 90, with higher scores indicating increased cognitive decline. Secondary outcome measurements included the MMSE. This ranges from 0 to 30, with higher scores indicating less cognitive decline.

At baseline, the mean (SD) ADAS-cog14 score was 28.9 [8.3] in the solanezumab group and 29.7 [8.5] in the placebo group ($P = .02$). MMSE scores at baseline were 22.8±2.8 and 22.6±2.9, for the solanezumab group and the placebo group, respectively ($P = .12$). Study results did not show a significant between-group difference at 80 weeks for the mean (SD) ADAS-cog14 score (35.09 [13.28] vs 36.11 [14.27] for solanezumab vs placebo; between-group difference, −0.80; $P = .10$).

Since the primary outcome measurement failed to reach significance, secondary outcomes were considered descriptive and measured without significance testing. There was a decrease in between-group MMSE scores for both groups, indicating a worsening of cognitive function (19.62±5.30 in the solanezumab group, and ±14.27 in the placebo group; estimated difference at 80 weeks, 0.49; 95% confidence interval). Likewise, other secondary outcome measurements did not show disease improvement with drug therapy.

The most common adverse events that occurred in the solanezumab group were vitamin D deficiency, nasal congestion, spinal osteoarthritis, and dysuria. For the placebo group, the most common adverse events were gait disturbance and somnolence. Furthermore, the percentage of

adverse events that led to discontinuation of the trial for the solanezumab and placebo groups were 4.5% and 3.6%, respectively.

“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,” concluded Dr Honig and colleagues. “The rationale for further trials with solanezumab with different doses and timing may require examination.”

The study was sponsored by the Department of Neurology and Taub Institute for Research on Alzheimer’s Disease and the Aging Brain, Columbia University Medical Center, and Eli Lilly.

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