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Study examines immunotherapy and cerebrospinal fluid biomarkers in patients with Alzheimer's disease

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Immunotherapy with the antibody bapineuzumab in patients with mild to moderate Alzheimer disease resulted in decreases in a cerebrospinal fluid biomarker, which may indicate downstream effects on the degenerative process, according to a report published Online First by *Archives of Neurology*.

Alzheimer disease (AD) is a progressive neurodegenerative disease characterized by, among other things, deposits of extracellular β-amyloid (Aβ) plaques and intraneuronal neurofibrillary tangles with accompanying decreases in cerebrospinal fluid (CSF) Aβ and increases in CSF tau proteins. Bapineuzumab is an anti-Aβ monoclonal antibody, and immunotherapy with antibodies against Aβ is one of the major disease-modifying therapeutic approaches being evaluated for AD, the authors write in their study background.

Kaj Blennow, M.D., Ph.D., of the University of Gothenburg, Sweden, and colleagues conducted a combined analysis of two double-blind, placebo-controlled trials that included 46 patients with mild to moderate AD. A total of 27 patients were treated with bapineuzumab and 19 with placebo. The researchers evaluated whether bapineuzumab affected the CSF levels of the downstream biomarkers, total tau (T-tau) and phosphorylated tau (P-tau), and the primary biomarker Aβ in the completed trials.

"The reduction in the downstream biomarker CSF P-tau following treatment with bapineuzumab suggests that bapineuzumab reduces brain levels of P-tau, which may also reduce the formation of tangles in the brain," the authors note.

Although there was a reduction in CSF T-tau, it did not reach statistical significance compared with placebo. No clear-cut differences were observed for CSF Aβ, the study results indicate. But the observed decrease in both P-tau and T-tau require further examination, the authors note.

"An important question remains whether such changes in CSF biomarkers correlate with clinical benefit. This question will be addressed in the ongoing bapineuzumab phase 3 trials," the authors conclude.

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