Small study shows association between medication and reduction in brain amyloid levels related to AD

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Although it is a small study and more clinical trials are needed, treatment with the medication gantenerumab appeared to result in a reduction in brain amyloid levels in patients with Alzheimer disease, according to a report published Online First by *Archives of Neurology*.

"Genetic and neuropathological evidence suggests that the accumulation of amyloid-β (Aβ) peptides in the brain is a key event in the pathophysiology of Alzheimer disease (AD)," the authors provide as background information. They note that there are several therapeutic approaches currently being investigated to lower the levels of Aβ amyloid in the brain. "We previously reported the development of gantenerumab, a potent and fully human anti-Aβ antibody that binds specifically to Aβ plaques."

Susanne Ostrowitzki, M.D., from F. Hoffmann-La Roche Ltd., Neuroscience, Basel, Switzerland, and colleagues investigated whether treatment with gantenerumab leads to a measureable reduction in the level of Aβ amyloid in the brain and to try to figure out the mechanism of amyloid reduction. The study included patients with mild-to-moderate AD and was conducted at three university medical centers. Two consecutive groups of patients were randomized to receive two to seven infusions of intravenous gantenerumab (60 or 200 mg) or placebo every four weeks. Additionally, brain tissue from two patients who had AD (tissue obtained during tumor surgery) was coincubated with

gantenerumab as an ex vivo study.

"Sixteen patients with end-of-treatment positron emission tomographic scans were included in the analysis," the authors report. "The mean [average] percent change from baseline difference relative to placebo (n = 4) in cortical brain amyloid level was -15.6 percent for the 60-mg group (n = 6) and -35.7 percent for the 200-mg group (n = 6)." The authors note that "Gantenerumab induced phagocytosis [a process the body uses to destroy dead or foreign cells] of human amyloid in a dose-dependent manner ex vivo."

"Our study demonstrates that two to seven months of treatment with gantenerumab led to dose-dependent amyloid reduction in the brains of patients with AD. Additionally, our findings in the placebo-treated patients support previous reports indicating that amyloid load continues to increase in many patients with mild-to-moderate AD." The authors suggest the treatment may work through an "effector cell-mediated mechanism of action."

"…it is still unclear whether any reduction in brain amyloid level will translate into clinical efficacy. A phase two clinical trial is under way to investigate whether a clinical benefit can be achieved in gantenerumab-treated patients with prodromal [early symptoms] AD," the authors conclude.

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