Authors and Disclosures

Journalist

Emma Hitt, PhD

Emma Hitt is a freelance editor and writer for Medscape.

Disclosure: Emma Hitt, PhD, has disclosed no relevant financial relationships.
Dr. Hitt does not intend to discuss off-label uses of drugs, mechanical devices, biologics, or diagnostics not approved by the FDA for use in the United States.
Dr. Hitt does not intend to discuss investigational drugs, mechanical devices, biologics, or diagnostics not approved by the FDA for use in the United States.

From Medscape Medical News

TNF Inhibitors Associated With Decreased Risk for AD in RA

Emma Hitt, PhD

November 17, 2010 (Atlanta, Georgia) — Tumor necrosis factor (TNF) inhibitor therapy reduces the risk of developing Alzheimer's disease (AD) in patients with rheumatoid arthritis (RA), according to the results of a nested case–control study.

Richard C. Chou, MD, PhD, from Dartmouth-Hitchcock Medical Center in Milton, Massachusetts, and colleagues presented the findings here at the American College of Rheumatology 2010 Annual Meeting.

The study investigated the relation between various RA treatments and AD. "Our study showed that RA patients are more likely to have dementia," Dr. Chou told *Medscape Medical News*. "Anti-TNF therapy is the only treatment modality that will lower the risks for AD."

A cohort of 42,193 patients with preexisting RA was derived from medical and pharmacy claims data from January 2000 to November 2007. From this set, 165 patients with AD (cases) were matched for age, sex, length of exposure, assessment period, and methotrexate treatment to 1383 control patients without AD.

Exposure to several RA therapies was analyzed, including sulfasalazine, prednisone, rituximab, and 3 anti-TNF agents (infliximab, etanercept, and adalimumab).

The study found that anti-TNF therapy significantly decreased the risk of developing AD in patients with RA (adjusted odds ratio, 0.440; 95% confidence interval [CI], 0.223 - 0.868; *P* = .0178), whereas other agents used to treat RA did not. Similar results were observed after adjustment for the covariates of hypertension, hyperlipidemia, diabetes mellitus, peripheral vascular disease, and coronary artery disease (adjusted odds ratio, 0.448; 95% CI, 0.225 - 0.892; *P* = .0222).

"Our study shows how a systemic immunosuppressive therapy for RA with anti-TNF agents can lower the risk of a local process of AD in the central nervous system in RA patients," said Dr. Chou. He added that "it raises new

questions about the mechanisms and therapy for AD."

Independent commentator Edward Tobinick, MD, medical director at the Institute for Neurological Research, a privately funded medical research and clinical center in Los Angeles, California, and assistant clinical professor of medicine at the University of California at Los Angeles, has been a pioneer in the use of locally (as opposed to systemically) delivered etanercept for the treatment of AD for several years.

"Dr. Chou's study showed that the risk of Alzheimer's in [RA] patients was decreased through the use of other anti-TNF agents, although etanercept appeared to be the most effective, with a decrease in Alzheimer's risk of 70%," he told *Medscape Medical News*.

"What our work shows and what Dr. Chou's work shows is that TNF is centrally involved in the pathogenesis of [AD]," Dr. Tobinick explained, "although we used a perispinal method of administration, not the systemic method that was studied in Dr. Chou's trial. It's different."

According to Dr. Tobinick, RA is associated with elevated levels of TNF in the periphery, whereas AD is associated with elevated levels of TNF in the cerebrospinal fluid.

"It may be that the systemic administration of these anti-TNF molecules is affecting the systemic levels of TNF," he said. "Potentially, the risk of the disease could be affected by changes in systemic levels of TNF in patient populations, such as those with rheumatoid arthritis, that are known to have elevated levels of TNF in the periphery."

Dr. Chou has disclosed no relevant financial relationships. Dr. Tobinick reports holding multiple issued and pending patents detailing methods of using etanercept and other anti-TNF biologics for neurological indications.

ACR 2010 Annual Meeting: Abstract 640. Presented November 8, 2010.