Anti-TNF-Alpha Tied to Lower Heart Risk in RA

BY DIANA MAHONEY

DESTIN, FLA. — The benefits of tumor necrosis factor blockade extend beyond the joints to the hearts and minds of rheumatoid arthritis patients, Dr. Iain McInnes reported at the Congress of Clinical Rheumatology.

Findings from two new studies suggest that anti-TNF treatment can inhibit the cytokine-induced chain of events that leads to the increased risk of cardiovascular disease and clinical depression in RA.

Along with lead investigator Dr. Mike J.L. Peters of VU University Medical Center in Amsterdam, Dr. McInnes and colleagues at the University of Glasgow (Scotland) have shown, for the first time, that anti-TNF-alpha therapy decreases circulating levels of the cardiac neurohormone N-terminal prohormone brain natriuretic peptide (NT-proBNP) in patients with rheumatoid arthritis (RA) who do not have evident heart failure.

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Major Findings: TNF-alpha blockade resulted in an 18% reduction in levels of NT-proBNP, a biomarker for heart failure, as well as altered serotonin transporter availability, affecting depression.

Data Source: Two studies of 171 and 6 patients.

Disclosures: Dr. McInnes has financial ties with Schering-Plough, Roche, Bristol-Myers Squibb, and Wyeth and has served as a consultant for Schering-Plough and Roche.

Previously identified as a clinically relevant biomarker for heart failure, NT-proBNP is independently associated with cardiovascular risk. Thus, the observed reduction in NT-proBNP suggests a "potential beneficial effect of [TNF-alpha] blockers with respect to vascular risk and ventricular function in rheumatoid arthritis," Dr. McInnes said.

The study measured serum NT-proBNP at baseline and after 16 weeks of biweekly adalimumab treatment in 171 consecutive RA patients without heart failure (Ann. Rheum. Dis. 2010 April 7 [doi:10.1136/ard.2009.119412]). After week 16, the investigators observed an approximately 18% reduction in NT-proBNP levels, providing biological evidence that TNF-alpha blockade does not worsen ventricular function in patients with RA who do not have prevalent heart failure, and supporting epidemiologic findings that indicate it may reduce overall cardiovascular risks in these patients, Dr. McInnes said.

In a separate study, Dr. McInnes and colleagues sought to assess the functional effects of anti-TNF-alpha therapy on the brains of depressed patients with RA, and determined that TNF-alpha blockade mediates altered serotonin transporter availability and induces an improvement in depression measures.

"This is critically important," Dr. McInnes stressed, referring to a 2006 report suggesting that the prevalence of major depressive disorder exceeds 40% in RA patients (Rheumatology [Oxford] 2006;45:1325-7).

Findings from earlier research have shown that proinflammatory cytokines can increase the density and activity of the serotonin transporter (SERT), a primary target for antidepressant therapy. On that basis, Dr. McInnes and his associates hypothesized that TNF blockade might be associated with altered SERT activity in RA patients, he said. They tested this hypothesis in a clinical, proof-of-concept study by measuring SERT density using SPECT (single-photon emission CT) in six patients with seropositive RA 2 weeks before the initiation of adalimumab therapy and 4 days after the last treatment, he said.

After anti-TNF-alpha therapy, "there was a significant decrease in the [SERT] density in all of the patients," as well as overall improvements in physical and mental functioning, Dr. McInnes said.

Although it is yet unclear whether the observed SERT alterations are specific to RA or are related to cytokine action in general, "the findings provide important insight into the biology linking clinical depression and rheumatoid arthritis." If confirmed in larger studies, the findings may offer guidance for developing treatment strategies, he said. ■