# Septic Arthritis Risk Raised With Anti-TNF Use

BY DENISE NAPOLI

PHILADELPHIA — Septic arthritis was twice as likely to occur in patients taking anti–tumor necrosis factor drugs for rheumatoid arthritis as in patients with the disease who did not take anti-TNFs.

However, the results may not be fully translatable to a U.S. population of RA patients, according to Dr. Deborah P. Symmons, who presented the findings during a press briefing at the annual meeting of the American College of Rheumatology.

In the United Kingdom, she explained, patients must have failed two disease-modifying antirheumatic drugs and have a high disease activity score in order to be eligible for treatment with TNF blockers. "Those people may have more serious disease" than do patients who take these agents in the United States, said Dr. Symmons, professor of rheumatology and musculoskeletal epidemiology at the University of Manchester (England).

Dr. Symmons and her associates studied the records of 11,757 RA patients from the British Society for Rheumatology Biologics Register who received anti-TNF drugs from October 2001 through May 2008. Patients were followed for 6 months or until death. Septic arthritis was counted in all patients who received that diagnosis either while taking anti-TNFs or within 90 days of their last dose.

A comparison group of 3,515 patients with active RA who were taking only DMARDs was also followed.

According to Dr. Symmons, 179 cases of septic arthritis that met study criteria occurred during the study period, for an incident rate of 1 per 200 patients (5 cases per 1,000 patient-years). In contrast, among the DMARD-only control group, there were

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there were 17 cases of septic arthritis, for an incidence of 1.9 cases per 1,000 patient-years.

That amounted to a hazard ratio for contracting septic arthritis of 2.0 for the anti-TNF patients, compared with controls (95% confidence interval, 1.1-3.5) after adjustment for age, sex, disease severity, prior joint replacement, comorbidity, and steroid use.

The investigators reported that 51% of septic arthritis cases occurred in patients' "native" joints (that is, not prosthetic joints), which are generally considered to have a higher risk of septic arthritis. However, "in both groups, having a replaced joint increased the patient's risk for an infection, but that risk was not further increased by use of an anti-TNF drug," Dr. Symmons said.

**Compared with controls, patients on anti-TNF agents had a 2.0 hazard ratio for contracting septic arthritis.**

DR. SYMMONS

The risk was highest with the use of etanercept, compared with infliximab and adalimumab.

Staphylococcus bacteria caused half of the infections in the DMARD group and 75% of infections in the anti-TNF group.

Dr. Symmons, along with one other researcher on the study, reported affiliation with the British Society for Rheumatology, on whose registry data the study was based. The researchers wrote that they had no other conflicts to disclose. ■

# Anti-TNF Drugs Tied to Skin Cancer

BY DENISE NAPOLI

PHILADELPHIA — Two studies showed an increased risk for nonmelanoma skin cancer in rheumatoid arthritis patients who take anti–tumor necrosis factor therapies, and should prompt evaluation of the use of these drugs in patients at risk for skin cancer, according to the researchers.

Previous studies have been too small to show a definitive link between biologic therapy for RA and skin malignancy, although RA previously has been well established as a risk factor for skin cancer, Dr. Prahba Ranganathan said.

She presented the results of her retrospective cohort study of RA patients in the Department of Veterans Affairs national database at the annual meeting of the American College of Rheumatology.

Among 16,829 patients with RA, 3,096 were treated with anti-TNF drugs at VA medical centers between Oct. 1, 1998, and Sept. 30, 2006. The incidence of nonmelanoma skin cancer was 25.9 per 1,000 patient-years in this cohort, compared with 19.6 per 1,000 patient-years in the biologic-naive cohort, a 34% increased risk.

The incidence of melanoma also was increased by about 50%, with about 3.7 cases per 1,000 patient-years seen in the anti-TNF-treated group vs. 2.6 cases per 1,000 patient-years in the biologic-naive cohort. Both results were significant.

A second study presented at the press conference mirrored these findings. Dr. Kimme Hyrich of the University of Manchester (England) looked at RA patients from the British Society for Rheumatology's biologics register, a prospective cohort study begun in 2001 to monitor the long-term safety of anti-TNF agents.

Dr. Hyrich found that among 11,598 RA patients who were treated with anti-TNF drugs and had no prior nonmelanoma skin cancer, the incidence of a malignancy was 3.5 per 1,000 patient-years. In contrast, among 8,975 similar patients who were treated with nonbiologic therapies, the incidence of new nonmelanoma skin cancers was 2.4, for a 70% increased risk for the anti-TNF–treated patients, although the data were not significant, Dr. Hyrich reported. Dr. Hyrich pointed out that patients treated with anti-TNF drugs typically have more contact with their physicians, which could have introduced a surveillance bias.

Dr. Ranganathan cautioned that even for patients who have multiple skin cancer risks, anti-TNF agents are still a good choice for patients who have failed other treatments.

"People with risk factors should be watched more closely and maybe have periodic skin exams," she said, adding, "I don't think [having risk factors] would be an absolute contraindication."

Dr. Ranganathan, Dr. Hyrich, and their respective research teams did not have any financial disclosures. ■