TNF Blockers' Infection Risk Greatest in First Year

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AMSTERDAM — Rheumatoid arthritis patients on a tumor necrosis factor antagonist in clinical practice have an increased rate of hospitalization for serious, non-TB infections, but that risk appears to be considerably less than previously reported, Dr. Lars Klareskog said at the annual European Congress of Rheumatology.

Moreover, the Swedish national clinical experience indicates that the rate of hospitalization for serious infections doesn't escalate with increasing time spent on the tumor necrosis factor (TNF) inhibitor. The risk is greatest during the first year; thereafter, it drops off and remains fairly static, according to Dr. Klareskog, professor of rheumatology at the Karolinska Institute, Stockholm.

He presented data from the Swedish Biologics Register, a national population-based registry of all patients on a TNF inhibitor for rheumatoid arthritis (RA). The analysis included 2,465 patients given a TNF inhibitor during 1999-2003. The comparison group consisted of 35,450 Swedish RA patients not treated with an anti-TNF agent; this group included historical controls treated for RA as early as 1964.

It's widely recognized that anti-TNF therapy increases the risk of TB. But that risk remains small, on the order of 0.1 case per 100 person-years on the drug.

Of much greater practical concern is the potential for increased risk of other, more common serious infections. That risk has not been well defined. Some relatively small observational studies have quoted a twofold elevation in risk, while others have found no increase.

A recent metaanalysis of randomized clinical trials reported a twofold increased risk of serious infection in RA patients on TNF inhibitors (JAMA 2006;295:2275-85). However, those trials were of relatively short duration and included a narrow spectrum of patients.

The new analysis of Swedish registry data was designed to help clarify the picture using a large real-world patient experience, Dr. Klareskog said at the meeting, which was sponsored by the European League Against Rheumatism.

The rate of hospitalization for serious infection did not escalate with increasing time on the drugs.

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With 253 hospitalizations for infection in Swedish patients during 4,471 person-years of therapy with their first TNF inhibitor, the crude rate of infection was 5.7 per 100 person-years, compared with 5.3 per 100 person-years in patients not treated with a TNF antagonist. After adjustment for sex, age, comorbidities, and propensity for hospitalization, patients on their first TNF inhibitor had a significant 28% increased relative risk of hospitalization for serious infection, compared with RA patients who had never taken a TNF antagonist.

In the smaller group of 528 patients on their second TNF inhibitor because their first was ineffective or poorly tolerated, the hospitalization rate for infection was 7.1 per 100 person-years. This represented an adjusted 64% increase in relative risk over that of RA patients who never received a TNF antagonist.

No particular type of infection predominated; the risks of hospitalization for skin, articular, bloodstream, and other infection sites were similarly increased in users of TNF antagonists. The data revealed no big surprises. These data fill out the picture of the risks associated with these agents in real-world practice. ■

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