TNF Blocker Registry Tracks Legionellosis, TB Risk

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VERSAILLES, FRANCE — A preliminary report from a French registry collecting severe reactions to anti–tumor necrosis factor–α therapy suggests that patients may be at greater risk than realized of developing legionellosis and tuberculosis.

"What was most surprising was the 13 cases of legionellosis," investigator Dr. Florence Tubach said at the 12th European Pediatric Rheumatology Congress. "[This] was quite unexpected."

Dr. Tubach of Hôpital Bichat in Paris reported on the first 137 cases in the multidisciplinary RATIO (Recherche Anti-TNF Infections Opportunist) registry, which began accepting cases on Feb. 1, 2004. Four hundred eighty-six French centers have agreed to report severe infections and lymphomas in patients on TNF-α antagonists to the project, which is soliciting information quarterly.

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The patients recorded so far have had 60 severe bacterial infections and 63 opportunistic infections (including 20 TB, 15 virosis, and 13 legionellosis). They also had 13 cases of lymphoma, and one of myeloma, Dr. Tubach said.

Rheumatoid arthritis was the most common underlying disease, occurring in 98 patients. The next most common underlying conditions were ankylosing spondylitis in 17 patients and Crohn's disease in 7 patients. Eight other diseases accounted for the remaining cases. Only two of the patients were children.

Dr. Tubach warned against making assumptions based on the number of patients who were taking infliximab, etanercept, or adalimumab. "We must be cautious with these numbers because we are in very small numbers, and infliximab has been available a long time, and adalimumab for only a short time," she said.

The median duration of anti-TNF therapy when patients presented with TB was 26 weeks, with a range of 2-173 weeks, Dr. Tubach reported in a presentation on the first 13 cases of TB. "Despite preventive guidelines TB is a persistent risk, complicating anti-TNF therapy," she said. "TB may occur later than previously reported."

Before starting anti-TNF therapy, all but 2 of the 13 patients who became infected had intradermal tuberculin tests. The results were less than 5 mm in six patients, 5-10 mm in four patients, and more than 15 mm in one patient, Dr. Tubach said.

Though five patients had a history of exposure to TB, she said none had a personal history of TB, and no one received any chemoprophylaxis against TB. All had normal chest x-rays.

Based on these findings, she said France has decided to modify guidelines for prevention "to include in the definition of latent TB patients with a history of exposure to TB." Authorities have also decreased the cut-off for positivity on the intradermal tuberculin test to 5 mm, she said.

The lymphoma cases included four Hodgkin's lymphomas, five diffuse large B-cell lymphomas, three T-cell lymphomas, and one mucosa-associated lymphoid tissue (MALT) B-cell lymphoma. Physicians detected Epstein-Barr virus in one Hodgkin's patient.

Dr. Tubach described the registry as "a good example of partnership between scientific societies, manufacturers, and the national authorities." It is supported by a grant from the three manufacturers of anti-TNF-α drugs: Abbott, Schering-Plough, and Wyeth.

Since one of the goals is to identify risk factors for infection, Dr. Tubach said that the investigators plan to match each case in which infection is reported with two controls. One would be a patient who never received anti-TNF-α therapy. The other would be a patient who had taken one of the drugs, and stopped without becoming infected.

In response to an audience question, she said the registry is not prepared to give information on incidence of infection because it only collects information on patients who meet the inclusion criteria. ■