Methotrexate Combo Prolongs Anti-TNF Use

BY HEIDI SPLETE

FROM ANNALS OF THE RHEUMATIC DISEASES

Patients who received methotrexate in combination with other disease-modifying antirheumatic drugs were significantly more likely to remain on anti–tumor necrosis factor therapy than were patients who received methotrexate monotherapy or other DMARDs without methotrexate, based on data from more than 10,000 patients in the British Society for Rheumatology Biologics Register.

Previous studies have examined the impact of DMARDs on the continuation of anti-TNF therapy, but most of these did not compare the effects of specific DMARDs, said Dr. Moetaza M. Soliman of the University of Manchester (England) and colleagues (Ann. Rheum. Dis. 2011 Feb. 17 [doi:10.1136/ard.2010.139774]).

After 5 years of follow-up, patients who received methotrexate (MTX) in combination with either sulfasalazine or hydroxychloroquine or a combination of the two agents were significantly less likely to discontinue anti-TNF therapy, compared with those who received MTX alone. The adjusted hazard ratios were 0.76, 0.81, and 0.80, respectively, compared with methotrexate alone.

Patients who received no DMARDs were 40% more likely to discontinue anti-TNF, compared with those who received MTX. Patients who received leflunomide or sulfasalazine were 41% and 23% more likely, respectively, to discontinue anti-TNF therapy, compared with those who received MTX.

The study population included 3,339 patients receiving no DMARDs, 4,418 on MTX, 610 taking leflunomide, 308 receiving sulfasalazine, 902 on MTX plus sulfasalazine, 401 taking MTX plus hydroxychloroquine, and 418 on MTX plus a sulfasalazine and hydroxychloroquine combination. The average age of the patients was 56 years, and the average disease duration was 13 years.

The results were similar when the researchers controlled for reasons for discontinuation, including adverse events and lack of efficacy. The results support the use of MTX alone or in combination with other DMARDs as a way to extend compliance with anti-TNF therapy, the researchers noted. ■

VITALS

Major Finding: Methotrexate combined with other DMARDs prolonged anti-TNF therapy adherence in rheumatoid arthritis patients

Data Source: A prospective, observational cohort study of 10,396 adults with RA.

Disclosures: The study was funded by the British Society for Rheumatology, which receives some income from pharmaceutical companies including Abbott Laboratories, Amgen, Roche, Schering-Plough, and Wyeth Pharmaceuticals.

EULAR Issues Vaccine Guidance for Adults With AIIRDs

BY HEIDI SPLETE

FROM ANNALS OF THE RHEUMATIC DISEASES

Inactivated flu vaccine is an option for patients with autoimmune inflammatory rheumatic diseases, but any vaccination should occur during periods of stable disease, according to new recommendations from the European League Against Rheumatism.

Patients with autoimmune inflammatory rheumatic diseases (AIIRDs) are at increased risk for infections, but vaccination can cause flares of the disease, wrote Dr. Sander van Assen of the University Medical Center Groningen (the Netherlands), and colleagues. To help rheumatologists make informed decisions about patient vaccinations, EULAR convened a task force that developed 13 evidence-based recommendations (Ann. Rheum. Dis. 2011;70:414-22).

"For the most part, such recommendations have been lacking and the field has been changing very quickly as new drugs are developed and roll into the marketplace," according to infectious disease specialist Dr. Kevin Winthrop of the Oregon Health and Science University in Portland.

"New drugs and new vaccines make these recommendations a moving target, and it was extremely important for the expert group to sit down, review the latest data, and codify their thoughts.

"For the most part, there is a lack of data regarding the efficacy and utility of many of these vaccines in these patients, and it is often unclear how their immunosuppressive medications and underlying diseases affect vaccine responsiveness.

"With certain biologics, we know that some vaccines are diminished in their immunogenicity and it is important to clarify for physicians when these vaccines can and should be given," he said. The expert committee members represented 11 European countries.

They reviewed studies from 1966 through October 2009, as well as abstracts presented at EULAR in 2008 and 2009 and at the American College of Rheumatology annual meeting in 2007 and 2008.

Their evidence-based recommendations on the use of vaccination in adults with AIIRDs include:

► Assess vaccination status of an AIIRD patient at an initial work-up.

► Vaccinate patients during times of stable disease whenever possible.

► Avoid live, attenuated vaccines whenever possible in immunosuppressed patients.

► Vaccinate patients before starting B-cell–depleting biologic therapy if possible, but vaccines can be given during the use of DMARDs and TNFi agents.

► Strongly consider inactivated flu vaccine for patients with AIIRD.

► Strongly consider PPV23 (23-valent pneumococcal polysaccharide vaccination) for AIIRD patients.

► Vaccinate AIIRD patients for tetanus toxoid in accordance with recommendations for the general population.

► Consider herpes zoster vaccination in AIIRD patients.

► Consider human papillomavirus vaccination for selected patients with AIIRD (young women with systemic lupus erythematosus up to age 25 years).

► Vaccinate hyposplenic or asplenic patients who have AIIRD with vaccines for influenza, pneumococcal, *Haemophilus influenzae* type b, and meningococcal C.

► Vaccinate only at-risk AIIRD patients for hepatitis A and/or hepatitis B.

► Vaccinate traveling AIIRD patients according to the general rules for travelers, but avoid the use of live, attenuated vaccines whenever possible in those patients who are immunosuppressed.

► Do not vaccinate AIIRD patients with the BCG vaccine.

In an interview with RHEUMATOLOGY NEWS, Dr. Winthrop noted that the "EULAR statement includes a thoughtful discussion of needed research.

"Clearly, we need better information regarding the risk of vaccine-preventable diseases in this population, as well as the outcomes of such infections and how these outcomes are modulated by certain immunosuppressive therapies [that are used in patients with AIIRDs].

"Such research would help better clarify the potential benefits of vaccination.

"On the adverse event side, further research is certainly necessary to better understand the risk of such vaccines (particularly live vaccines) and how that risk is modulated by immunosuppressive therapies, most notably biologic therapies.

"Lastly, studies evaluating the safety and efficacy of new vaccines [such as zoster vaccine and the new conjugated pneumococcal vaccine PCV13] in the context of existing and new biologic therapies remains an important area of study," Dr. Winthrop noted.

The study that produced the guidelines was funded by the European League Against Rheumatism. The researchers had no financial conflicts to disclose. Dr. Winthrop said he had no relevant financial disclosures to make. ■

VIEW ON THE NEWS

Zoster Vaccine Needs Evaluation in AIIRD

Because of the immune dysregulation seen inpatients with AIIRD, some vaccine-preventable infections seem to be more common or more severe. Yet the immunosuppressive therapies given to these patients can blunt the vaccine efficacy or, theoretically, be associated with primary infection from certain live and attenuated vaccines. There is only a limited amount of information obtained in the controlled-trial setting to provide guidance. Hence, a structured review of published data with expert discussion is of value in helping to provide guidance as to when specific vaccination is either appropriate or should be avoided. This is a common question from our patients: "Should I get [a specific vaccine]?"

The likelihood of a patient's getting a severe infection without having gotten a vaccine, the degree of immunosuppression, and the safety of the vaccine are all factors that rheumatologists should consider when counseling patients about vaccinations. Influenza and pneumococcal vaccine decisions are easy: Efficacy may be blunted in some settings, but the vaccines are safe and any potential efficacy would be beneficial. A decision to vaccinate patients who are about to receive rituximab must take into consideration the data that B-cell–directed therapy clearly lowers the efficacy of the vaccine, so vaccination ideally should be given prior to this therapy. This takes some planning and careful review of the patient's vaccination history in advance. We need outcome-based studies of clinical, not just serologic, efficacy of certain vaccines in the setting of immunosuppression. I would particularly like to see formal studies on safety and efficacy of the zoster vaccine.

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