Rituximab Seems Safe in RA Lung Disease

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FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

To date, no new significant safety signals associated with rituximab therapy in patients with severe rheumatoid arthritis who also have lung disease have been identified in an ongoing observational study of such patients, according to Dr. Shouvik Dass.

Overall, the incidence of serious infections has been low and is about what would be expected in these patients, who already have significant comorbidity because of longstanding RA and preexisting lung disease, said Dr. Dass, of the department of rheumatology, University of Leeds (England).

Because interstitial lung disease and various other lung diseases are more common among patients with RA, they may be considered contraindications to treatment with anti–tumor necrosis factor therapy, because of reports that the anti-TNF agents may cause, or at least may be associated with, major deteriorations in interstitial lung disease. Although these data are not definitive, as a result, the use of rituximab – a CD20-directed cytolytic antibody – may be increasing among patients with RA and pulmonary disease, said Dr. Dass.

"The effect of biologic therapies as a whole on lung disease is not completely clear," he said in an interview. He also referred to data – mostly case reports– in the hematologic literature associating rituximab with worsening lung disease.

He and his associates reviewed the records of 67 patients with RA and concomitant lung disease who were treated with rituximab between 2004 and 2010 at their center, which he said has one of the largest single cohorts of RA patients treated with rituximab. The patients' mean age was 60 years and most (56) were female. The most common pulmonary diagnosis was interstitial lung disease (ILD) in 48 patients; 14 patients had chronic obstructive pulmonary disease (COPD), and 5 patients had bronchiectasis; 2 patients also had had a previous pulmonary empyema.

All patients received two infusions of 1,000 mg rituximab with methylprednisolone per course, which was repeated when RA became active again, at intervals of no less than 6 months. Half of the patients received at least two treatment cycles.

Over a median of about 2 years of follow-up (the range was about 8 months to 6.5 years) after treatment with rituximab, there were three deaths among these patients: 2 of the 48 patients with ILD and 1 of the 14 patients with COPD. The patient with COPD died of an infective COPD exacerbation 12 months after the third cycle of rituximab. One of the patients with ILD died of pneumonia and possible acute progression of ILD, Dr. Dass said, noting that clinical and CT changes attributable to either condition were observed 4 weeks after the patient had been treated with the first cycle of rituximab. Suicide was the cause of death in the second patient with ILD, 3 months after treatment with the first course of rituximab. Another three patients had a single episode of serious respiratory tract infection, which required hospital admission or treatment with intravenous antibiotics.

Based on these cases, there were no definite new significant safety signals that were observed "beyond that which might be expected in this group of patients with longstanding severe RA and concomitant lung disease," Dr. Dass said.

However, he pointed out that the one death caused by respiratory deterioration was temporally related to rituximab therapy.

"B-cell depletion is now an important therapy for RA, and therefore this study aims to add insight into the safety and practical usage of rituximab," he noted in the interview. "We hope to encourage ongoing review and follow-up of such patients."

In the United States, rituximab is marketed as Rituxan by Genentech, a member of the Roche Group, and is a registered trademark of Biogen Idec.

Dr. Dass and two of his six coauthors disclosed that they are consultants for Roche. Dr. Dass received an award from EULAR for this research. ■