Statin Use May Limit Effect of Rituximab in RA

Investigators: this is the first study to show a significant interaction of statins and rituximab.

BY SHARON WORCESTER

FROM THE ANNALS OF RHEUMATIC DISEASES

Statins can inhibit the beneficial effects of rituximab on disease activity in rheumatoid arthritis patients, according to a study of 187 patients from the Dutch Rheumatoid Arthritis Monitoring registry.

After 6 months of treatment, the mean reduction in disease activity score using 28 joint counts (DAS28) was lower in 23 of 187 RA patients who were treated with both statins and rituximab (RTX) than in 164 patients treated with RTX alone (mean reduction of 0.5 vs. 1.0 point).

Compared with patients taking just rituximab, those taking a statin in addition to the biologic agent experienced a shorter period of rituximab efficacy (9 months vs. 7 months).

The difference was of borderline statistical significance after adjustment for age, sex, baseline DAS28 score, and rheumatoid factor positivity, Dr. E.E.A. Arts of Radboud University Nijmegen (the Netherlands) Medical Center and colleagues reported.

Compared with the RTX-only patients, those exposed to statins also had a shorter effective period following RTX treatment (median of 9 months vs. 7 months), and were more likely to experience a failure event (hazard ratio, 2.3), after adjustment for the same confounders, the investigators said (Ann. Rheum. Dis. 2010 Oct. 18 [doi:10.1136/ard.2010.136093]).

All of the patients who participated in the DREAM registry were included in the prospective cohort study, and all received 50 mg of prednisone with the first RTX infusion.

Patients in both the RTX plus statin and the RTX-only groups had similar DAS28 scores at baseline.

The statin group was older (mean age, 66 vs. 58 years) and included a greater proportion of men than the RTX-only group (48% vs. 20%), but the groups were otherwise similar in demographic characteristics.

Although the study had a small sample size, it was sufficiently powered and showed a clinically relevant difference in DAS28 score changes over the 6-month study period, noted the investigators, who added that lack of randomization was another limitation of little concern, because "confounding by indication is unlikely."

More studies to replicate these findings and measure the magnitude of the effect are needed, they said.

"Significant interactions of statins with RTX in RA have not previously been shown.

"A critical review of common practice regarding concomitant use of statins in RTX-treated patients with RA is needed," according to Dr. Arts and co-investigators. ■

VITALS

Major Finding: After 6 months of treatment, the mean reduction in disease activity score using 28 joint counts (DAS28) was lower in 23 of 187 RA patients who were treated with both statins and rituximab (RTX) than in 164 patients treated with RTX alone (mean reduction of 0.5 vs. 1.0 point).

Data Source: A prospective cohort study involving 187 patients from the DREAM registry.

Disclosures: The DREAM registry is funded by the Dutch affiliations of Wyeth Pharmaceuticals, Abbott Laboratories, Schering-Plough, Roche Pharmaceuticals, UCB Pharma, and Bristol-Myers Squibb.

Statin Use Linked to 57% Reduction in Knee OA Incidence

BY MITCHEL L. ZOLER

FROM THE WORLD CONGRESS ON OSTEOARTHRITIS

BRUSSELS – Statin therapy may exert yet another beneficial clinical effect – preventing development of knee osteoarthritis and slowing its progression – based on an analysis of more than 3,000 people who were enrolled in a prospective cohort study.

In an analysis of people in the Rotterdam Study, statin use was significantly linked with a more-than-50% reduced rate of knee osteoarthritis (OA) incidence, and a more-than-50% reduced rate of knee OA progression after adjustment for several baseline risk factors, Dr. Stefan Clockaerts said at the congress.

In contrast, statin use had no significant impact on the incidence or progression of hip OA.

The findings suggest that knee OA may be at least partly a metabolic disease, said Dr. Clockaerts of Erasmus University, Rotterdam, the Netherlands, and the University of Antwerp (Belgium).

"We think that there is a difference in the pathogenesis of hip and knee osteoarthritis, and that several systemic factors – such as cholesterol, body mass index, and diabetes – appear to influence knee osteoarthritis" but not deterioration of the hip, Dr. Clockaerts said in an interview.

"Our idea is that metabolic alterations are more important for knee osteoarthritis than for hip osteoarthritis."

For example, Dr. Clockaerts cited prior reports that cholesterol may have a damaging effect on cartilage, and it may increase the formation and activity of bone marrow lesions. "Cholesterol is probably not good for knee osteoarthritis," he said. Synovial fluid contains cholesterol, and statin treatment would reduce the level.

A key difference in the pathogenesis of knee and hip OA is that that knee OA may be at least partly a metabolic disease, judging from these findings.

An additional hypothesis is that vascular pathology may contribute to the OA disease process, and that the beneficial effects of statin treatment on atherosclerosis and vascular function may also link statins and knee OA. The anti-inflammatory effect of statins most likely also plays a role.

"The systemic and intra-articular anti-inflammatory effects of statins are the most plausible explanations for the effect," Dr. Clockaerts said.

The Rotterdam Study began in 1990 and enrolled 7,983 men and women aged 55 years or older into a longitudinal cohort study.

The analysis by Dr. Clockaerts and his associates focused on participants with knee and hip x-rays that were available from baseline and follow-up and were evaluable for scoring on the Kellgren-Lawrence (KL) scale. They excluded study participants with a history of rheumatoid arthritis, gout, ankylosing spondylitis, or a leg fracture that was treated with a prosthesis.

Information on statin use came from computerized pharmacy records for the Rotterdam suburb where participants lived. The analysis considered to be a statin user anyone who received a statin prescription for at least 100 days for at least 50% of the drug's recommended daily dosage.

They identified incident OA of the knee or hip in people with a baseline KL score of 0 or 1 that subsequently became 2 or greater.

They defined a case of OA progression to be a person with a baseline KL score of 1, 2, or 3 whose score later increased by at least 1 point. Average follow-up was 6 years.

The analysis showed that among 3,056 people who were evaluable for incident knee OA, statin users had a statistically significant, 57% reduced rate of knee OA, compared with nonusers, after adjustment for baseline age, diabetes, BMI, total cholesterol:HDL cholesterol ratio, and bone mineral density, said Dr. Clockaerts at the congress, which was presented by the Osteoarthritis Research Society International. (See box.)

Progression of knee osteoarthritis among 1,412 people with a baseline KL score of 1-3 occurred 53% less often in the statin users, compared with nonusers after adjustment for age, BMI, and BMD, which was a statistically significant difference.

The analysis did not look at the impact of specific statin types.

A similar analysis showed no significant interaction of statin use and the incidence of new-onset or progressing hip OA in more than 4,000 people who were evaluable for one of these end points, according to Dr. Clockaerts.

Further studies should directly test a statin's effect in an animal model for OA, such as the STR/ort mouse, which also shows metabolic derangements, he said.

Dr. Clockaerts said that he had no disclosures. ■