Statins May Aid Arthritis Patients With High CRP

BY SALLY KOCH KUBETIN

NEW YORK — Patients with rheumatoid arthritis and elevated C-reactive protein levels would be likely to benefit from treatment with a statin to lower their CRP levels and consequently their risk for a cardiovascular event, regardless of their cholesterol levels, according to Dr. Jeffrey Greenberg.

This insight comes from a review of data from the 2008 JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) study of almost 18,000 people, all of whom had high-sensitivity CRP (hs-CRP) levels above 2 mg/L, but relatively normal LDL cholesterol levels of less than 130 mg/dL. They were randomized to either 20 mg rosuvastatin or placebo.

The trial planned to run 5 years, but it was stopped after 2 years when the statin dropped LDL cholesterol levels by 50% on average, while CRP levels dropped by 37%. Of clinical note, the patients on the statin had significantly fewer episodes of nonfatal myocardial infarction, any MI, nonfatal stroke, and any stroke (N. Engl. J. Med. 2008;359:2195-207).

Although, strictly speaking, the findings from JUPITER cannot be extrapolated to rheumatoid arthritis patients, "clinical trials of this magnitude are rarely conducted in RA populations," noted Dr. Greenberg.

Another compelling finding concerning the role of hs-CRP in increasing heart disease risk emerged after Dr. Greenberg's presentation: It was reported from the American College of Cardiology's annual meeting that JUPITER investigators doing subset analysis said that the effect of the statin on lowering the risk for cardiac events stemmed from its hs-CRP–lowering properties, rather than from its effect on cholesterol.

During his presentation, Dr. Greenberg, associate director of clinical and translational sciences in the division of rheumatology at New York University Medical Center, reviewed an earlier trial's findings suggesting that statins can act like a DMARD in RA. TARA (Trial of Atorvastatin in Rheumatoid Arthritis) involved 116 patients, randomized to placebo or 40 mg atorvastatin for 6 months. All patients were on DMARD therapy and some were taking a corticosteroid. Use of a statin reduced all components of their disease activity score, including erythrocyte sedimentation rate, hs-CRP level, swollen joint count, and plasma viscosity (Lancet 2004;363:2015-21).

Cardiovascular disease is the leading cause of death in patients with RA, and is estimated to account for 50% of mortality in that group. Mounting evidence suggests that the inflammation of the RA disease process acts on coronary vessels, increasing fatty streak deposition and contributing to the accumulation and possible rupture of plaque, Dr. Greenberg noted.

Findings from recent studies suggest that RA patients are more likely than other patients with CVD to have silent myocardial infarctions and sudden death (Arthritis Rheum. 2005;52:402-11). Another study found that RA patients who present with acute coronary syndrome may be more likely than other patients to have a second event and not to survive it (Ann. Rheum. Dis. 2006;65:348-53).

Given RA patients' increased risk for CVD and its propensity for atypical presentation, physicians must increase their vigilance to identify risk factors and intervene to lower them, he said. In addition to statin therapy, RA patients are likely to benefit from smoking cessation. Like other patients with CVD, they also should be advised to lose weight. ■

Corticosteroid-Induced Bone Loss Occurs Within 3 Months

BY PATRICE WENDLING

CHICAGO — Fracture risk increases in arthritis patients within about 3 months of starting corticosteroids and remains high, according to Dr. Nelson Watts.

"How much of this is steroids and how much of this is the underlying disease is unanswered," said Dr. Watts, an endocrinologist and director of the bone health and osteoporosis center at the University of Cincinnati.

Glucocorticoid-induced osteoporosis results from a variety of systemic effects of corticosteroids, but it's the combination of reduced bone formation and increased bone resorption that causes a "double whammy" for patients—a troubling aspect for rheumatologists, who regularly dispense corticosteroids for their patients, Dr. Watts said at a symposium sponsored by the American College of Rheumatology.

The exact dose at which corticosteroids increase fracture risk is also difficult to tease out because of the underlying disease. One study observed that fracture risk was dose dependent and significantly higher with 2.5 mg/day or more of oral prednisone, with increases of 61% in hip and 160% in vertebral fractures (J. Bone Miner. Res. 2000;15:993-1000).

"It may well be that people who need 2.5 [mg]/day of prednisone are at increased risk for fracture not because of prednisone, but because of their rheumatoid arthritis; … clearly, as the dose goes up, the risk increases," he said.

The American College of Rheumatology's current guidelines on glucocorticoid-induced osteoporosis highlight lifestyle modifications, such as calcium and vitamin D supplementation, weight-bearing exercise, and minimization of alcohol intake.

The value of calcium and vitamin D supplementation is unclear, Dr. Watts said. In a relatively small trial in 96 RA patients on prednisone, daily supplementation with 500 IU of vitamin D and 1,000 mg of calcium carbonate per day significantly improved bone mineral density, at a rate of 0.72% in the lumbar spine and

The combination of reduced bone formation and increased bone resorption causes a 'double whammy.'

DR. WATTS

0.85% in the trochanter per year, compared with losses of 2% and 0.9%, respectively, among patients on placebo (Ann. Intern. Med. 1996;125:961-8).

In four prospective studies in 173 patients who recently started corticosteroid therapy, however, bone loss occurred at a rate of 3%-5% per year, despite daily supplementation with 500-800 mg of calcium. Two other studies that Dr. Watts highlighted reported no bone loss in patients who were given up to 1,000 mg per day of calcium and up to 500 IU per day of vitamin D.

Pooled data show a significant 70% decrease in vertebral fractures with risedronate vs. placebo, Dr. Watts said. New prescribing information also shows that bone mineral density changes were significantly better with zoledronic acid than alendronate.

Dr. Watts disclosed relationships with Amgen Inc., Eli Lilly & Co., Procter & Gamble Co., Sanofi-Aventis, Novo Nordisk Inc., and Novartis Pharmaceuticals Corp., which manufactures Reclast. ■

Golimumab Approved for RA, PsA, Ankylosing Spondylitis

BY ELIZABETH MECHCATIE

Golimumab, the first once-monthly, injectable tumor necrosis factor–alpha antagonist, was recently approved for treating adults with moderately to severely active rheumatoid arthritis, active psoriatic arthritis, and active ankylosing spondylitis, based on data from five studies of more than 2,500 patients.

The Food and Drug Administration approved the TNF inhibitor for use in combination with methotrexate in patients with RA; with or without methotrexate for psoriatic arthritis; and for use alone in patients with ankylosing spondylitis. It not been approved for pediatric use. Recommended dosage (50 mg administered subcutaneously once a month) is the same for all indications.

Golimumab will be marketed as Simponi by Centocor Ortho Biotech Inc., and has been available since its approval on April 24, according to a spokesperson for the company. The annual cost of golimumab is $18,900, which is based on the list price and is comparable with the cost of other subcutaneous biologics that are used to treat these three indications, he said.

Medicare and some private insurance carriers have adopted a fourth tier of copayment that requires patients to pay 40% of the price of particularly costly drugs.

Dr. John Kay, a lead investigator in the phase II and III trials, said in an interview that "having another TNF antagonist available allows patients who are inadequate responders to one or more of the currently available TNF agents to have an alternative agent to treat their disease."

Golimumab "can be dosed less frequently, allowing the patient more flexibility," said Dr. Kay, director of clinical trials in the rheumatology unit at Massachusetts General Hospital, Boston.

Dr. Kay served as a consultant to Centocor and as a member of the steering committee for clinical trials; he was on the steering committee for the GO-AFTER (Golimumab After Former Anti-TNF Therapy Evaluated in RA) study of 461 patients who were treated previously with at least one anti-TNF-alpha treatment and had stopped treatment for various reasons.

Approval for the three indications was based on five simultaneous phase III trials of more than 2,000 patients with RA, psoriatic arthritis, and ankylosing spondylitis, which included three studies of 1,542 patients with moderately to severely active RA who had had the disease for 1-9 years.

The three RA studies were the GO-AFTER study and two other studies (one that evaluated golimumab in 637 patients who were naive to methotrexate and who had not been previously treated with a TNF-blocker, and another that evaluated golimumab in 444 patients with inadequate responses to methotrexate). In the three studies, a greater proportion of patients achieved American College of Rheumatology responses at 14 weeks (in two studies) and at 24 weeks (all three studies), compared with the proportion of patients achieving those responses on methotrexate alone.

As with other TNF blockers, the label for golimumab has a boxed warning about the risk of tuberculosis and invasive fungal infections associated with treatment, and the FDA is requiring a risk evaluation mitigation strategy to address the potential serious risks associated with golimumab. ■

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