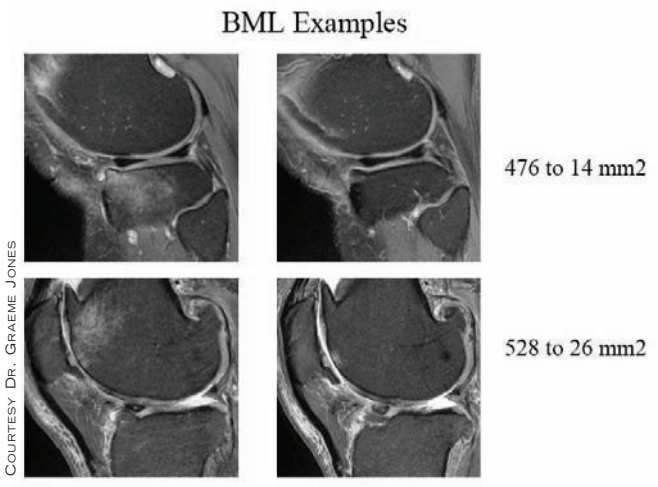

MRI knee scans from two patients taken before (left) and 6 months after treatment with zoledronic acid show shrinkage of bone marrow lesions.

COURTESY DR. GRAEME JONES

Zoledronic Acid Shrinks Bone Marrow Lesions

BY MITCHEL L. ZOLER

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

LONDON – A single 5-mg infusion of zoledronic acid, a bisphosphonate, in patients with knee osteoarthritis led to significant pain reduction and shrinkage of bone marrow lesions in a randomized, placebo-controlled study with 59 patients.

The zoledronic acid treatment led to an average 15-point drop in pain (on a visual analog scale of 0-100) beyond what occurred in the placebo group, and the active treatment was also linked with an average 170-mm^2 reduction in maximal bone marrow lesion (BML) area beyond the placebo-treated patients, which was a

VITALS

Major Finding: A 5-mg infusion of zoledronic acid given to 31 patients with knee OA and associated bone marrow lesions reduced pain by 15 points more on a visual analog scale than did placebo, and reduced maximal bone marrow lesion area by 170 mm^2 after 6 months, compared with patients who received a placebo infusion.

Data Source: A single-center, randomized study with 31 patients who received a zoledronic acid infusion and 28 patients who received a placebo infusion.

Disclosures: The study was funded by Novartis, which markets zoledronic acid. Dr. Jones said that he has received speaker fees, travel sponsorship, and research support from Novartis and several other drug companies. Dr. Conaghan said that they had no disclosures.

cut in BML area of about 37%, compared with the starting BML area, Dr. Graeme Jones said at the meeting. Dr. Jones visualizes BMLs using MRI knee scans.

"This is the first intervention shown to work on BMLs" in patients with osteoarthritis (OA), said Dr. Jones, professor of rheumatology and epidemiology and head of the musculoskeletal unit at the Menzies Research Institute Tasmania, Hobart, Australia.

"This is exciting for treating existing OA. It is one of the first positive structure modification trials," commented Dr. Philip Conaghan, professor and chairman of musculoskeletal medicine at the University of Leeds (England).

"Results from several studies have linked BMLs with pain and cartilage damage in OA patients. The larger the BML, the faster the cartilage loss and the worse the pain," Dr. Jones said in an interview. Based on studies his group has done, about 20% of BMLs that are associated with knee OA spontaneously enlarge over the course of 3 years, another 20% shrink in size, and about 60% remain the same, he said. Their earlier research findings also showed that BMLs are independently linked with fast progression of OA and the need for knee replacement. "If you reduce BMLs, it should produce good outcomes in patients," he said.

"The next step is to show that treatment with zoledronic acid not only reduces BML size but also slows cartilage loss. Sixty patients followed for 12 months were not enough to assess cartilage. We will need about 400 patients followed for 2 years," Dr. Jones added.

Despite not yet having information on cartilage effects, he said that his results so far have convinced him that treatment with zoledronic acid is reasonable for patients with painful knee OA and BMLs.

"I use it off label. Patients need to know it's off label, and they [therefore] must be willing to pay for it, but I use it. It's been shown to work, and nothing else works. Zoledronic acid [Reclast] is available, we know about its safety, and it's been used for a long time to treat osteoporosis and cancers. If you have OA patients with BMLs, this is something to actively consider for them. Patients with OA have very limited treatment options. This can make a large difference in their pain, and it has long-lasting benefit so it can be given once a year," Dr. Jones said.

The benefits of zoledronic acid that were seen in his study might be a class effect that may be replicated by treatment with another bisphosphonate, but zoledronic acid is more potent than oral bisphosphonates and hence the drug's beneficial effect on pain and BML shrinkage may exceed the effect that other bisphosphonates might have, he said.

The pain benefit appeared to start wearing off about a year after the zoledronic acid injection. Dr. Jones said that he has a small number of patients whom he has infused a second time, which produced a second round of pain reduction.

The 59 patients who were enrolled in the study had an average age of about 60 years, with an average knee pain score of about 52 on the visual analog scale; all patients had BMLs as seen on MRI scans of their affected knees. In all, 31 patients received a 5-mg infusion of zoledronic acid and 28 patients received a placebo infusion. All patients also continued their conventional pain medication regimens.

The Food and Drug Administration has approved zoledronic acid under a number of brand names to prevent or treat osteoporosis in postmenopausal women or patients who are at risk for osteoporosis because they are taking or have taken corticosteroid therapy; to manage Paget's disease; and to prevent chemotherapy-induced bone fractures or fractures in patients with multiple myeloma or cancer that has metastasized to the bones from other locations. ■