Ups Spinal BMD

Osteoporosis *from page 1*

new bone formation," said Dr. Saag, professor of medicine and epidemiology at the University of Alabama at Birmingham.

Steroids are known to have apoptosis-mediated deleterious effects on both osteocytes and osteoblasts that lead to decline in bone function and an abrupt increase in fracture risk independent of bone mineral density (BMD). Osteoclasts are also unfavorably impacted because of cross talk and the indirect effects of sex steroids, insulin-like growth factor, and a modest effect of secondary hyperparathyroidism mediated through altered calcium absorption. In addition, higher-dose steroids have adverse effects upon muscle that can independently lead to a higher fracture rate, the rheumatologist explained.

The FDA has approved alendronate, zoledronic acid (Reclast), risedronate (Actonel), and teriparatide (Forteo) for treatment of GIOP. More recently, raloxifene (Evista) has joined the ranks of agents shown to increase BMD in patients on long-term steroids; this came in the form of a double-blind, placebo-controlled, 12-month study (Ann. Rheum. Dis. 2011;70:778-84).

Subcutaneous daily teriparatide for up to 2 years also has the approval of the Food and Drug Administration for use in adults at high fracture risk because they are on sustained systemic steroid therapy.

There is no definitive study demonstrating that any of these agents actually prevents fractures in patients with GIOP. Nor is it likely such a study will be undertaken. Such trials require large numbers of patients and lengthy follow-up, and pharmaceutical companies have little incentive to mount such a costly project given that the medications are already approved for use in patients on steroids, Dr. Saag noted.

However, data from a study in which Dr. Saag was lead investigator showed that teriparatide-treated patients had significantly fewer vertebral fractures than those assigned to alendronate. The study was a 36-month randomized, double-blind, clinical trial that assessed fracture rates as a preplanned secondary end point. The radiographic and clinical vertebral fracture rates in 169 alendronate-treated patients were 7.7% and 2.4%, respectively, compared to 1.7% and 0% in 173 teriparatide-treated patients ($P = .007$ and .037). No significant difference in nonvertebral fractures was found between the two treatment arms.

The primary study end point was the change in BMD from baseline. Here again teriparatide proved significantly more effective than the bisphosphonate, with a mean 11% increase at the lumbar spine, compared to 5.3% with alendronate.

Teriparatide-treated patients also had a 5.2% increase in BMD at the total hip and a 6.3% boost at the femoral neck, compared to 2.7% and 3.4%, respectively, with alendronate (Arthritis Rheum. 2009;60:3346-55).

Confirmation of teriparatide's superior BMD-building effect came from the EuroGIOPs trial presented by Dr. Claus C. Glüer at the ASBMR meeting.

EuroGIOPS was an 18-month, open-label, phase III clinical trial in which 92 men with GIOP were randomized to teriparatide or risedronate.

Teriparatide has achieved the status of a first-line drug in the management of CIOP thanks in part to an ASBMR commentary that recommended it for high-risk patients without reservation.

At 6 months the mean increase in lumbar spine BMD was 5.7% in the teriparatide group, compared with 3.3% in the risedronate arm. At 18 months – the primary study end point – the teriparatide group averaged a 16.3% BMD increase over baseline, while the risedronate arm had a 3.8% rise.

Intriguingly, new clinical fractures occurred during 18 months of therapy in five patients on risedronate and none on teriparatide, a difference that came within a hair of statistical significance ($P = .056$).

Bone strength as formally measured in terms of anterior bending, axial compression, and axial torsion was also significantly greater in the teriparatide group, according to Dr. Glüer, who is professor of medical physics at the department of diagnostic radiology, University Hospital Schleswig-Holstein in Kiel, Germany.

The 2010 update of the American College of Rheumatology guidelines for the prevention and treatment of GIOP recommend bisphosphonates but not teriparatide for older adults at high risk of fracture who are taking less than 5 mg/day of prednisone for less than 1 month (Arthritis Care Res. 2010;62:1515-26). The ACR guidelines recommend reserving use of teriparatide for high-risk patients – that is, those with a prevalent fracture or a World Health Organization Fracture Risk Assessment Tool (FRAX) score indicative of a greater than 20% 10-year risk of a major osteoporotic fracture – who are on at least 6 mg/day of prednisone for less than 1 month or on any dose of glucocorticoids for longer than 1 month.

Although Dr. Saag was a coauthor of the ACR guidelines, he was pleased to see a new commentary on the ACR guidelines published by the Professional Practice Committee of the ASBMR. The review recommends teriparatide or any of the bisphosphonates for high-risk patients, period.

Dr. Saag, who wasn't involved in the ASBMR review, recommended it as useful reading both for its areas of agreement with the ACR guidelines as well as for raising several patient scenarios in which the ASBMR committee believes the ACR recommendations either don't apply or might be improved upon.

The ASBMR commentary also lays out a research agenda, identifying key areas for future study. For example, what's the best management strategy in lupus patients and others who may need to be on systemic steroids for a decade or more, given that teriparatide is FDA approved only for 2 years of daily use and the clinical trials of bisphosphonates for GIOPS were only 1 or 2 years long (J. Bone Miner. Res. 2011;26:1989-96).

Dr. Glüer declared having no financial conflicts regarding the Eli Lilly–funded EuroGIOPs trial. Dr. Saag disclosed that he has received research grants from and serves as a paid consultant to Amgen, Eli Lilly, Merck, and Novartis. ■

Rheumatologists Do a 'Pretty Good' Job on GIOP Therapy

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR BONE AND MINERAL RESEARCH

SAN DIEGO – Physicians overall are doing a less than stellar job of recognizing glucocorticoid-induced osteoporosis and prescribing bone-protective medications for affected or high-risk patients.

But some specialties are doing significantly better than others.

"While many rheumatologists and endocrinologists are doing a pretty good job, we know that collectively, internationally, this still continues to be a major therapeutic dilemma, and steroids still constitute the most common form of drug-induced osteoporosis," said Dr. Kenneth G. Saag.

He cited a recent as-yet-unpublished study led by University of Alabama epidemiologist Ryan C. Outman, who, together with his coinvestigators, analyzed 106,310 patients in the Medco Pharmacy database who were at high risk for glucocorticoid-induced osteoporosis (GIOP) by virtue of having received more than 90 days of systemic corticosteroid therapy during the study years of 2004-2007.

The primary study outcome was prescription of any form of anti-GIOP medication within 12 months after patients reached the 90-day mark of steroid therapy. The 12-month mark is the point on the therapeutic time line when, according to American College of Rheumatology guidelines, physicians are supposed to initiate bone-protective therapy.

The steroids were prescribed by a total of 53,766 physicians. During the 12-month window, the physicians ordered bone mineral density tests in just 4.6% of the patients, and 23.5% of patients received a prescription for an anti-GIOP medication, according to Dr. Saag, professor of medicine and epidemiology at the University of Alabama, Birmingham.

The results varied by physician specialty. In a multivariate analysis adjusted for patient age, gender, and other potential confounders, endocrinologists were 61% more likely to prescribe anti-GIOP medication for patients having more than 90 days of exposure to systemic steroids than were internists, who served as the reference standard. Rheumatologists were 59% more likely than internists to prescribe therapy.

Nephrologists, pulmonologists, and gastroenterologists were 37%, 34%, and 15%, respectively, more likely to have prescribed bone-protective medications for their at-risk patients than were internists.

Dermatologists and physicians in all other specialties who prescribed steroids for longer than 90 days were, collectively, 22% less likely to introduce anti-GIOP therapy than were internists.

Rates of prescription of anti-GIOP medications were particularly low in men of all ages and in premenopausal women. During the 12 months after more than 90 days of exposure to systemic steroids, 36.8% of affected women aged 50 years or older were prescribed bone-protective medication, compared with 11.4% of affected women under age 50 years and 14.7% of men of any age, said Dr. Saag, who was not involved in the study.

"We've got a lot of work to do in terms of initiating therapy, but adherence is a big problem, too. Less than half of patients who start on any bone-protective drug are still taking it a year later," he said.

Dr. Saag disclosed that he has received research grants from and serves as a paid consultant to Amgen, Eli Lilly, Merck, and Novartis. ■