Zoledronic Acid Now Indicated for Prevention

BY MICHELE G. SULLIVAN

Osteoporosis

BY BRUCE JANCIN

Bisphosphonates Don’t Raise Atrial Fibr Risk, Study Shows

ORLANDO — Further evidence that bisphosphonates do not really increase the risk of atrial fibrillation has come from an observational study involving more than 47,000 patients.

“Were unable to find an association between bisphosphonate therapy and atrial fibrillation. However, patients who received bisphosphonates were older and had more comorbidities and therefore were predisposed to the increased arrhythmia risk reported in other trials,” Dr. John D. Day reported at the annual meeting of the American College of Cardiology.

The study population comprised 37,485 enrollees in a Rocky Mountain health plan followed for an average of 4.6 years and 9,623 consecutive patients in a coronary angiography cohort followed up an average of 8.6 years. The 7,489 health plan enrollees on bisphosphonate therapy for osteoporosis and fracture prevention had a 37% baseline prevalence of hyperlipidemia, significantly greater than the 30% rate among plan members not on a bisphosphonate. The bisphosphonate users were older, too. Yet their rates of new-onset atrial fibrillation, MI, and all-cause mortality during follow-up were no different than nonusers’, according to Dr. Day of Intermountain Medical Center, Murray, Utah.

In the coronary angiography cohort, the patients on bisphosphonates were significantly older than were bisphosphonate nonusers, were more likely to be hypertensive by a margin of 36% to 45%, and had a 4.1% history of cardiac failure compared with 0.7% in patients not on a bisphosphonate. A prior MI was present at baseline in 12.2% of bisphosphonate users and 4.8% of nonusers.

The all-cause mortality rate was 32.7% in bisphosphonate users in the angiography cohort and 18.8% in nonusers. Yet the rates of new-onset atrial fibrillation were essentially the same: 10.2% among bisphosphonate users, 10.1% in nonusers.

In November 2008, the Food and Drug Administration reported that based on its review of the data from clinical trials involving nearly 40,000 patients treated with alendronate (Fosamax), ibandronate (Boniva), risedronate (Actonel), zoledronic acid (Zometa), or placebo, there is “no clear association” between the use of drugs in this class and the rate of serious or nonserious atrial fibrillation. The FDA report concluded that physicians “should not alter their prescribing patterns for bisphosphonates.”

However, because of discordance among some of the studies, agency officials left the door open to possible future epidemiologic studies addressing the issue, prompting Dr. Day and co-investigators to look at their data in the context of the new indication.

Another study presented at the osteoporosis symposium shed light on zoledronic acid’s role in preventing bone loss in women who’ve already had a hip fracture. A subanalysis of a second HORIZON study showed that zoledronic acid indeed benefits patients with a recent fracture—and particularly the very elderly and those with the poorest bone quality.

The HORIZON Recurrent Fracture Trial included 2,127 patients with a recent hip fracture who were randomized to an annual infusion of 5 mg zoledronic acid or placebo and followed up for 5 years. HORIZON-RFT concluded that the drug reduced the rate of recurrent fracture by 35% (N. Engl. J. Med. 2007;357:1799-809).

The subanalysis examined response rates within specific patient groups, said Denise Orwig, Ph.D., who presented the trial data during a poster session at the meeting. The analysis showed that patients at the highest risk for a recurrent fracture—those who were at least 85 years old or who had a T score of less than –2.5 at the total hip—benefited the most from the treatment.

Although Dr. Orwig said it’s unclear why the oldest, least-dense bones benefited the most, the finding does carry a strong positive clinical implication. On “these patients who are at the highest risk are also the ones who are the least likely to be treated,” said Dr. Orwig of the department of epidemiology and preventive medicine at the University of Maryland Medical Center, Baltimore.

“The thought may be that they have already had multiple fractures and there is probably not a lot more that can be done. But this study showed us that these individuals can benefit and that we can have a big short-term impact on their bone density and possibly even reduce the risk of more fractures due to continued bone loss,” said Dr. Orwig. Novartis Pharmaceuticals Corp. sponsored the HORIZON studies. Dr. Orwig has received research funding from the company. Dr. Recknor and Dr. Zaidi are on the Novartis speakers bureau.

Diana Mahoney contributed to this report.