Six-Year Zoledronic Acid Regimen Safe, Effective

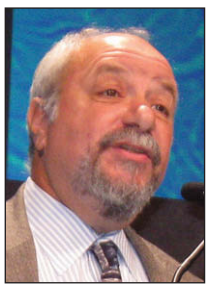
BY MITCHEL L. ZOLER

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

TORONTO – Patients who continued annual treatment with zoledronic acid for 6 years had significantly better bone mineral density and fewer morphometric vertebral fractures than did patients who received 3 years of treatment and then stopped, according to results of a controlled study with more than 1,200 subjects.

Six continuous years of annual zoledronic acid treatment also proved safe, making continued treatment with this bisphosphonate formulation an option for patients who might benefit, Dennis M. Black, Ph.D., said at the meeting.

"After 3 years, it might be beneficial for some women, particularly those at high vertebral fracture risk, to continue zoledronic acid for an additional 3 years," said Dr. Black, professor of epidemiology and biostatistics at the University of California, San Francisco.



The decision to continue bisphosphonate treatment long term must be individualized.

DR. BLACK

"These new findings show that continued treatment with zoledronic acid for 6 years continues to maintain bone mass and reduced vertebral fracture risk with no change to its favorable safety profile compared with discontinuation of treatment after 3 years," he said in a written statement.

On the other hand, the decision to continue bisphosphonate treatment long term must be individualized, he said.

It may be possible to identify women who would benefit from a drug holiday, he added.

In light of the new finding, zoledronic acid joins other bisphosphonates, such as alendronate, shown to prevent loss of bone density when the drug is continued after several years of treatment.

In a previous report, continuing treatment with alendronate for 5 years following an initial 5 years of treatment led to less bone density loss than in patients who switched from alendronate to placebo (JAMA 2006;296:2927-38).

The same alendronate study failed to show that continued bisphosphonate treatment led to a reduced rate of morphometric vertebral fractures, compared with stopping alendronate.

The new zoledronic acid findings came from an extension of the Health Outcomes and Reduced Incidence With Zoledronic Acid Once Yearly (HORIZON) Pivotal Fracture Trial, which compared a single, annual infusion of zoledronic acid with placebo in postmenopausal women with osteoporosis during 3 years of treatment (N. Engl. J. Med. 2007;356:1809-22).

Dr. Black and his associates randomized 1,233 women who completed the zoledronic acid arm of the study to either continue with another 3 years of annual infusions of 5 mg zoledronic acid or switch to placebo.

The average age of the study subjects was 76 years, and approximately 55% had a femoral neck T score of less than –2.5.

At the conclusion of the study, the percent change in femoral neck bone mineral density, compared with the level at entry into the study, averaged 1% higher in patients who were treated with zoledronic acid, a statistically significant difference in the study's primary end point.

Femoral neck bone mineral density in the zoledronic acid–treated patients increased by an average of 1.4% over baseline 6 years earlier (when they started on the drug), compared with those who switched off the bisphosphonate after 3 years, a statistically significant difference.

The rate of morphometric vertebral fractures during the 3 years of the new study totaled 6% in the patients who were on placebo and 3% in those who

were on zoledronic acid, a statistically significant difference.

The two treatment arms showed no significant difference in their rates of nonvertebral fractures. Continued zoledronic acid treatment also led to reduced blood levels of a marker of bone turnover compared with the patients who received placebo injections.

Six years of annual zoledronic acid treatment appeared safe, with no excess of adverse events or serious adverse events compared with the patients on 3 years of placebo. The researchers looked especially closely at cardiovascular events; the only significant, between-treatment difference was in new hypertensive adverse events, which occurred significantly more often in the patients who received placebo for 3 years. ■

VITALS

Major Finding: Postmenopausal women with osteoporosis who received an annual injection of zoledronic acid for 6 years maintained their femoral neck bone mineral density significantly better than did those treated with the drug for 3 years followed by 3 years on placebo.

Data Source: Extension of the HORIZON Pivotal Fracture Trial, a randomized, multicenter extension trial with 1,233 women.

Disclosures: The HORIZON Pivotal Fracture Trial was funded by Novartis, which markets zoledronic acid (Aclasta). Dr. Black said that he has served as a consultant and done teaching for Amgen and Nycomed, and that he has received research contracts from Amgen, Merck, Novartis, and Roche/Genentech.