Once-a-year drug reduces fractures from osteoporosis

May 2 2007

A treatment for osteoporosis delivered once a year is as effective as current monthly or weekly osteoporosis regimens at reducing the incidence of bone fractures, according to a new study led by a UCSF research team.

Results from a three-year, international study of 7,736 postmenopausal women with osteoporosis are reported in the May 3, 2007 issue of the "New England Journal of Medicine." Study findings also are available online at content.nejm.org.

The study showed that treatment with zoledronic acid (marketed as Reclast) was very effective in reducing the incidence of all types of fractures in women with postmenopausal osteoporosis, the researchers said. Impact included a 70 percent reduction in the risk of spinal fractures and a 40 percent reduction in the risk of hip fractures. The effect was sustained over three years.

"The reductions in hip and spine fractures were at least as large as those seen with other drugs in this category," said Dennis Black, PhD, a professor of epidemiology and biostatistics in the UCSF School of Medicine, who led the study. "But even more remarkable were the strong, significant and consistent effects across all fracture types."

Reclast is an investigational drug in the bisphosphonate drug category that is being developed by Novartis Pharmaceuticals Corp., a U.S. affiliate of the Swiss-based Novartis AG. It is the only once-yearly

bisphosphonate treatment being studied for osteoporosis and is still in the approval process through the Food and Drug Administration.

Three other drugs in the bisphosphonate family (marketed as Fosamax, Actonel and Boniva) are currently available and most commonly used as a once per week or once per month pill.

"For the first time, women could have the option of being treated once a year for osteoporosis, instead of having to remember to take a weekly pill," Black said. "Adherence to these weekly and monthly regimens is often a problem, so an annual treatment means patients are far more likely to actually receive valuable protection against potentially devastating fractures."

Postmenopausal osteoporosis affects millions of women worldwide, Black said, including more than 50 million women in the United States, Europe and Japan combined. Half of those women over age 50 will suffer from an osteoporotic fracture in their lifetime and, of women over age 65 who fracture a hip, 21 percent will die within one year as a result of poor underlying health status, in addition to the acute effects of the fracture.

The study, formally called Health Outcomes and Reduced Incidence with Zoledronic acid Pivotal Fracture Trial, known as HORIZON, was a multinational, randomized, placebo-controlled trial. It evaluated the potential of using a once-yearly infusion of 5 mg of zoledronic acid to decrease the risk of vertebral and hip fractures in postmenopausal women with osteoporosis.

The study also closely examined and put to rest several questions of other side effects of zoledronic acid, such as the renal damage and bone deterioration that has been seen at much larger doses in oncology treatments. The HORIZON study showed no such findings at the lower

dose required for osteoporosis treatments.

The study did observe a small increase in the incidence of atrial fibrillation in patients who received zoledronic acid (1.3 percent for zoledronic acid versus 0.5 percent for placebo). Atrial fibrillation is a condition of abnormal heart rhythms, which is one risk factor for stroke.

"The observed increase in atrial fibrillation was very small – less than one in 100 patients – so it needs to be weighed against the reduction in fracture risk," Black said. This increase was unexpected and has not been seen in other studies of zoledronic acid. He recommends that it be further examined.

The May 3 issue of "NEJM" also includes a letter regarding a separate study on a different drug in the bisphosphonate family, which showed a similar, but not statistically significant, increased risk of atrial fibrillation. That study also was conducted by the UCSF group.

As was expected, there was also a slight increase in minor side effects, such as fever or muscle pain. Those effects were seen within three days of the first infusion but not after the second or third.

Source: University of California - San Francisco