Alendronate Praised for Osteoporosis Prevention

BY JONATHAN GARDNER
London Bureau

Alendronate is the only proven cost-effective medication for initiation of primary or secondary prevention of osteoporosis, according to draft assessments issued March 5 by the agency that determines which drugs the National Health Service uses in England and Wales.

If affirmed later this year, the National Institute for Health and Clinical Effectiveness (NICE) draft document would rule out the use of strontium ranelate, etidronate, risedronate, and raloxifene for primary prevention of osteoporosis in women with at least one clinical risk factor.

For initiation of secondary prevention, a separate NICE document would rule out those four drugs and teriparatide.

NICE found that nonproprietary alendronate, the second-cheapest drug, was as effective as risedronate, etidronate, strontium, and raloxifene. As a result, NICE's drafts ruled that alendronate was the most cost-effective medication. Only etidronate, at £85.65 ($171) a year, could match alendronate on price. However, the committee questioned the evidence regarding etidronate's effectiveness.

At an annual cost of £95.03 ($190) for once-weekly treatment, generic alendronate for primary prevention in patients at high risk of osteoporosis was estimated to cost £17,632 ($35,288) or less per quality-adjusted life year, a measurement of a single year in perfect health, compared with no treatment, according to the NICE committee that appraised the medications.

For initiation of secondary prevention among women with bone mineral density more than 2.5 standard deviations below normal confirmed by bone-density scanning, it was estimated to cost less than £27,422 ($54,881) per quality-adjusted life year, depending on age and treatment strategy, the committee said.

A NICE document on secondary prevention of osteoporosis issued in January 2005 recommended the use of all three bisphosphonates, raloxifene, and teriparatide for secondary prevention in postmenopausal women who have already had an osteoporosis-related fracture. ■

Previous Fall History, Age Above 80 Years Are Predictors of Future Falls

BY KERRI WACHTER
Senior Writer

WASHINGTON — Postmenopausal women with a prior fall or those 80 years of age or older have a significantly greater risk of a subsequent fall, according to data presented at an international symposium sponsored by the National Osteoporosis Foundation.

Specifically, the investigators found that women with a prior fall had an odds ratio of 2.7 and those 80 years or older had a odds ratio of 1.5 for a future fall, based on a analysis of potential risk factors for falls among 66,134 women enrolled in the National Osteoporosis Risk Assessment (NORA) study, said Dr. Elizabeth Barrett-Connor, chief of epidemiology in the department of family and preventive medicine at the University of California at San Diego.

The NORA study enrolled over 200,000 community-dwelling, postmenopausal women between 1997 and 1999. Women had to be at least 50 years old without a diagnosis of osteoporosis. They could not have had a bone mineral density measurement in the previous year or be taking an osteoporosis-specific medication. At baseline, BMD was measured at the heel, forearm, or finger. The women were followed up at 1, 3, and 6 years with surveys asking if they'd had a fracture in the previous year.

The sample of women in this study responded to all of the surveys. At baseline, the average age was 63 years. Most (91%) were white. The average T score was –0.78. In all, 38% reported at least one fall in the past year.

The researchers included a long list of potential risk factors. These included age, body mass index, a self-rating of health as being poor/fair, functional limitations, smoking and alcohol use, early menopause, height loss, peripheral T score, personal history of fracture after age 45, maternal history of fracture and/or osteoporosis, first-degree relatives with a history of fracture, history of estrogen therapy, calcium supplementation, use of certain medications (oral corticosteroids, thyroid medication, an osteoporosis-specific drug), history of depression, osteoporosis self-knowledge, and self-report of a fall within the previous 12 months at the year 1 survey. They also included arthritis, coronary artery disease, hypertension, diabetes, kidney/liver disease, breast cancer, other cancers, memory problems, stroke, hyperthyroidism, hypothyroidism, epilepsy, poor vision, and poor hearing.

In addition, history of depression and of stroke increased the risk of falling by over 40%. An additional nine factors were identified that significantly increased fall risk by 9%-23%. The number of baseline risk factors was linearly associated with a risk of falling.

The NORA study has several limitations. First, participants were volunteers and may not be a representative sample. Second, falls were self-reported and limited to a 12-month recall period. The gaps between surveys likely mean falls were underreported. Longitudinal attrition resulted in a slightly younger and healthier analytic sample. No data were collected on factors known to be associated with falls, such as prescription medications, environment, gait, balance, and muscle strength. Lastly, the cause of falls was not known.

Dr. Barrett-Connor disclosed research support from several pharmaceutical companies and is a consultant for Merck & Co. Two of her collaborators are employees of Merck. ■

Teriparatide Boosts Bone Mass In Secondary Osteoporosis

BY KERRI WACHTER
Senior Writer

WASHINGTON — Teriparatide appeared to increase lumbar spine bone mineral density and showed some promise in reducing nonvertebral fractures in patients on glucocorticoid therapy with low bone mineral density or a prior fragility fracture, according to data presented at an international symposium sponsored by the National Osteoporosis Foundation.

"In patients with glucocorticoid-induced osteoporosis treated with teriparatide or alendronate for 18 months, teriparatide resulted in significantly greater increases in lumbar spine bone mineral density (BMD) compared with alendronate. Significantly fewer patients had new vertebral fractures with teriparatide, compared with the alendronate group," said Margaret R. Warner, Ph.D., a researcher with Eli Lilly & Co., which funded this trial.

In terms of biomarkers of bone turnover, the teriparatide patient group showed increases in serum P1NP—a marker of bone formation—and in CTX.

At 18 months, lumbar spine BMD increased 7.2% for patients treated with teriparatide and 3.4% for those treated with alendronate. Differences could be seen between the two treatment groups as early as 6 months.

Teriparatide (Forteo), made by Eli Lilly, contains recombinant human parathyroid hormone (1-34) and is currently indicated for the treatment of postmenopausal women with osteoporosis who are at high risk for fracture. The drug also is indicated to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture. Teriparatide is the only osteoporosis drug shown to stimulate new bone growth.

Glucocorticoid therapy is the most common cause of secondary osteoporosis. Currently, only the bisphosphonates risedronate (Actonel, made by Procter & Gamble Pharmaceuticals) and alendronate (Fosamax, made by Merck & Co.) are indicated for the prevention and treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and who have low BMD.

The trial included men and women at least 21 years of age who had taken a minimum dose of 5 mg/day of prednisone (or its equivalent) for 3 months or longer prior to screening. All patients had total hip, femoral neck, or lumbar spine T scores of at most –2.0 or at most –1.0 with a prior fragility fracture. A total of 428 patients (80% women) were randomized to receive 20 mcg/day teriparatide injection and an oral placebo tablet or 10 mg/day oral alendronate and an injectable placebo. All patients in the trial received calcium and vitamin D supplements. Patients were followed for 18 months.

The primary end point was the effect of teriparatide on lumbar spine BMD in patients with glucocorticoid-induced osteoporosis compared with alendronate. The researchers also looked at the effect of teriparatide versus alendronate on total hip and femoral neck BMD, on markers of bone turnover, and on the incidence of vertebral and nonvertebral fractures.

BMD was assessed using dual-energy x-ray absorptiometry. Vertebral fractures were assessed using semiquantitative visual scoring of radiographs taken at baseline and at 18 months. Nonvertebral fractures were assessed with radiograph or radiologist report. Both vertebral and nonvertebral fractures were assessed at a central reader site.

In addition, markers of bone turnover were analyzed in roughly half of the patients in each group. Adverse event data were collected throughout.

At baseline, both groups were fairly evenly matched in terms of gender, race, age, average prednisone dose, and average duration of prednisone use. Both groups were evenly matched in average BMD at the total hip, femoral neck, and lumbar spine, and vertebral and nonvertebral fractures. Three-quarters of patients in both groups had rheumatologic disease. Rheumatoid arthritis was the most common, accounting for 69% of those in the alendronate group and 61% of those in the teriparatide group.

Total hip BMD rose 3.6% for the teriparatide group, versus 2.2% for the alendronate group. Femoral neck BMD rose 3.7% for the teriparatide group, versus 2.1% for the alendronate group.

In terms of biomarkers of bone turnover, the researchers measured serum procollagen type 1 N-propeptide (P1NP)—a marker of bone formation—and serum C-terminal telopeptide of type 1 collagen (CTX)—a marker of bone resorption. "In the teriparatide group, there were increases in serum P1NP and CTX, whereas with the antiresorptive agent there were decreases in serum P1NP and CTX," said Dr. Warner.

Adverse event profiles were similar between groups. In the teriparatide group there were 182 adverse events, with 45 considered serious. There were 170 adverse events in the alendronate group, and 39 were considered serious. ■