

Ibandronate Helps Avert Anastrozole Bone Loss

After 1 year, women on the bisphosphonate showed a significant increase in BMD at both the hip and spine.

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

SAN ANTONIO — Monthly ibandronate appears to prevent, and perhaps even reverse, bone loss in women who are taking anastrozole for estrogen receptor-positive breast cancers, Dr. J.E. Lester reported in a poster at the Sixth International Meeting on Cancer-Induced Bone Disease.

While she said that further follow-up is required, her randomized placebo-controlled trial showed that after 1 year, women taking the bisphosphonate showed a significant increase in bone mineral density (BMD) at both the hip and spine, while those taking the placebo experienced a significant decrease at both sites.

Dr. Lester, of the Cancer Research Centre of Weston Park Hospital, Sheffield,

England, examined ibandronate's effects in 131 postmenopausal women with estrogen receptor-positive breast cancers. The women were grouped according to baseline BMD: 68 had normal BMD (mean age 63 years), 50 were osteopenic (mean age 67 years), and 13 were osteoporotic (mean age 71 years).

All patients were taking calcium and vitamin D supplements in addition to anastrozole. Those with normal BMD continued on the supplements. Osteopenic patients were randomized to either 150 mg oral ibandronate every 28 days (25 patients) or placebo (25 patients). All osteoporotic women received the same monthly ibandronate treatment.

Ibandronate significantly increased BMD at the hip and spine in both treated groups. At 1 year, osteopenic women had a mean increase of 2.8% at the lumbar

Treatment	Normal	Osteopenia	Osteoporosis	Withdrawal
Ibandronate for osteopenia (n = 25)	5	18	0	2
Placebo for osteopenia (n = 25)	0	23	2	0
Ibandronate for osteoporosis (n = 13)	0	7	5	1

Source: Dr. Lester

spine and 1.4% at the hip. After 1 year, five of the previously osteopenic women were found to have normal BMD.

Women in the placebo group had a decrease of BMD at both sites (mean -2.6% at the lumbar spine and -2.3% at the hip).

During the blinded period, two osteopenic patients lost more than 10% of their BMD at either the spine or hip. They were withdrawn and unblinded; both had been taking the placebo and both were offered open-label ibandronate.

Among the osteoporotic women, the mean increase in BMD was 2.6% at the lumbar spine and 2.6% at the hip. Seven previously osteoporotic patients were found to be osteopenic at 1-year follow-up.

Of the 68 women with initially normal BMD untreated with ibandronate, 20 were followed for 2 years. Follow-up scans showed a mean BMD decrease of -4% at the lumbar spine and -3% at the hip. Despite these changes, however, none of the women developed osteoporosis. ■

5 More Years of Alendronate Show Little Added Benefit

BY BARBARA RUTLEDGE
Contributing Writer

Postmenopausal women who discontinue alendronate after 5 years of treatment may experience a moderate decline in bone mineral density but are not at a significantly higher risk for fracture compared with those who continue alendronate for an additional 5 years, reported Dennis M. Black, Ph.D., of the University of California, San Francisco, and his colleagues.

"For many women, discontinuation of alendronate after 5 years for up to 5 more years does not significantly increase fracture risk, but women at high risk of clinical vertebral fractures, such as those with vertebral fracture or very low [bone mineral density], may benefit by continuing beyond 5 years," Dr. Black wrote (JAMA 2006;296:2927-38).

This conclusion was based on findings from a 5-year extension of the Fracture Intervention Trial (FIT), a randomized, placebo-controlled trial designed to evaluate the effect of daily alendronate on bone mineral density (BMD) and fracture risk in postmenopausal women with low BMD. The FIT Long-Term Extension (FLEX) study was open to women who had been assigned to the alendronate treatment arm in FIT and who had completed at least 3 years of alendronate treatment. Women with a total hip BMD of less than 0.515 g/cm² at baseline were ineligible to participate in FLEX.

Participants were randomly assigned to receive daily treatment with 10 mg alendronate (30%), 5 mg alendronate (30%), or placebo (40%). The primary study end point was total hip BMD.

Of 1,099 women participating in FLEX, 437 were assigned to placebo, 329 were assigned to 5 mg alendronate, and 333 were assigned to 10 mg alendronate.

The treatment groups did not significantly differ in adverse events or other safety parameters during the study, and no cases of osteonecrosis were observed.

After 5 years, total hip bone mineral density declined 3.38% (0.22) from baseline values in the placebo group and 1.02% (0.18) in the combination of the two alendronate groups for a mean difference of 2.36% (95% CI: 1.81%-2.90%; *P* less than .001). The combined alendronate group experienced a mean 5.26% (0.24) increase from FLEX baseline in lumbar spine BMD compared with a mean 1.52% (0.29) increase in the placebo group (mean difference of 3.74%; 95% CI: 3.03%-4.45%, *P* less than .001). Notably, mean BMD levels remained at or above FIT baseline levels in all treatment groups after 5 years.

The two alendronate groups did not differ significantly in their incidence of total clinical fractures or nonvertebral fractures.

However, the risk of clinical vertebral fractures was significantly higher in the placebo group (5.3%) than in the combined alendronate group (2.4%). ■

PTH Response Could Explain Racial Differences in Osteo-Related Fractures

BY JEFF EVANS
Senior Writer

ARLINGTON, VA. — African Americans may have a lower rate of osteoporosis-related fractures than whites because of adaptations in calcium homeostasis, bone turnover and resorption, and response to parathyroid hormone, Dr. Felicia Cosman said at a conference sponsored by the American Society for Bone and Mineral Research.

It is "very surprising" that at all ages, black individuals have a lower rate of fractures and higher bone mineral density (BMD) than white individuals, even though blacks generally have higher rates of vitamin D deficiency or insufficiency, said Dr. Cosman, medical director of the clinical research center at Helen Hayes Hospital, West Haverstraw, N.Y.

Mean serum levels of 25-hydroxyvitamin D [25(OH)D] are known at all ages and in both genders to be generally lower in blacks than in whites. This is the result of reduced skin production of vitamin D and a lower dietary intake of vitamin D, Dr. Cosman said.

An alteration in the vitamin D-endocrine system in blacks was first proposed by Dr. Norman Bell; it was based on evidence that blacks have a greater prevalence of vitamin D deficiency and relative secondary hyperparathyroidism, lower levels of bone turnover, and increased urinary calcium retention as an adaptive means to maintain calcium homeostasis without sacrificing the skeleton (J. Clin. Invest. 1985;76:470-3).

In many studies, parathyroid hormone (PTH) levels are higher, on average, in blacks than in whites. The PTH levels found in blacks occur within the context of low calcium intake in addition to low 25(OH)D levels, which may be related to "real or perceived" lactose intolerance, Dr. Cosman said. As a consequence of high PTH levels, blacks have generally been measured with higher 1-25 dihydroxyvitamin D [1,25(OH)₂D] levels than have whites.

"We would expect that with higher

1,25(OH)₂D levels, you would see greater [dietary] calcium absorption in black individuals compared to whites," but studies have reported inconsistent data, many of which have shown no significant interracial differences, she said.

One also would expect blacks to have higher bone turnover levels because of high PTH levels, but in general this has not been true, Dr. Cosman said. However, nearly all studies of the kidney have found that blacks have lower urinary calcium excretion than whites.

In addition, supplementation of 1,25(OH)₂D has been shown to cause a significantly greater decrease in urinary calcium excretion in blacks than in whites. Markers of bone formation also increased more among blacks than among whites, whereas bone resorption indices showed no racial differences (Osteoporos. Int. 2000;11:271-7). In a separate study, administration of PTH also caused blacks to retain urinary calcium to a greater degree than it did in whites, but it did not cause any racial differences in bone formation markers. After receipt of PTH, blacks also did not have as great an increase in bone resorption markers (J. Bone Miner. Res. 1997;12:958-66). This finding directly confirms "the hypothesis that the black skeleton could be resistant to the acute bone resorptive effects of PTH," she said.

Studies of histomorphometric differences in bone have shown significantly reduced bone formation rates and a longer total bone formation period in blacks, compared with whites. The results of those studies are consistent with evidence that blacks have a lower level of serum osteocalcin—which has been the most sensitive indicator of a racial difference in bone turnover levels—and that blacks respond more slowly to bone remodeling therapies.

"The bottom line message ... for these measurements is that in a relative secondary hyperparathyroid state you really expect to see high [bone] turnover," Dr. Cosman said. "We never see that. We see either the same or, in most cases, lower turnover in blacks." ■