

# Consider Risk Factors in Osteoporosis Therapy

*Increased fracture risk seen in those with T scores below -1.8, previous fracture, and fair or poor health.*

BY NANCY WALSH  
New York Bureau

NEW YORK — While bone mineral density T scores clearly are predictive of a postmenopausal woman's osteoporotic fracture risk, treatment decisions should take into account other factors, including her overall health and history of previous fractures, Stephen Honig, M.D., said at a rheumatology meeting sponsored by New York University.

"We have to do better than the T score in deciding who needs treatment for osteoporosis, because the long-term use of bisphosphonates has not been determined to be safe," said Dr. Honig, director of the osteoporosis center at the Hospital for Joint Diseases Spine Center in New York.

Very long-term bisphosphonate therapy may lead to oversuppression of bone turnover, he said. This superhardening can hinder subsequent fracture healing, as was seen in a recent report of nine patients who sustained spontaneous, nonhealing fractures while on alendronate therapy (*J. Clin. Endocrinol. Metab.* 2005;90:1294-301).

These patients showed histomorphometric evidence of markedly suppressed bone formation, Dr. Honig said.

This new finding has heightened interest in targeting osteoporosis treatment. Research findings have begun to provide guidance on which patients can most benefit from treatment.

Most notable was the National Osteoporosis Risk Assessment (NORA) study, which enrolled 200,160 postmenopausal women aged 50 and older.

In that study, bone mineral density (BMD) measurements were obtained at baseline, and the participants were followed for 1 year.

At follow up, one-third of all fractures and one-fifth of all hip fractures in particular occurred in women aged 50-64. Although the majority of fractures did occur in women 65 and older, the high number in the younger cohort "was a little surprising," said Dr. Honig.

Another finding that emerged from NORA was that 80% of the women who had fractures during the yearlong study had T scores that were higher than -2.5 and therefore did not meet the World Health Organization definition of osteoporosis.

Most fell between -1 and -2.5, the osteopenic range, he said.

"We want to identify patients at risk in this middle range and not wait until they

have obvious fractures," he commented.

The NORA investigators subsequently followed 57,421 osteopenic women and developed an algorithm for determining risk.

As it turns out, identifying patients with a previous fracture, a T score below -1.8, a self-reported health status of fair or poor, and poor mobility were all factors significantly predictive of fracture risk (*Arch. Intern. Med.* 2004;164:1113-20).

Another prospective study conducted in France followed 672 healthy postmenopausal women for more than 5 years,

and found an annual incidence of osteoporotic fractures of 21 per 1,000 women per year (*Bone* 2003;32:78-85).

The French investigators identified the key risk factors (listed in order of importance) to be a past fracture, hip BMD, low physical activity, low grip strength, age over 65, maternal fracture history, and past falls.

Other studies have also suggested additional risk factors, including smoking, low body mass index, and increased markers of bone absorption.

Based on the available data and tools at hand, Dr. Honig recommends that clini-

cians now consider treatment for the following patients:

► Women 65 and older, with or without a history of fracture, who have low BMD or other risk factors, such as low BMI and family history.

► Women 50 and older with a previous fracture and a T score of -1.8 or less.

► Women in poor overall health with mobility problems and low BMD.

► Women with low BMD and increased markers of bone resorption.

But questions remain, he said. How long can a bisphosphonate be used?

When should teri-

paratide or a selective estrogen receptor modulator be used? What place does hormone therapy have in treatment strategies?

"There is some new evidence that postmenopausal women with certain levels of endogenous estradiol levels have a lower incidence of fractures. This may translate into using very low-dose [hormone therapy], which conceivably could be safer than what was seen in the Women's Health Initiative," he said.

Dr. Honig disclosed that he receives support from Eli Lilly & Co. and is on the speakers' bureau of Sanofi-Aventis. ■

**Very long bisphosphonate therapy may lead to oversuppression of bone turnover, which can hinder the healing process in subsequent fractures.**

## Vitamin D Levels Low in Many Women on Osteoporosis Tx

BY HEIDI SPLETE  
Senior Writer

WASHINGTON — Vitamin D levels are inadequate in up to half of postmenopausal women who receive treatment for osteoporosis, Ethel Siris, M.D., reported during an international symposium sponsored by the National Osteoporosis Foundation.

Vitamin D inadequacy was significantly worse among women who took less than 400 IU of vitamin D supplementation daily, compared with women who took at least 400 IU of vitamin D daily (63% vs. 45%).

Previous study findings suggest that serum 25-hydroxyvitamin D concentrations of at least 30 ng/mL are needed to stabilize serum parathyroid hormone levels, Dr. Siris, director of the metabolic bone diseases program at Columbia University, New York, and her colleagues, wrote in a poster presentation.

In a cross-sectional, observational study conducted between November 2003 and March 2004, the investigators collected

blood samples from 1,536 postmenopausal women, mean age 71 years, at 61 sites throughout North America.

They used several cut points of serum 25-hydroxyvitamin D to define inadequacy—less than 9 ng/mL, less than 20 ng/mL, less than 25 ng/mL, and less than 30 ng/mL.

Parathyroid hormone values stabilized among patients with serum 25-hydroxyvitamin D concentrations of at least 29.8 ng/mL, which suggests that concentrations of approximately 30 ng/mL are important for healthy parathyroid levels.

Additional factors significantly related to vitamin D inadequacy in a multivariate analysis included age older than 80 years, BMI greater than 30, lack of exercise, and lack of physician counseling about the importance of vitamin D.

More than half (59%) of the women reported that they had not discussed vitamin D with a doctor.

Dr. Siris is a paid consultant for Eli Lilly & Co., Merck & Co., Sanofi Aventis, Procter and Gamble Pharmaceuticals, and Novartis. ■

## Monthly Oral Ibandronate Therapy Boosts BMD as Well as Daily Dose

BY HEIDI SPLETE  
Senior Writer

WASHINGTON — A monthly dose of oral ibandronate is at least as safe and as effective at increasing bone mineral density as a daily dose, according to data from a study of more than 1,200 postmenopausal women with osteoporosis.

The Monthly Oral Ibandronate in Ladies (MOBILE) study, a multinational randomized, double-blind, phase III study of women aged 55-80 years, will continue for 2 years, Michael Bolognese, M.D., explained in a poster presented at an international symposium sponsored by the National Osteoporosis Foundation. Dr. Bolognese and his colleagues presented their 1-year results at the meeting.

A total of 318 women received a 2.5-mg dose of oral ibandronate (Boniva) daily; another 328 women received a 50/50 mg dose (two 50-mg single doses on 2 consecutive days) monthly; 311 received one 100-mg dose monthly; and 320 received one 150-mg dose monthly.

After 1 year, the increase in BMD at the lumbar spine was 3.9% in the daily group, compared with 4.3%, 4.1%, and 4.9% in the groups receiving, respectively, 50/50 mg, 100 mg, and 150 mg monthly.

Increases in the total hip BMD were 2.2% in the daily group, compared with 2.2%, 2.7%, and 3.1% in the 50/50 mg, and monthly groups, respectively.

Similar increases occurred at the femoral neck and hip trochanter.

In addition, all treatment groups demonstrated significant decreases in serum C-terminal cross-linking telopeptide of type I collagen (CTX), a bone resorption marker that's used to measure the effectiveness of treatment. The 150-mg group showed the most robust response.

"The once-monthly oral ibandronate has a comparable safety profile with the daily, and therefore seems like it should provide an effective, well-tolerated, and practical alternative to daily and weekly oral bisphosphonate," Dr. Bolognese

said in his oral presentation of the data.

The dosage of the newly approved monthly formulation of ibandronate (Boniva) is 150 mg, and it has been shown to have maximal effectiveness when taken 60 minutes before eating meals, said Dr. Bolognese, of Bethesda (Md.) Health Research.

The incidence of adverse events and withdrawal rates were comparable across all treatment groups.

Approximately 70%-80% of the adverse events were gastrointestinal, which remains a concern with bisphosphonate therapy, but the incidence was relatively low and comparable across all treatment groups. In fact, the rate of discontinuation due to upper GI events was lower among patients in the 150-mg group (3.3%), 100-mg group (4.0%), and 50/50-mg group (4.0%), compared with the daily group (5.3%).

Dr. Bolognese is a consultant for Eli Lilly & Co. and Procter & Gamble, and he has received grants or research support from Sanofi-Aventis, Pfizer, Lilly, and Wyeth Pharmaceuticals. ■