Strontium Ranelate Cuts Vertebral Fracture Risk

BY BRUCE JANCIN
Denver Bureau

VIENNA — Strontium ranelate reduced the risk of new vertebral fractures 41% over 3 years in a very-high-risk population of osteoporotic women with at least two prevalent vertebral fractures at baseline, Sergio Ortolani, M.D., reported at the annual European congress of rheumatology.

That's as robust a relative risk reduction as seen in much lower-risk postmenopausal osteoporotic women with no previous vertebral fractures, noted Dr. Ortolani of the Center for Metabolic Bone Disease, Milan. "It appears we have a new first-line treatment for postmenopausal osteoporosis."

Dr. Ortolani presented a prespecified subgroup analysis drawn from two large phase III multinational placebo-controlled randomized trials of strontium ranelate for the reduction of fracture risk in osteoporotic postmenopausal women. The Spinal Osteoporosis Therapeutic Intervention (SOTI) involved 1,649 women randomized to 2 g/day of oral strontium ranelate or placebo, while the Treatment of Peripheral Osteoporosis Study (TROPOS) included 5,091 women. Both Servier Laboratories–sponsored trials will run for 5 years, although the 3-year primary outcome data have been published.

'It appears we have a new first-line treatment for postmenopausal osteoporosis.'

DR. ORTOLANI

Among 2,605 combined study participants without prior vertebral fractures at baseline, the 3-year incidence of new vertebral fractures was 14.4% with placebo and 7.5% with strontium ranelate, for a 48% relative risk reduction. Among the 734 participants with two or more prevalent vertebral fractures at enrollment, the absolute 3-year new vertebral fracture rates were far higher—42.7% in the placebo group, compared with 28.5% in those taking strontium ranelate—but the relative risk reduction conferred by strontium ranelate remained robust at 41%.

Strontium ranelate has a unique mode of action. It simultaneously increases bone formation and reduces bone resorption. The antiresorptive effect is less potent than with bisphosphonates; however, in combination with the simultaneous bone-forming effect, strontium ranelate becomes a highly effective antiosteoporosis medication, Dr. Ortolani said.

The chief adverse effect is diarrhea, which was limited to the first few months of therapy in the trials. When data from TROPOS and SOTI were pooled, there was a statistically significant increase in deep venous thrombosis, but no increase in strokes or cardiovascular events.

Strontium ranelate is approved in several European countries and will be marketed in Europe. The Food and Drug Administration requested that Servier conduct a U.S. trial before filing for marketing approval in the United States. ■

Back Pain Is Reduced for at Least 30 Months After Stopping Teriparatide

BY BRUCE JANCIN
Denver Bureau

VIENNA — The risk of developing new-onset back pain is markedly decreased during and for at least 30 months after stopping teriparatide (Forteo) for the treatment of osteoporosis, Jean-Yves Reginster, M.D., Ph.D., reported at the annual European congress of rheumatology.

He presented a metaanalysis of four Eli Lilly–sponsored randomized double-blind clinical trials involving 1,222 teriparatide-treated patients and 691 controls. The control groups in two of the trials received placebo. In the other two, controls got 10 mg/day of alendronate or hormone therapy. The median follow-up after discontinuing teriparatide was more than 31 months.

The incidence of any new back pain during 4,157 patient-years at risk was 6.9 cases per 100 patient-years among subjects in the teriparatide-treated group, compared with 9.3 cases per 100 patient-years in controls. (See box.)

There was no significant difference in the incidence of new back pain in patients who received 20 mcg/day of subcutaneous teriparatide and in those who got 40 mcg/day. Rates in teriparatide-treated patients and controls appeared to diverge after 6 months of therapy, noted Dr. Reginster, director and professor of epidemiology, public health, and health economics at the University of Liège, Belgium.

The relative risk of developing severe back pain during teriparatide therapy or for 30 months after treatment ended was reduced by 61%, compared with controls. The risk of developing moderate or severe back pain was reduced by 28%. And the risk of any new-onset back pain was 27% lower in the teriparatide group.

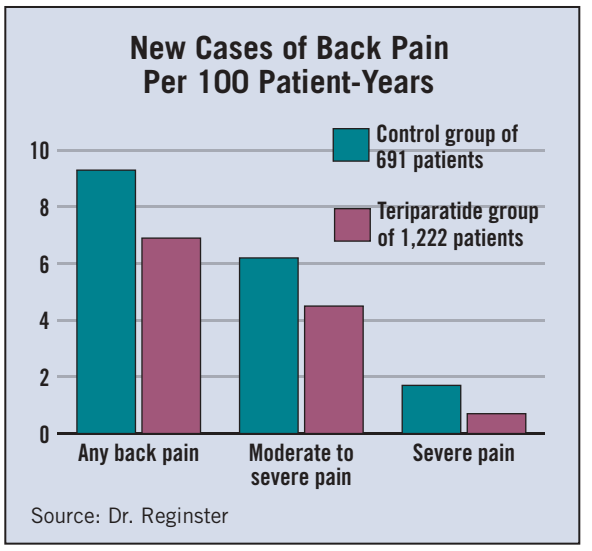
In a separate presentation, Thomas Nickelsen, M.D., said that postmenopausal osteoporotic women showed a significant decrease in self-assessed back pain after 1 and 6 months of teriparatide in the ongoing European Forteo Study (EUROFORS). At baseline, the women rated their back pain as scoring a mean of 50 points out of 100 on a visual analog scale. After 6 months of open-label teriparatide, their score dropped by a 10-point absolute margin, or 20%.

Postmenopausal osteoporotic women showed a decrease in back pain after 1 and 6 months of teriparatide.

DR. NICKELSEN

These back pain findings are incidental to the primary purpose of EUROFORS, which is to study the impact of sequential antiosteoporosis therapy—a year of teriparatide followed by a year of raloxifene—compared with 2 years of teriparatide, explained Dr. Nickelsen of Lilly Deutschland GmbH, Bad Homburg, Germany.

EUROFORS involves 866 severely osteoporotic postmenopausal women who fall into one of three subgroups: those with no history of antiresorptive therapy, those who'd been on antiresorptive therapy—primarily with bisphosphonates—prior to EUROFORS and responded adequately to it, and inadequate responders to prior antiresorptive agents. Women in all three groups receive a year of teriparatide. Those in the first two groups are then randomized to a year of raloxifene or a second year on teriparatide. For ethical reasons, all prior inadequate responders to antiresorptive therapy get 2 years of teriparatide.



Source: Dr. Reginster

The primary end point in EUROFORS will be the 2-year change in lumbar spine bone mineral density (BMD). After 6 months of teriparatide, mean lumbar spine BMD was up by 5.2% in the treatment-naive patients, 4.2% in prior adequate responders to antiresorptive therapy, and 3.7% in the inadequate responders. There was also a small but statistically significant increase in hip BMD in treatment-naive patients, no change in the adequate responders, and a small but significant decrease in the prior inadequate responders.

Side effects were similar to those seen in other teriparatide trials: nausea in 10% of patients, arthralgias in 5%, headache in 6%, pain in the extremities in 3%, and hypercalcemia in 2.1%. ■

Most Women Treated For Osteoporosis Are Deficient in Vitamin D

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — More than half of North American women receiving treatment for osteoporosis have suboptimal serum vitamin D levels, Anne E. de Papp, M.D., and her associates reported in a poster at the annual meeting of the American Association of Clinical Endocrinologists.

Inadequate vitamin D concentrations can lead to alterations in calcium and phosphate homeostasis, secondary hypoparathyroidism, bone loss, osteoporosis, and an increased risk of fractures.

Yet, data from a cross-sectional study of 1,536 postmenopausal women at 61 North American sites suggest the problem is often overlooked in osteoporosis patients, said Dr. de Papp, of Merck & Co. Inc., West Point, Pa., and her associates.

"We advocate the use of vitamin D supplementation and patient counseling regarding the importance of vitamin D in all women with osteoporosis," they said in the poster.

The patients had a mean age of 71 years (range, 47-103 years) and a mean body mass index (BMI) of 26.4 kg/m^2. A total of 92% were Caucasian and 35% resided at latitude greater than or equal to 42°N (Boston), while 24% lived below 35°N (Memphis). All had been taking medication to treat or prevent osteoporosis for at least 3 months. The medications used included alendronate, calcitonin, etidronate, raloxifene, risedronate, and teriparatide.

Vitamin D supplementation at 400 IU/day or more was reported by 59.5%. The rest were taking less. The mean serum level of the active vitamin D metabolite 25-hydroxyvitamin D was 30.4 ng/mL. Most (52%) had levels below 30 ng/mL, the minimum to maintain optimal serum parathyroid hormone levels (Osteoporos Int. 1997;7:439-43), while 36% had 25-hydroxyvitamin D levels below 25 ng/mL, and 18% were below 20 ng/mL. Suboptimal 25-hydroxy vitamin D levels were found in 63% taking less than 400 IU/day of vitamin D, and in 45% of those receiving 400 IU or more per day.

Risk factors include having less than a 12th-grade education, lack of exercise, concomitant medication use, BMI of 30 or higher, nonwhite race, and age over 80 years.

The study was funded by Merck. ■