ONJ Less Than 1% With Bevacizumab

BY BRUCE JANCIN

SAN ANTONIO — The largest-ever analysis of osteonecrosis of the jaw occurring in women receiving the antiangiogenesis agent bevacizumab for advanced breast cancer indicates the incidence is less than 1%, even in patients receiving bisphosphonates.

The analysis involved more than 3,500 bevacizumab-treated women with locally recurrent or metastatic breast cancer prospectively followed in large clinical trials.

As such, it provides a much more accurate—and reassuring—risk estimate than the 16% incidence recently reported by Greek investigators in patients on a bisphosphonate plus bevacizumab (Avastin) or another antiangiogenesis agent, sunitinib (Sutent), for various advanced cancers (Oncology 2009;76:209-11).

The Greek report was a retrospective analysis based on 116 bisphosphonate-treated patients, only a subset of whom were on an antiangiogenesis agent, Dr. Valentina Guarneri noted at the San Antonio Breast Cancer Symposium.

In contrast, she reported on 3,560 patients on bevacizumab combined with a taxane or other standard chemotherapy as first-line treatment for locally recurrent or metastatic breast cancer. The women were participants in the open-label ATHENA study or the randomized RIBBON-1 or AVADO trials.

In the randomized trials, the incidence of osteonecrosis of the jaw (ONJ) was 0.3% in patients on bevacizumab and zero with placebo during follow-up of 10-19 months. In ATHENA, the incidence was 0.4% during 13 months of follow-up of more than 2,200 women on bevacizumab.

The incidence of ONJ was higher in bevacizumab-treated patients with prior or current exposure to bisphosphonates, but not close to the 16% figure cited in the small Greek study. In ATHENA, the incidence of ONJ was 2.4% in bevacizumab-treated patients who had been exposed to bisphosphonates and zero in those who had not.

In the two randomized trials, the rate was 0.9% in patients who had been on a bisphosphonate, compared with 0.2% in those who had not, according to Dr. Guarneri of the University of Modena and Reggio Emilia (Italy).

Detailed analysis of all ONJ cases in this series showed that dental/oral hygiene issues—a recent extraction, a loose tooth, maxillary fracture repair—were present in one-third. Thus, dental examination and avoidance of invasive dental procedures are important in patients on intravenous bisphosphonates, regardless of whether they're on bevacizumab, she added. ■

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Combo Tx Improves BMD at Spine, Hip

VITALS

Major Findings: Treatment with teriparatide plus zoledronic acid increased spinal bone mineral density more than either drug alone.

Source of Data: One-year study of 412 postmenopausal women with previously untreated osteoporosis.

Disclosures: The study was sponsored by Novartis, which makes Zometa. Dr. Cosman reported that she has received consulting fees from Novartis and other pharmaceutical companies.

BY KERRI WACHTER

DENVER — Bone mineral density at the spine and hip increased more rapidly and to a greater degree with combined teriparatide and zoledronic acid than with either agent alone in a 1-year study of 412 postmenopausal women with previously untreated osteoporosis.

"Combination therapy could therefore be considered in some patients at high risk for hip and other fractures," Dr. Felicia Cosman said at the annual meeting of the American Society for Bone and Mineral Research.

Clinical fractures were assessed as part of serious adverse event monitoring and were confirmed using radiographic reports. There were 13 fractures in the zoledronic acid (Zometa) group, 8 in the

teriparatide (Forteo) group, and 4 in the combination therapy group.

At 1 year, the increase in spine BMD was 4.4% with zoledronic acid alone, 7.1% with the teriparatide alone, and 7.5% with combination therapy. Spine BMD increased more rapidly with combination therapy, but it eventually caught up to similar levels with teriparatide alone.

Similarly significant increases in total hip BMD occurred in all treatment groups, said Dr. Cosman, medical director of the clinical research center at Helen Hayes Hospital in West Haverstraw, N.Y.

The study included three active treatment groups: 5 mg zoledronic acid at baseline (open arm), 20 mcg daily subcutaneous teriparatide (placebo infusion at baseline), and a combination of the two. All patients received calcium and vitamin D supplements. Average age at baseline was 65 years. The women had a mean spine T score of –2.9, and a mean total hip T score of –1.9. Baseline variables did not differ among the three groups.

The researchers also measured two bone markers: Beta C-terminal telopeptide of type I collagen (CTx) is a marker of bone resorption, and amino-terminal propeptide of type 1 procollagen (P1NP) is a marker of bone formation.

"In the combination group, there is first a small increase and then a brief but modest decline in P1NP, followed by a progressive rise thereafter," she said. The decline in P1NP for the combination group is not as great as for those on zoledronic acid alone.

For patients on zoledronic acid alone, there was a rapid and robust suppression of beta CTx up to 4 weeks, when the levels trended back toward baseline. There was no change in beta CTx in patients on teriparatide alone for the first month. Then beta CTx levels began to increase, peaking at about 6 months. In the combination group, there was a prominent suppression of beta CTx (bone resorption) similar to that of zoledronic acid over the first 2 months. A gradual increase followed, with levels greater than at baseline for the latter half of the year.

For P1NP, there is a lag in suppression compared with beta CTx with zoledronic acid treatment, followed by prominent suppression with a nadir/plateau at 6 months. For those on teriparatide alone, there is a doubling of baseline P1NP levels by 4 weeks, with levels peaking at about 6 months. ■