Osteoporosis Challenges Grow With Tx Options

BY DAMIAN McNAMARA

EXPERT ANALYSIS FROM THE AMDA - DEDICATED TO LONG TERM CARE MEDICINE ANNUAL MEETING

TAMPA – The treatment of osteoporosis is in flux because of a variety of forces, including a substantial increase in the number of aging patients deemed eligible for treatments, a leading geriatrician said. Just as baby boomers begin reaching senior status, a recently developed tool for assessing people's fracture risk is increasing the number of patients considered suitable for preventive therapy.

Meanwhile, those therapy options are multiplying, and emerging evidence suggests that one, bisphosphonates, is associated with an increased risk for atypical fractures, although the absolute risk appears to be low, Dr. Barbara Messinger-Rapport, said at the meeting.

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The assessment tool making a difference is the Web-based Fracture Risk Assessment Tool (FRAX), released by the World Health Organization in 2008. FRAX guides clinicians to consider drug therapy for patients with T scores (deviations from healthy bone density) of –2.5 or lower at the femoral neck or spine, a T score between –1.0 and –2.5 as well as a 3% or higher calculated risk for hip fracture over 10 years, or a 20% or greater risk of major osteoporosis-related fracture.

Even if a person's T score never reaches –2.5, his or her hip fracture risk can climb to 3% or higher, said Dr. Messinger-Rapport, director of the Center for Geriatric Medicine at the Cleveland Clinic and medical director of the Fairfax Health Care Center Nursing Home, also in Cleveland. "This could widen the number of people who could be put on treatment."

Bisphosphonates remain the most-common treatment strategy, but optimal duration of therapy, timing of drug holidays, and how age and gender play into risk for adverse events remains unclear, she said.

A newer option, the monoclonal antibody denosumab (Prolia, Amgen), significantly reduced vertebral fractures compared with a placebo in published studies. Administered as a subcutaneous injection every 6 months, denosumab also may be more convenient than agents requiring infusion, Dr. Messinger-Rapport said.

Higher cost is a consideration, however. Wholesale cost of denosumab is approximately $850/60-mg subcutaneous injection. In contrast, generic alendronate costs $100-$200/year; brand-name oral bisphosphonate costs up to $1,000/year; and zoledronic acid, delivered via intravenous infusion, is approximately $1,100/year, she said.

Denosumab's impact on clinical care is not yet known, Dr. Messinger-Rapport said. She suggested that clinicians consider this agent in high-risk elders, women or men with osteoporosis, men with prostate cancer with androgen deprivation, patients with metastatic prostate or breast cancer, and possibly patients with renal impairment (denosumab clearance is not renal). Also consider denosumab for patients who cannot tolerate a bisphosphonate either orally or by infusion, she added.

Researchers showed a 68% decrease in vertebral fractures, a 40% decline in hip fractures, and a 20% decrease in nonvertebral fractures with denosumab versus placebo in the FREEDOM study of osteoporotic women treated for 36 months (N. Engl. J. Med. 2009;361:756-65). A similar 62% decrease in vertebral fractures with denosumab, compared with placebo, was observed in a 24-month study of men with androgen deprivation for prostate cancer (N. Engl. J. Med. 2009;361:745-55).

Researchers also have examined reports of atypical femoral fractures asso-

ciated with bisphosphonate use and found an association. For example, in a study published last year, 17 of 20 atypical femoral fractures occurred in patients taking oral bisphosphonates (N. Engl. J. Med. 2010;363:1848-9).

In a letter (N. Engl. J. Med. 2010; 362:1848-9), the researchers stated that although they found the association, "overall the anti-fracture effects of bisphosphonates far outweigh their potential risks."

More recently, other investigators found an increased risk of subtrochanteric and femoral shaft fractures in women treated for 5 years or more with oral bisphosphonates (JAMA 2011;305:783-9). The authors stated that the absolute risk of the atypical fractures is low, however.

Dr. Messinger-Rapport listed the contraindications to bisphosphonates as a prior allergic reaction, vitamin D depletion (less than 30 ng/mL), hypocalcemia, dysphagia, esophageal disorders, and severe gastroesophageal reflux disorder.

A person attending the meeting asked if it is appropriate to continue bisphosphonate therapy after a patient's T score improves. "Yes, even if the T score only improves by a few percentage points," Dr. Messinger-Rapport replied, because there is a disproportionate benefit in terms of fracture risk reduction.

Dr. Messinger-Rapport has disclosed that she is a member of the editorial board for the National Osteoporosis Foundation. ■

To watch an interview with Dr. Messinger-Rapport, scan this QR code with a smartphone.