Drug Combo Boosts Rebuilding of Bone Mass

BY SALLY KOCH KUBETIN

PHILADELPHIA — Combining once-a-year zoledronic acid and daily teriparatide significantly increased bone mass in key skeletal sites and lowered serum levels of bone turnover biomarkers in postmenopausal women with osteoporosis, according to a study presented at the annual meeting of the American College of Rheumatology.

Previous research has not shown a bone mineral density (BMD) benefit from using the two types of drugs together. In fact, certain bisphosphonates have been shown to blunt the beneficial effects of recombinant human parathyroid hormone analogs such as teriparatide (Forteo).

However, findings from animal studies suggested that zoledronic acid (Reclast) did not blunt the effect of recombinant human parathyroid hormone analogs, a finding that led the investigators to undertake the latest trial.

Use of the two drugs in combination increased bone mineral density at the spine more than did teriparatide alone, and at the hip more than did zoledronic acid alone.

Both drugs have Food and Drug Administration approval for the management of osteoporosis in men and woman. Teriparatide also has an indication to treat corticosteroid-induced osteoporosis. Zoledronic acid has an additional indication for use in the treatment of osteoporosis in patients who have osteoporosis and have already had a fracture.

The trial included 412 postmenopausal women considered to be at high risk for fracture. They were diagnosed with osteoporosis on the strength of having a T score that was 2.5 standard deviations below peak bone mass, or having a slightly better T score but a history of at least one fracture. The women were randomized to treatment with zoledronic acid alone (137), with both zoledronic acid and teriparatide (137), and with teriparatide alone (138). The zoledronic acid dosage was 5 mg intravenously once per year. Teriparatide was given daily in a subcutaneous dose of 20 mcg.

Use of the two drugs in combination increased BMD at the spine more than did teriparatide alone, and at the hip more than did zoledronic acid alone, according to study presenter Dr. Kenneth G. Saag, the Jane Knight Lowe Chair of Medicine in Rheumatology at the University of Alabama at Birmingham.

BMD at the spine increased 7.51%, 7.05%, and 4.37% in the combination arm, teriparatide arm, and zoledronic acid arm, respectively. Combination therapy significantly increased lumbar spine BMD at week 13 and 26 and total hip BMD at weeks 13, 26, and 52, compared with teriparatide alone.

Changes in BMD were calculated as the difference of least square means (LSM) from a two-way analysis of variance model calculated including the percent change in lumbar spine and total hip BMD at weeks 13, 26, and 52 in all three treatment groups.

In terms of serum markers of bone turnover, C-telopeptide declined within 4 weeks and rose progressively thereafter in the combination arm, with levels above baseline within 39 weeks. N-propeptide of type 1 collagen increased for up to 4 weeks, declined to a nadir at week 8, and then rose progressively with levels above baseline by week 26. Levels of both markers were lower with combination therapy than with teriparatide alone throughout the trial.

The incidence of serious adverse events was 9.5%, 14.6%, and 10.9% in the combination, zoledronic acid, and teriparatide arms, respectively. Transient postinfusion flulike symptoms were more common in the combination and zoledronic acid groups than in the teriparatide group.

Dr. Saag disclosed financial relationships with Eli Lilly & Co., Merck & Co., Novartis, Amgen Inc., Roche, Procter & Gamble Co., NPS Pharmaceuticals Inc., Pfizer Inc., Sanofi-Aventis, TAP Pharmaceutical Products Inc., and GlaxoSmithKline. ■