

THERAPY

Raising BMD—two drugs are better than one

A combination of teriparatide and denosumab increases BMD more efficaciously than monotherapy with either agent, reveals a randomized, controlled trial in postmenopausal women with osteoporosis.

Previous attempts to improve efficacy of current osteoporosis medications by combining multiple agents, for example, an antiresorptive bisphosphonate with parathyroid hormone, have not shown additive effects of these agents. Moreover, animal studies have yielded conflicting results regarding the effects of combination therapy on bone.

To determine the efficacy of combined therapy with teriparatide and the RANKL inhibitor denosumab, a team of investigators at the Massachusetts General Hospital in Boston randomly allocated 100 postmenopausal women with osteoporosis to receive 20 µg teriparatide daily, 60 mg denosumab every 6 months, or both. BMD was measured at baseline and at follow-up after 3, 6 and 12 months.

A modified intention-to-treat analysis showed a marked increase in areal BMD at all sites with combination therapy compared with single-agent therapy. Of note, the changes in femoral-neck and total-hip BMD observed after 12 months of combination therapy were greater than those previously reported for approved postmenopausal osteoporosis medications, state the authors.

“This finding raises some important questions,” says Clifford J. Rosen (Maine Medical Center Research Institute), who is not an author of the study. “Unfortunately, the study was not powered to determine effects on fracture, so we do not know whether the increase in BMD translates into greater fracture



prevention or not. Nevertheless, this trial is the first to really show synergistic or more likely additive effects of the two drugs.”

Interestingly, biochemical markers of bone turnover showed profound suppression of both formation and resorption despite the use of the anabolic agent teriparatide. “It is hard to understand how both drugs could be working synergistically if bone formation is suppressed at a time when denosumab suppresses resorption,” comments Rosen.

The findings by Tsai *et al.* are promising; but whether improved efficacy of combination therapy extends to a reduction in fractures remains to be determined. Also, questions about cost-effectiveness and safety remain. “Quantitative CT to assess the changes seen by dual-energy X-ray absorptiometry would be an important additional set of studies to gain insights,” concludes Rosen.

Linda Koch

Original article Tsai, J. N. *et al.* Teriparatide and denosumab, alone or combined, in women with postmenopausal osteoporosis: the DATA study randomised trial. *Lancet* doi:10.1016/S0140-6736(13)60856-9