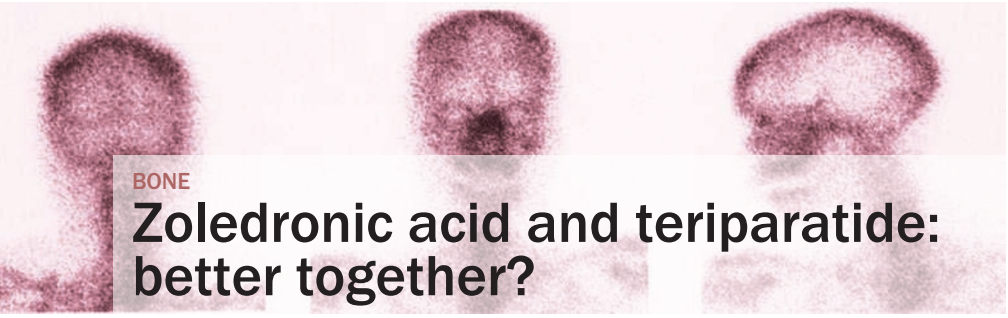

BONE

Zoledronic acid and teriparatide: better together?

Intravenous zoledronic acid plus teriparatide has a greater beneficial effect on BMD in postmenopausal women with osteoporosis—when considering increases in both the spine and hip—than either therapy alone, report researchers of a multicenter, randomized controlled trial.

Although both teriparatide—a recombinant, human fragment of the parathyroid hormone ($rhPTH_{1–34}$)—and bisphosphonates are used alone to treat women with postmenopausal osteoporosis, research to determine whether combination therapy could be beneficial has produced inconsistent results. The inconsistencies seem to reflect whether participants were treatment naive or not and the particular antiresorptive agent used, amongst other factors. Interestingly, concomitant use of a bisphosphonate may blunt the anabolic effects of rhPTH. Studies in rats, however, suggest that a single intravenous dose of a bisphosphonate might circumvent this problem. Consequently, Cosman and co-investigators used a single intravenous administration of zoledronic acid in this 1-year study to evaluate the effects of combination therapy on BMD and bone turnover.

The researchers randomly allocated 412 postmenopausal women with osteoporosis to receive a single intravenous infusion of 5 mg zoledronic acid plus daily subcutaneous injections of 20 μg teriparatide ($rhPTH_{1–34}$) or either agent alone. Participants had no prior use of PTH or bisphosphonates for >3 consecutive months and a 1-year washout was required for short-term use. The investigators measured participants' lumbar spine and total hip BMD by dual-energy X-ray absorptiometry at screening and at weeks 13, 26 and 52, and markers of bone formation (*N*-terminal propeptide of type I collagen) and resorption (β-C-telopeptide of type I collagen) at baseline and 4, 8, 26, 39 and 52 weeks.

At 1 year, lumbar spine BMD had increased by 7.5% in the combination therapy group, by 7.0% in the teriparatide group and by 4.4% in the zoledronic acid group. Total hip BMD increases were 2.3%, 1.1% and 2.2% with combination therapy, teriparatide alone and zoledronic acid alone, respectively.

As the increases in BMD at both sites were most pronounced during the initial 3–6 months of combination treatment, the researchers speculate that co-administration of the agents expanded the anabolic window—the period of time when teriparatide displays maximal anabolic effects. Specifically, in the combination group, bone resorption rapidly declined in the first 8 weeks whilst bone formation generally increased throughout the 1-year period, only briefly declining between 4–8 weeks, which suggested that zoledronic acid had not prevented teriparatide's osteoblastic response. However, the period of zoledronic-acid-induced inhibition of bone resorption was stunted by teriparatide—the researchers speculate that this agent might promote rapid removal of zoledronic acid from the bone surface.

Although effects on fracture-risk reduction require assessment, the investigators conclude that the combination might be appropriate for patients at high risk of hip fracture.

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Original article Cosman, F. *et al.* Effects of intravenous zoledronic acid plus subcutaneous teriparatide [(1–34) rhPTH] in postmenopausal osteoporosis. *J. Bone Miner. Res.* doi:10.1002/jbmr.238