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# New osteoporosis drug combination outperforms current alternatives

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A combination of two FDA-approved osteoporosis drugs with different mechanisms of action was found to increase bone density better than treatment with either drug alone in a small clinical trial. As reported in paper receiving Online First publication in *The Lancet*, Massachusetts General Hospital (MGH) investigators found that treatment combining denosumab (Prolia) and teriparatide (Forteo) was superior to single-agent treatment in a 12-month trial in women with postmenopausal osteoporosis. The authors note that additional study is required before their findings should be put into clinical practice.

"We found that giving both of these drugs together increased bone mineral density more than treatment with just one drug and more than has been reported for any currently available therapy for postmenopausal osteoporosis," says Benjamin Leder, MD, of the MGH Endocrine Unit, corresponding author of the *Lancet* report. "This is particularly important since previous attempts to combine teriparatide with bisphosphonate drugs like Fosamax did not show any additional improvement."

Bone density in young adults is maintained by a constant interaction between cells called osteoclasts, which break down bone, and osteoblasts, that form new bone. After a woman goes through menopause, both processes accelerate, but the breakdown or resorption of bone increases more, leading to the overall loss of bone density and osteoporosis, a thinning of the bones leading to increased risk of fractures. While several types of drugs that increase bone density – teriparatide, which stimulates bone formation, and several that block

bone resorption – have been approved for the treatment of postmenopausal osteoporosis, none can reliably restore normal bone strength in most patients or eliminate osteoporosis-related fracture risk.

Previous trials combining teriparatide with bisphosphonates, which block breakdown, did not show improvement over treatment with a single drug. But some animal studies combining teriparatide with denosumab, which blocks resorption using a different mechanism, suggested a possible benefit, leading the MGH team to design the current trial. They enrolled 100 postmenopausal women determined to be at high fracture risk, based on their bone density and other risk factors, who were randomly divided into three groups.

Over the 12-month study period, one group received a subcutaneous 60 mg dose of denosumab every six months, another group self-administered daily 20-microgram injections of teriparatide, and the third received both drugs at the same dosage schedules. Bone density and blood tests were taken at the outset of the study and after 3, 6 and 12 months, and the final analysis included 94 participants who completed at least one follow-up visit.

Participants receiving treatment with both drugs had significantly better results than those receiving just one at several measured sites. For example, bone density measured at the lumbar spine increased 6.2 percent with teriparatide alone and 5.5 percent with denosumab, but combination treatment resulted in a 9.1 percent increase. Similar bone density improvements were seen at the hip.

In considering possible reasons for this combination's superiority over combined bisphosphonate and teriparatide, Leder explains that teriparatide actually stimulates both bone formation and resorption and that denosumab may more completely block teriparatide-induced resorption while only partially interfering with the drug's stimulation of

bone formation. An associate professor of Medicine at Harvard Medical School, he notes that longer studies are required in larger groups of patients to assess the combination's ability to reduce fracture risk and its long-term safety.

**More information:** www.thelancet.com/journals/lan … (13)60856-9/abstract

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