University of Pittsburgh researchers launching trial of new osteoporosis drug

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Endocrinologists at the University of Pittsburgh School of Medicine and UPMC are launching a human trial of a new drug that their research indicates holds great promise for building bones weakened by osteoporosis.

For the study, 105 participants will be randomly assigned to receive either teriparitide (Forteo®), a drug that already is FDA-approved for osteoporosis treatment, or an experimental agent called parathyroid hormone-related protein (PTHrP), explained principal investigator Mara J. Horwitz, M.D., an assistant Professor of Medicine in the Division of Endocrinology and Metabolism, Pitt School of Medicine, and a practicing metabolic bone specialist at UPMC.

"We are very eager to find out how this new drug compares to a therapy that is currently available," Dr. Horwitz said. "Our previous studies suggest that it may increase bone density more dramatically with fewer side effects, but this is the first head-to-head comparison."

On the cellular level, bone is constantly being broken down, a process known as resorption, and then rebuilt. In osteoporosis, this balancing act is off-kilter, leaving bones less dense and more vulnerable to fracture. Many drugs, such as alendronate (Fosamax®), and raloxifene (Evista®), work by decreasing bone resorption. They can improve bone density by two to 10 percent over several years to a decade and reduce fractures, but many patients' bone density already has been reduced by half when treatment begins.

Another kind of agent works on the other end of the bone metabolism see-saw: it promotes the creation of new bone. Teriparitide, a form of naturally occurring parathyroid hormone, currently is the only FDA-approved anabolic or bone-building agent in the United States. The experimental drug PTHrP, another protein made naturally by the body, also is an anabolic agent and appears to be unique in its ability to stimulate bone formation without simultaneously increasing bone breakdown. Both drugs are given as daily injections.

"When we studied PTHrP several years ago in small numbers of postmenopausal women with osteoporosis, we found that bone density increased by nearly 5 percent after only three months of treatment," said senior investigator Andrew F. Stewart, M.D., professor and chief of the Division of Endocrinology and Metabolism, Department of Medicine, Pitt School of Medicine. "And even at the highest doses, the side effects were negligible."

In findings published online last week in the *Journal of Clinical Endocrinology and Metabolism*, Drs. Horwitz and Stewart and their colleagues identified the maximum tolerable dose and therapeutic window of PTHrP. In this study, they were also able to show that PTHrP, at the tolerable doses, stimulated bone formation after only three weeks of treatment.

Provided by University of Pittsburgh