

CONTENTS

Adding to the Arsenal

BY PAUL ENGSTROM

New drugs in the research pipeline could prove valuable in protecting bone from osteoporosis in patients with or without cancer. Most of the agents suppress bone resorption, the same method as bisphosphonates.

Initially, the focus of such research is often narrow, with investigators studying the effectiveness of a compound in patients whose cancer has spread to bone. But experts are always hopeful some experimental drugs will also prove effective in osteoporosis patients without bone metastasis, says Catherine H. Van Poznak, MD, a medical oncologist at the University of Michigan in Ann Arbor. For instance, clinical trials of the bisphosphonate Zometa initially looked at its effectiveness in treating bone metastasis. Now, a new formulation of the drug is used to treat osteoporosis in postmenopausal women under the brand name Reclast.

Compared to current osteoporosis drugs, “one hopes the newer treatments will have fewer side effects,” says Allan Lipton, MD, a researcher and oncology division chief at the Milton S. Hershey Medical Center of Penn State College of Medicine in Hershey. While denosumab and osteoprotegerin are among the most promising new agents—though they still need to be evaluated in large-scale clinical trials to establish their value—other investigational agents include:

Strontium ranelate. Clinical trials in Europe suggest this compound suppresses the resorption of bone, thereby allowing unimpeded bone formation and a reduction of vertebral fractures. There are trace amounts of the element strontium throughout the skeleton.

Cathepsin K blockers. Osteoclasts attach to the bone surface and resorb calcium. Then they release cathepsin K, an enzyme, to degrade proteins in the bone matrix, which weakens bone if the bone formation and resorption process is out of balance. Researchers are studying a class of compounds that block cathepsin K.

Gallium nitrate (intravenous) and gallium maltolate (oral). Scientists have discovered these semi-metallic compounds directly inhibit the release of calcium from bone, mostly by lowering bone resorption. Gallium may also stimulate bone formation. The Food and Drug Administration has already approved gallium for treating cancer-related hypercalcemia, in which bone loss is so rapid that the kidneys are unable to eliminate excess calcium in the blood.

Small-molecule inhibitors. Another enzyme that fosters bone resorption—as well as the proliferation, metastasis, and other activities of human cancers—is Src tyrosine kinase. Researchers are experimenting with designer molecules that, in specifically targeting bone tissue, inhibit the enzyme’s activities and prevent osteoclasts from resorbing bone.

