

# BONE UP/date

OREGON OSTEOPOROSIS CENTER

## Special Edition: IV Zoledronic Acid Treatment for Osteoporosis

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The results of research evaluating a new intravenous treatment for osteoporosis have recently been released. The results of the major study with zoledronic acid were presented at a national scientific meeting in Philadelphia in September 2006. In that study, more than 7,000 women with osteoporosis received either intravenous zoledronic acid given once yearly or a placebo given every year for a total of three years. During the study, active treatment decreased the frequency of spine fractures by 70%. Hip fracture risk was reduced by 40% and the overall incidence of fracture was reduced by 24%.

There are several reasons why this new treatment schedule is appealing to both patients and to physicians. The purpose of treating patients with or at risk for osteoporosis is to prevent the progressive damage to bone tissue and to protect them from fractures. We now have several drugs that are capable of accomplishing this. The drugs in the class called bisphosphonates are most commonly used to treat osteoporosis. Drugs in this class include alendronate (Fosamax<sup>®</sup>), risedronate (Actonel<sup>®</sup>), and ibandronate (Boniva<sup>®</sup>). These drugs are the most commonly used because they have been proven in large clinical research studies to protect women with osteoporosis from fractures. Doctors have more confidence these drugs reduce fracture risk compared to the other available drugs, raloxifene (Evista<sup>®</sup>) and nasal calcitonin (Miacalcin<sup>®</sup>, Fortical<sup>®</sup>). The bisphosphonate drugs are usually very well tolerated, especially with the intermittent dosing regimens now used. Fosamax and Actonel are generally given once each week, and Boniva is available in higher dose tablet taken once a month.

Despite the good features of bisphosphonate tablets to treat osteoporosis, several problems exist with these treatments. Some patients experience

heartburn and other gastrointestinal symptoms when they take bisphosphonate tablets. The proportion of patients who have true intolerance to the medicine is not known, since most patients who are candidates for these drugs are older adults who have intermittent gastrointestinal symptoms even without the help of other medications. Having treatment options for those patients who do not tolerate oral bisphosphonates would be helpful in many patients.

Secondly, many older adults who are prescribed bisphosphonate tablets have other complicated medical problems. It is difficult to fit the special dosing requirements for oral bisphosphonates (fasting, not eating or taking other medicines for at least 30 minutes, etc.) into that schedule. This is a special problem for patients in nursing homes or in those who take many medicines each day. Being able to receive a treatment for osteoporosis at infrequent intervals that does not interfere with the rest of their medical regimen would be helpful.

Lastly, several studies have demonstrated that fewer than half of patients who begin any of the oral treatments for osteoporosis remain on treatment for more than one year. This means that the potential effectiveness of these medications is substantially reduced, and the healthcare costs of identifying patients who are candidates for treatment and having them begin therapy is simply wasted. Improving the ability to receive the benefit of treatment for a longer time would be both helpful to the patients and more cost effective.

For these reasons, there is strong interest in the availability of bisphosphonate drugs that are administered intravenously. Ibandronate (Boniva<sup>®</sup>) is already available to be given by injections into the vein once every three months. That drug is approved for the treatment of osteoporosis in women and is known to be as effective as is the

daily oral form of ibandronate. The availability of intravenous ibandronate and zoledronic acid will provide benefit for the three circumstances listed above, and the once-yearly dosing interval with zoledronic acid is especially appealing.

All drugs have side effects. The patients who received intravenous zoledronic acid did not experience upper GI side effects. However, a moderate number of patients did experience a flu-like illness that lasted for a few days after they received their intravenous treatment. These symptoms of muscle and joint aches, fever and headache were generally mild to moderate, lasted for only a few days, and were helped by taking medicines such as acetaminophen (Tylenol®). The symptoms most often occurred after the first dose, and did not occur after the second or third doses. Similar symptoms have occurred with intravenous Boniva and, less commonly, with the high-dose once monthly Boniva treatment.

The results of the major fracture prevention study with zoledronic acid will be submitted to the FDA for their review and for them to decide about approving this treatment regimen for women with postmenopausal osteoporosis. It takes several months after the filing of this information before the FDA arrives at that decision.

Zoledronic acid is already approved by the FDA for the treatment of patients with cancer who have high levels of blood calcium or have tumor that has spread to the bone tissue. Those patients receive very high doses of zoledronic acid (Zometa®), receiving IV treatments every 3-4 weeks. This treatment has been shown to slow the growth of tumor in the bone and to slow the progression of the bone complications of cancer. Zometa treatment has been associated with the development of a dental problem called osteonecrosis of the jaw. In some patients who are receiving the high doses of Zometa, the jaw bone does not heal after teeth are removed or after other dental procedures. A smaller number of patients have been seen with these jaw lesions who have taken oral bisphosphonates like Fosamax or Actonel for the treatment of osteoporosis, although the risk of developing jaw problems with bisphosphonate tablets appears to be very low. It is not known whether the dose of intravenous zoledronic acid that will be used for the treatment of osteoporosis will be associated with this complication.

Because zoledronic acid is available for the treatment of cancer patients, doctors can prescribe it for the treatment of other conditions such as osteoporosis. However, since treating osteoporosis is not yet an approved indication, many insurance companies and Medicare will not cover the cost of this treatment (about \$800 per IV treatment) since other approved treatments, including intravenous ibandronate (Boniva®), are available.

It is my opinion that intravenous zoledronic acid is an appealing new option for treating patients with osteoporosis in the near future. I personally think that it should not yet be used for the treatment of osteoporosis, except in very special circumstances, until the medicine has been approved and the full set of research data about both its effectiveness and safety have been carefully reviewed by the FDA and other scientists.

***Interested in Clinical Research?***

To obtain information about our clinical research activities or to discuss participation in one of our clinical trials, please call our research recruitment coordinator at (503) 215-1731.

*NOTE: The opinions expressed here are those of Dr. Michael McClung, the founding director of the Oregon Osteoporosis Center where consultation, diagnostic testing and clinical research activities are conducted. Dr. McClung is a board certified endocrinologist who has been interested in bone and calcium metabolism for more than 25 years. During that time, he has published many articles and book chapters and has become a national expert in the fields of osteoporosis and bone density testing. Dr. McClung is a well-known speaker and educator, and is an active member of multiple international societies focusing on bone diseases and their treatment. He is an*



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