

Introduction: This is a very interesting study from the standpoint that I do not prescribe bisphosphonates for osteoporosis because there are safer work-arounds for this problem. This class of drugs also has some very problematic side effects for those women with root canal teeth causing in some what is known as “fossy-jaw” or the complete destruction of the jawbone around root canal teeth. This is an irreparable condition. What is interesting to me is the aspect of looking at calcium interplay, particularly the mevalonate pathway which is also the metabolic pathway to break down statins which, coincidentally, also have anti tumor properties. I do not prescribe statins for similar reasons. But a 60% relative reduction in the risk of colorectal cancer is worthy of some study. PBMD

Bisphosphonates Now Linked to Lower Risk for Colorectal Cancer

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January 27, 2011 (San Francisco, California) — Taking bisphosphonates for osteoporosis for more than a year is associated with a reduced risk for colorectal cancer, according to a new study from the same Israeli group that reported a reduced risk for breast cancer.

Both sets of results come from an analysis of postmenopausal women who were taking mainly oral bisphosphonates, such as alendronate, for osteoporosis, and were reported by Gad Rennert, MD, PhD, and colleagues from the Clalit Health Services National Cancer Control Center in Haifa, Israel, at the 2011 Gastrointestinal Cancers Symposium, which is cosponsored by the American Society of Clinical Oncology and other societies..

The [previous study](#), showing a reduction in breast cancer risk, was published last year; a similar finding has been reported by 2 independent groups from 2 different populations of postmenopausal women taking bisphosphonates.

These findings stirred great interest in the potential anticancer effects of bisphosphonates, but some experts raised concerns about the breast cancer data. They pointed out that postmenopausal women who were taking bisphosphonates for osteoporosis were likely to have low levels of estrogen, which led to the osteoporosis, and lower levels of estrogen are known to reduce the risk for breast cancer.

Dr. Rennert told *Medscape Medical News* that his team specifically set out to investigate the effect of bisphosphonates on tumor sites other than the breast to address these concerns. Demonstration of a protective effect at a site other than the breast "would help clear the question" of whether the effect seen with breast cancer is a drug effect or simply a reflection of low estrogen leading to osteoporosis and requiring bisphosphonates, but also reducing the risk for breast cancer in itself.

"Our new data about a similar effect in the colon suggest that it is the drug itself," Dr. Rennert reported.

Further studies are ongoing. "We are working with more tumor sites and seeing a similar effect to what we are seeing with statins," he said. "It definitely looks like a class effect, with a mechanism that possibly involves the mevalonate pathway, which is also involved in the metabolism of statins."

New Data on Colorectal Cancer

"The use of oral bisphosphonates for more than 1 year was associated with a 60% relative reduction in the risk of colorectal cancer, similar to the recently reported

association of this drug class with reduction in breast cancer risk," Dr. Rennert and colleagues told the meeting.

The results come from a population-based case-control study of colorectal cancer — the Molecular Epidemiology of Colorectal Cancer — conducted in northern Israel. The data on bisphosphonate use were collected from a subset of 933 postmenopausal women with colorectal cancer and 933 control subjects (matched for age, religion, and residence) from the Clalit Health Services, using computerized pharmacy controls.

Bisphosphonate use was recorded in 97 patients and 138 control subjects, Dr. Rennert reported. "But our finding is for [those who have used] bisphosphonates for more than 1 year," he explained (53 of 933 women with colon cancer and 100 of 933 control women; $P < .001$ in univariate analysis).

The use of bisphosphonates for more than 1 year prior to the diagnosis of colorectal cancer, but not for less than a year, was associated with a significantly reduced risk for colorectal cancer (odds ratio, 0.50; 95% confidence interval, 0.35 to 0.71).

This association remained statistically significant after adjustment for vegetable consumption, sports activity, family history of colorectal cancer, body mass index, and use of low-dose aspirin, statins, vitamin D, and hormone replacement therapy, the researchers note. Concomitant use of bisphosphonates and statins did not reduce the risk any further.

Intense Interest in Bisphosphonates

There is an intense interest in the potential anticancer effects of bisphosphonates, prompted by several intriguing findings in recent years. In addition to the data suggesting a protective effect against cancer discussed above, there have been several studies suggesting that these drugs have anticancer effects in patients who already have cancer.

The most positive of these results come from an [Austrian study](#), which showed that breast cancer recurrence and death were reduced by a third in women taking bisphosphonates.

However, the most recent study on this was negative overall. The AZURE study found no effect from the potent bisphosphonate zoledronic acid (*Zometa*, Novartis) on the recurrence of breast cancer or on overall survival. However, a subset analysis showed a significant effect in postmenopausal but not premenopausal women; breast cancer recurrence and deaths were reduced by about a third.

Results from the AZURE study, presented in December 2010 at the San Antonio Breast Cancer Symposium, were described as unexpected and puzzling, and sparked much discussion at the meeting, as [reported](#) by *Medscape Medical News* at the time. This story will continue, because several more studies addressing this issue are underway.

Dr. Rennert and colleagues have disclosed no relevant financial relationships.

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