Potential breast cancer prevention drug found to cause significant bone loss

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A drug that has been shown to prevent breast cancer in postmenopausal women at high risk of developing the disease, and is poised for widespread use, appears to significantly worsen age-related bone loss, according to an Article published Online First in The *Lancet Oncology*.

"Exemestane worsens age-related decreases in bone mineral density by about three times, even in the setting of adequate calcium and vitamin D intake", explains Angela Cheung from the University Health Network, Toronto, Canada, lead author of the study.

Aromatase inhibitors work by suppressing oestrogen production and are the standard treatment for postmenopausal women with early stage hormone-receptor-positive breast cancer. But despite being generally well-tolerated, concerns have been raised about their effects on bone loss and increased fracture risk. To date, one of the problems with obtaining clear evidence about the impact of aromatase inhibitors on bone health is that most studies have been done with tamoxifen as the comparison, a treatment with known beneficial effects on bone in postmenopausal women.

Preliminary research suggests that exemestane, a third generation steroidal aromatase inhibitor, might cause less bone loss than other aromatase inhibitors and could even stimulate bone formation.

Here, Cheung and colleagues report the results of a bone-mineral and bone structure substudy of patients included in the Mammary Prevention

3 (MAP.3) trial, to quantify the effect of exemestane on bone-mineral density (BMD) and structure in postmenopausal women.

The MAP.3 randomised trial examined the effect of exemestane at preventing breast cancer in over 4500 healthy postmenopausal women at high risk of developing the disease (eg, with a family history of breast cancer). Exemestane reduced the risk of developing breast cancer by 65% compared with placebo. 351 women without osteoporosis were included in the bone substudy, 176 given exemestane and 175 given placebo. BMD was measured by conventional dual-energy x-ray absorptiometry and new high-resolution peripheral quantitative CT.

After 2 years of treatment, women given exemestane had a significant loss of BMD at the distal radius (a common site for fractures related to osteoporosis) and distal tibia compared with at the start of the study.

Additionally, in the exemestane group, cortical thickness and area declined by almost 8% compared with a 1% decline in the placebo group. Exemestane substantially affected the loss of cortical bone compared with trabecular bone. This finding is important because most fractures (80%) in old age are the result of greater loss of cortical rather than trabecular bone and account for most disability.

The authors caution: "Women considering exemestane for the primary prevention of breast cancer should weigh their individual risks and benefits. For women taking exemestane, regular bone monitoring plus adequate calcium and vitamin D supplementation are important. Long-term studies are needed to assess the effect of our findings on fracture risk."

In an accompanying Comment, Jane Cauley from the University of Pittsburgh, Pennsylvania, USA says: "Most bone loss occurs after 65 years of age, within the cortical compartment. Thus, if aromatase

inhibitors increase cortical porosity, this effect could be a key cause of bone loss strength and non-vertebral fractures associated with their use. Thus, one might not be too reassured about the use of exemestane in the prevention setting."

More information: www.thelancet.com/journals/lan … (11)70389-8/abstract

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