Effects of AIs on Bone Metabolism

Marker	Estimated % change		
	Anastrozole	Letrozole	Exemestane
Bone ALP	2.0	2.9	6.6
P1NP	13.6	11.3	23.4
CTX	16.4	27.8	23.0
PTH	–7.7	–10.7	–20.5

Note: AI = aromatase inhibitor, ALP = alkaline phosphatase, P1NP = propeptide of type I procollagen, CTX = C-telopeptide crosslinks, PTH = parathyroid hormone.

Source: Dr. McCloskey

Three Aromatase Inhibitors Found to Have Similar Effects on Bone Turnover

BY KERRI WACHTER
Senior Writer

Elsevier Global Medical News

PHILADELPHIA — Steroidal and nonsteroidal aromatase inhibitors appear to have very similar effects on bone metabolism, which result in increased bone turnover, according to data presented at the annual meeting of the American Society for Bone and Mineral Research.

"Anastrozole, letrozole, and exemestane in this study seem to have similar effects on bone biochemical measurements, and thus bone turnover. … The increase in bone turnover doesn't appear to be significantly different with the steroidal versus nonsteroidal aromatase inhibitors," said Dr. Eugene McCloskey, a senior clinical lecturer in metabolic bone disease at the University of Sheffield in England.

Aromatase inhibitors have been associated with increased bone turnover, particularly in the setting of adjuvant therapy for breast cancer. Some preclinical studies have suggested that there may be differences between the effect of the steroidal (exemestane) and nonsteroidal (letrozole and anastrozole) aromatase inhibitors on bone turnover.

With the Letrozole, Exemestane, and Anastrozole Pharmacodynamics (LEAP) trial, Dr. McCloskey and his colleagues compared the effects of these three aromatase inhibitors on safety parameters such as serum markers of bone formation and resorption, lipid profiles, and adrenal function in healthy postmenopausal women with normal bone mineral density at the spine and hip.

Letrozole (Femara) is made by Novartis Pharmaceutical Corp., exemestane (Aromasin) by Pfizer Inc., and anastrozole (Arimidex) by AstraZeneca. The study was sponsored by AstraZeneca, and Dr. McCloskey disclosed that he has received research grants from the company.

In the study, healthy postmenopausal women were randomized to receive letrozole (2.5 mg/day), exemestane (25 mg/day), or anastrozole (1 mg/day) once daily for 24 weeks. The women were followed for another 12 weeks after the end of therapy. Overall, 102 women were randomized and 96 are included in this analysis (32 on letrozole, 34 on exemestane, and 30 on anastrozole).

The researchers measured changes from baseline bone alkaline phosphatase (a formation marker), serum C-telopeptide crosslinks (a marker of resorption), parathyroid hormone, and propeptide of type I procollagen (a marker of formation).

For bone alkaline phosphatase (ALP) all three drugs showed a trend toward increased levels but only exemestane reached statistical significance. However, there was no statistical difference among the three groups.

There was a nonstatistical increase for all three groups in terms of propeptide of type I procollagen (P1NP) but no statistical difference between the groups.

Serum C-telopeptide crosslinks (CTX) levels were also increased in all three groups but there was no significant difference among the groups.

To look at these formation and resorption marker increases in more detail, the researchers calculated the uncoupling index, which is a measure of the difference between formation and resorption. To do this, they calculated *z* scores for the resorption marker (CTX) and formation markers (ALP and P1NP). *z* Scores for formation markers were subtracted from *z* scores for CTX. The results indicated that resorption generally exceeds formation for all three drugs. With regard to change in parathyroid hormone (PTH) levels, the decrease with exemestane was greater than with anastrozole. The difference was statistically significant. ■

Pages 16a—16b