Short Communication

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Problems with the Use of Aromatase Inhibitors in Breast Cancer

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The use of Aromatase Inhibitors (AI's) in the adjuvant therapy of operable breast cancer is ubiquitous. All guidelines in widespread use advocate their use in hormone-receptor-positive breast cancer in post-menopausal women. Pre-menopausal hormone-receptor-positive women who are considered at high risk of relapse are also treated with drug- or surgically-induced ovarian suppression plus an AI following chemotherapy, producing somewhat better results than those seen with chemo followed by tamoxifen [1]. A major side effect of these drugs is the accelerated loss of bone mineral density (BMD). The use of bone-sparing agents such as bisphosphonates has become widespread but not routine in these patients. Whether or not they receive bone-sparing agents, patients on AI's should receive periodic assessment of bone density. How do doctors comply with this common-sense approach? The answer: not as often as they should. The best data on this practice was published in the *Journal of Oncology Practice* in May 2017 from a group of investigators at Yale [2]. Using the SEER Medicare database they identified over 135,000 women diagnosed with breast cancer from 2007 to 2010. Using robust exclusion criteria for such things as metastasis at presentation, too brief exposure to bisphosphonates, in situ only cancer, and prior diagnosis of osteoporosis, they identified 2409 women who met all entry criteria and served as the population studied. Within this group only 51% received a DEXA scan at initiation of AI and only 34% had a second scan within three years of being on therapy. What the authors were not able to ascertain was how many of these patients were placed on a prophylactic bisphosphonate or equivalent at the start of AI therapy. What was clear is that age and race had a lot to do with who received a DEXA scan. 30% of women over 85 vs. 56% ages 67-69 were scanned. 53% of caucasian women were scanned vs. 33% non-caucasian. Women with higher stage and more comorbidities were also less likely to have been scanned.

A subsequent study looked at the addition of denosumab, a RANKL inhibitor that prevents the development of osteoclasts, to AI therapy with or without chemotherapy. They found an improvement in lumbar bone density of 8% and in hip bone density of 6% over a two-year period [3]. The enrollees in this trial had their BMD measured every four months.

What can we learn from these data? First of all, we seem not to have, but are sorely in need of, data on what percentage of women on an AI are also on supportive measures to prevent bone loss. Second, physicians who administer AI's need to be put on notice as to the need to monitor their patients rigorously. Closed health-care plans with carefully structures electronic health records are the ideal venue to accomplish this sort of peer review, but it could be conducted in a variety of other settings. The Yale study speaks to the haphazard approach to following BMD that characterizes contemporary practice patterns. Fractures associated with osteoporosis are very morbid and result in excess mortality when the hip joint is involved. Oncologists in particular need to take a holistic approach to patient care, including monitoring for the development of bone mineral loss; and need to seriously consider adding a bone-sparing drug

to their patients' regimen. Finally, it is very clear that the addition of bone-enhancing drugs adds BMD when used appropriately in conjunction with aromatase inhibitors.

To summarize, women given adjuvant AI's to prevent breast cancer metastasis are not being evaluated appropriately for a major potential complication of therapy; and data on the frequency of use of supportive-care bone strengthening agents in these patients is sorely lacking, despite the abundance of data that they help prevent loss of bone. Fixing these problems should be easy but thus far they have defied a solution. We can do better.

References

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