Switching AIs Often Effective for Joint Symptoms

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SAN ANTONIO — More than half of breast cancer patients who experience joint symptoms on one nonsteroidal aromatase inhibitor don't experience them on the other, results of a randomized, prospective trial suggest.

Moreover, at least three-quarters of patients who develop joint pain and/or stiffness on the nonsteroidal aromatase inhibitors (AIs) anastrozole (Arimidex) or letrozole (Femara) no longer experience joint symptoms if they are switched to tamoxifen, study investigator Dr. J. Michael Dixon reported at the San Antonio Breast Cancer Symposium.

"The message is, if you get joint symptoms on one drug, try switching to something else because there's probably something out there they can tolerate," Dr. Dixon, of the University of Edinburgh, explained in an interview.

The AIs are increasingly prescribed for up to a 5-year course in lieu of tamoxifen as adjuvant hormonal therapy in women with hormone receptor–positive early invasive breast cancer because of their superior efficacy in reducing the risk of recurrence.

New-onset musculoskeletal complaints are common in patients on the AIs. They are a leading cause of poor compliance and treatment discontinuation. To better understand these important side effects, Dr. Dixon and coworkers randomly assigned 182 women with early invasive breast cancer to 3 months of standard dosages of either anastrozole or letrozole, followed by 3 months on the other AI. After that 6-month period, all participants were placed on tamoxifen, because 5 years of tamoxifen was the standard practice in Scotland at the time.

Patients were evaluated in detail for side effects after 1, 2, and 3 months on each drug. Twelve subjects were forced to withdraw from the study because they couldn't complete at least 1 month on both AIs because of joint symptoms.

The investigators' hypothesis was that joint symptoms and bone turnover would be worse on letrozole, since it's the more potent of the two AIs in terms of reducing circulating estrogen levels. But their hypothesis wasn't borne out.

Of the 170 patients who completed the study, 131 reported new-onset joint pain while on an AI. But there was no significant difference between the rates associated with anastrozole and letrozole. Ten women reported joint stiffness.

A total of 56% of patients who reported joint problems on letrozole didn't experience them on anastrozole. And 55% of those who had joint symptoms on anastrozole didn't have them on letrozole.

Moreover, 85% of patients with joint problems on anastrozole had no joint problems when placed on tamoxifen. The same was true for 74% of women who had joint symptoms on letrozole.

On the other hand, 74% of patients who didn't experience joint problems while on anastrozole did have them on tamoxifen, as did 57% of those who didn't have joint symptoms on letrozole.

Dr. Dixon said that trying to wait out significant joint symptoms in the hope that they will abate over time is not a winning strategy. The large clinical trials of the AIs versus tamoxifen, such as the landmark 6,241-patient ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial, clearly demonstrate that the joint symptoms don't abate with time if patients remain on the offending drug. Indeed, in ATAC the prevalence of joint symptoms climbed steadily during the 5 years of treatment with either drug. He added that, in his own experience, NSAIDs "don't help all that much" for AI-associated joint symptoms. Other physicians at the conference estimated that about half of their affected patients benefit from NSAID therapy.

With regard to AI-induced bone turnover, Dr. Dixon and coworkers found that 2.5 mg/day of letrozole and 1 mg/day of anastrozole had virtually identical effects on bone metabolism, as measured by changes in parathyroid hormone, type 1 procollagen peptides, bone-specific alkaline phosphatase, and N- and C-terminal telopeptides. Bone turnover was greater at 6 months than at 3 months. Based on these results, he concluded that there is unlikely to be any difference between the two AIs in osteoporosis or fracture rates.

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Dr. Dixon stated that he has no financial relationships relevant to this investigation to disclose. ■

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