Try Aromatase Inhibitor for Subset of Breast Ca

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An aromatase inhibitor should be considered as adjuvant therapy for all postmenopausal women with hormone receptor–positive breast cancer, according to an updated American Society of Clinical Oncology clinical practice guideline.

The optimal timing and duration of aromatase inhibitor (AI) treatment are not yet resolved, but it appears to reduce the risk of recurrence when taken at some time during adjuvant therapy – either alone as monotherapy, as sequential therapy before tamoxifen therapy commences or after 2-3 years of tamoxifen treatment, or as extended therapy after 5 years of tamoxifen is completed, said Dr. Harold J. Burstein of the Dana-Farber Cancer Institute, Boston, and his associates on ASCO's Endocrine Therapy for Breast Cancer Update Committee.

The last update on the adjuvant use of AIs for hormone receptor–positive breast cancer was published in 2004. "Our panel carefully reviewed the explosion of research that has emerged in the past 5 years on anti-estrogen drugs, and filled in gaps in our understanding of how best to use these newer treatments, and what the trade-offs and side effects of therapy would be," Dr. Burstein noted in a press statement.

Their review focused on 12 prospective randomized clinical trials gleaned from 484 articles or abstracts from the medical literature, presentations, or posters.

The data are somewhat limited. Most of the studies had relatively short follow-up times, and the longest median follow-up was only 8 years. Because of that and

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patients' generally favorable prognoses, few breast cancer events occurred during follow-up.

In addition, the assessment of important subgroups of patients was limited by relatively small sample sizes, and the small samples also limited analysis of quality-of-life data, Dr. Burstein and his colleagues said (J. Clin. Oncol. 2010 [doi:10.1200/JCO.2009.26.3756]).

Among the major findings:

► Adding an AI to adjuvant therapy improves disease-free survival and reduces the risk of distant metastasis, locoregional recurrence, and contralateral breast cancer. The reduction is modest – typically less than 5% over several years – but these outcomes are clinically important to patients. Only a few trials demonstrated a statistically significant increase in overall survival.

► AI therapy should not extend beyond 5 years, as either initial or extended adjuvant treatment, because results on longer-term treatment are not yet available.

► The optimal length of time before switching from tamoxifen to an AI is not yet known. For sequential treatment, patients should receive an AI after 2-3 years of tamoxifen, for a total of 5 years of adjuvant endocrine therapy. Alternatively, patients who begin an AI but discontinue it before 5 years have elapsed can consider taking tamoxifen until a total of 5 years of endocrine therapy accrue. For extended therapy, patients can be offered an AI after they have taken 5 years of tamoxifen. The data on extended therapy, however, are not as extensive as with sequential therapy.

► As of now, no clinically important differences in effectiveness have been reported among the three commercially available AIs (anastrozole, letrozole, and exemestane).

► Research to date has not revealed a specific marker that identifies patients most likely to benefit from AI therapy, nor a clinical subset of patients most likely to benefit.

► AIs generally are well tolerated. The drugs have been linked to increased risk of hypercholesterolemia and hypertension, and possibly of cardiovascular disease, but longer follow-up is needed to determine potential CV toxicity.

AIs also often cause a mild to moderate musculoskeletal/arthralgia syndrome. They have been associated with a greater loss of bone mineral density and a 2%-4% increased risk of fracture, compared with tamoxifen, but the long-term impact of treatment on bone is not yet known.

AIs appear to have fewer gynecologic adverse effects than tamoxifen. An increased risk of uterine cancer, benign endometrial pathology, hysterectomy, and vaginal discharge has not yet been noted with AIs, as it has with tamoxifen. AIs may produce fewer hot flashes and less vaginal dryness than tamoxifen.

The committee stressed that the late effects of AI therapy, as well as the possible adverse effects of extended AI therapy, have not yet been fully characterized.

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The committee also noted that there is no evidence yet for or against the usefulness of AI therapy in men with breast cancer.

To facilitate treatment adherence, the updated guideline emphasized that clinicians should alert patients to common adverse effects and potential toxicities of AIs. Research shows that up to 40% of patients discontinue tamoxifen within 3 years and half do so within 5 years, and the findings with AIs are similar. The clear majority of patients who stop treatment prematurely do so because of adverse effects.

In particular, the musculoskeletal effects of AIs prompted discontinuation in more than 10% of women in one study. "Information support for patients about anticipated adverse effects and management of those adverse effects may increase persistence," according to the guideline.

Monetary constraints are another cause of nonadherence. In one study of tamoxifen, 60% of patients who discontinued treatment early said that the cost of the drug was a key factor. "It is likely that the out-of-pocket costs of AIs pose an even greater barrier to patients," the committee said. ■

The complete clinical practice guideline is available at www.asco.org/guidelines/endocrinebreast. A corresponding patient guide is available on ASCO's patient Web site, www.cancer.net.

***Disclosures:** Some of the update committee members reported ties to Pfizer, Novartis, and AstraZeneca.*