Exemestane Beneficial After Adjuvant Tamoxifen

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SAN ANTONIO — Breast cancer patients randomized to exemestane following 5 years of adjuvant tamoxifen were 56% less likely to experience a relapse than were those assigned instead to placebo in the National Surgical Adjuvant Breast and Bowel Project B-33 trial, Dr. Terry P. Mamounas said at a breast cancer symposium that was sponsored by the Cancer Therapy and Research Center.

This result underestimates the benefits of a course of exemestane (Aromasin) following tamoxifen, since 44% of participants randomized to placebo in the prematurely halted B-33 trial crossed over to exemestane and were on the aromatase inhibitor (AI) for much of the median 30-month follow-up, even though for the intent-to-treat analysis they were counted in the placebo arm, noted Dr. Mamounas, medical director of the Aultman Cancer Center in Canton, Ohio.

The NSABP B-33 trial thus shows that exemestane, like the other two approved AIs, is effective when employed in what has come to be called the extended adjuvant hormonal therapy strategy. This was previously shown to be the case for 5 years of letrozole (Femara) following 5 years of tamoxifen in the National Cancer Institute of Canada MA.17 trial, and for 5 years of anastrozole (Arimidex) after 5 years of tamoxifen in the Austrian Breast and Colorectal Cancer Study Group Trial 6.

Five years of tamoxifen—long the standard for adjuvant hormonal therapy in breast cancer—has given way to three alternative AI-based strategies, each shown in large randomized trials to be more effective than the former standard, although the alternatives haven’t hinged on head-to-head.

One strategy involves substituting 5 years of an AI for 5 years of tamoxifen. Another entails sequential therapy with 2-3 years of tamoxifen followed by an AI for the balance of a 5-year course of treatment.

The extended adjuvant therapy strategy is attractive for several reasons. More than half of breast cancer recurrences and more than two-thirds of deaths occur after 5 years on tamoxifen have ended. Most of these recurrent tumors remain hormone sensitive. And as shown in the NSABP B-14 trial, extending tamoxifen beyond 5 years gives no additional benefit, he said.

The double-blind B-33 trial was halted after enrollment of 1,598 of a planned 2,000 patients. On April 8, 2007, it was announced that the study would be unblinded to provide all study patients with exemestane, since most patients randomized to placebo had crossed over to the AI, which might provide an increased benefit over tamoxifen. The decision came after an independent data and safety monitoring committee concluded that the trial was unlikely to reach a significant difference in the primary endpoint of disease-free survival, compared with placebo, even though there was a 53% relative risk reduction, compared with the placebo arm.

Only 8% of patients randomized to placebo had received only tamoxifen; the majority had previously received an AI. Of the 1,598 randomized patients, 1,552 had received 5 years of tamoxifen, followed by 5 years of placebo or exemestane.