Tamoxifen/Anastrozole Sequence Ups Survival

BY BRUCE JANCIN

SAN ANTONIO — Adjuvant endocrine therapy with 2 years of tamoxifen, followed by 3 years of the aromatase inhibitor anastrozole, conferred a 22% reduction in overall mortality, compared with 5 years of tamoxifen alone in breast cancer patients in the large, randomized Austrian Breast and Colorectal Cancer Study Group trial 8.

This is the first clear evidence showing that sequential tamoxifen followed by anastrozole (Arimidex) for a total of 5 years confers a survival benefit compared with tamoxifen alone, Dr. Raimund Jakesz reported at the San Antonio Breast Cancer Symposium.

The Austrian study also demonstrated that the sequence (tamoxifen followed by anastrozole) improved recurrence-free survival by 27%, compared with tamoxifen alone, added Dr. Jakesz, professor and head of the division of general surgery at the Medical University of Vienna.

The ABCSG 8 trial randomized 3,714 postmenopausal women with operable low- to intermediate-risk, hormone receptor–positive breast cancer to one of these two adjuvant endocrine therapy strategies.

The study differed from other randomized trials that compared adjuvant endocrine therapy strategies in that it enrolled patients up to age 80 (fully two-thirds of participants were age 60 years or older), chemotherapy was not permitted, and it was limited to patients with invasive ductal or lobular breast cancer, the surgeon explained.

Nearly 800 patients who were randomized to the tamoxifen-only arm of ABCSG 8 elected to switch to anastrozole following widely publicized reports at the 2004 San Antonio symposium that 5 years of an aromatase inhibitor resulted in significantly better recurrence-free survival than did 5 years of tamoxifen.

In an analysis that excluded the crossover patients, the overall mortality rate was 8.4% in the planned sequential therapy arm of ABCSG 8 at a median 72 months of follow-up, which was significantly better ($P = .025$) than the 11.4% mortality rate in the tamoxifen-only group. This translated to an adjusted 23% relative risk reduction in all-cause mortality.

The tamoxifen/anastrozole sequence was associated with a 27% improvement in recurrence-free survival and a 22% improvement in overall survival, relative to tamoxifen alone.

The recurrence rate was 13.8% among patients in the sequential therapy arm, compared with 16.2% among those treated with tamoxifen only ($P = .038$), for an adjusted 21% relative risk reduction.

In an analysis based upon the treatment that patients actually received, allowing crossovers, the tamoxifen/anastrozole sequence was associated with a 27% improvement in recurrence-free survival ($P = .001$) and a 22% improvement in overall survival ($P = .032$), relative to tamoxifen alone.

The side effect profiles associated with the two adjuvant strategies differed in accord with prior reports from other major trials of tamoxifen vs. aromatase inhibitors: more bone and joint issues with the tamoxifen/anastrozole sequence (11% vs. 8% with tamoxifen alone), and more gynecologic problems with tamoxifen only (31% vs. 23% with the sequencial treatment).

There were no significant differences between the two groups in rates of cardiovascular disorders or eye, skin, or GI problems.

"I don't think 5 years of tamoxifen is now defensible as the best treatment—but you have to remember that it's very good treatment compared to no adjuvant therapy," said Dr. Alan Coates of the University of Sydney, who is cochair of the scientific committee of the International Breast Cancer Study Group.

The ABCSG 8 trial was supported by AstraZeneca. Dr. Jakesz reported having no financial conflicts of interest. ■

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