

IN EVERY ISSUE

Should Breast Cancer Patients Make the Switch?

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Doctors have known for years that hormonal therapies are effective at treating women with hormone-sensitive breast cancers (those positive for the estrogen or progesterone receptors).

But questions remained about switching from one type of drug to another for postmenopausal women: Is it best to start with tamoxifen and then switch to an aromatase inhibitor (AI), or should the AI come first? And is the sequential use of both agents better than treatment with either one alone?

Offering some answers were new data from the BIG (Breast International Group) 1-98 trial, a phase III study involving more than 8,000 women with early-stage breast cancer, which were presented this past December at the 31st Annual CTSC-AACR San Antonio Breast Cancer Symposium. Previous results reported in 2005 showed five years of Femara (letrozole) was more effective than five years of tamoxifen, so the purpose of the updated analyses was to determine whether giving both agents in a sequence would work better than Femara alone.

The amended BIG 1-98 trial compared five years of Femara, two years of Femara followed by three years of tamoxifen, and two years of tamoxifen followed by three years of Femara. There was no evidence that the sequential treatments improved disease-free survival compared with Femara alone. But after two years of initial treatment with Femara, the patients who switched to tamoxifen for three years “couldn’t be distinguished” from patients treated with Femara for the entire five years, study investigator Alan Coates, MD, of the University of Sydney in Australia, told *CURE* at the meeting.

This is important, Coates said, “because if you need to switch [because of the side effects or cost of Femara], you can afford to switch” without compromising efficacy.

Other data presented at SABCS addressed a related question: Is tamoxifen as effective in patients whose bodies do not fully metabolize the drug?

It turns out that tamoxifen has to be metabolized to a compound called endoxifen to be fully active, and one of the key enzymes responsible for this is CYP2D6.

Individuals inherit slightly different versions of genes that encode all proteins, including CYP2D6. In some studies looking at patients taking tamoxifen, those who inherited less active versions of these genes were found to have a higher

recurrence rate compared with those who have versions with normal enzyme activity.

American researchers found that in patients treated with tamoxifen only, those who had “slow metabolizing” CYP2D6 had a nearly four-fold higher chance of early recurrence compared with high metabolizers.

Experts say this finding provides more evidence supporting routine CYP2D6 assessment in patients receiving tamoxifen, and possibly the use of AIs in postmenopausal patients who are slow metabolizers. Ovarian removal or suppression would be necessary in premenopausal patients since AIs are only effective when the ovaries are not producing estrogen.

There is still controversy as to how this test should be interpreted and whether it should be routinely used to make treatment decisions. (Other enzymes metabolize tamoxifen, and several parts of the CYP2D6 gene harbor variations.) It is likely the research community will come together to deliberate on whether this and other findings warrant changes in recommendations for CYP2D6 testing.

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