

WEB EXCLUSIVES

A Winning Combination

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New Data Supports Tykerb Plus Femara for Metastatic Breast Cancer

The combination of Tykerb (lapatinib) and Femara (letrozole) may offer a first-line oral treatment approach for postmenopausal women with hormone receptor-positive, HER2-positive metastatic disease deemed suitable for endocrine therapy, according to a study presented Friday at SABCS.

In women with hormone receptor-positive and HER2-positive tumors, treatment with a combination of Tykerb and Femara delayed the time to disease progression slightly over five months longer than treatment with Femara alone, according to data from the EGF30008 study undertaken by Stephen Johnston, MD, a researcher at the Royal Marsden Hospital in London.

EGF30008 was a study of first-line treatment for 1,286 postmenopausal women with advanced breast cancer and tumors that were hormone receptor-positive. In a subgroup of 219 women with tumors that were both hormone receptor-positive and HER2-positive, treatment with Femara alone resulted in a median progression-free survival of three months, compared with over eight months for patients treated with the combination.

“Wow, this is huge improvement. This is very important information,” said Edith Perez, MD, when she was shown the data during an interview with *CURE*. Perez, a professor of medicine at the Mayo Clinic and a researcher not associated with the trial but who is studying HER2-positive breast cancer, said that based on Johnston’s data, “we should be very comfortable using the combination of lapatinib and letrozole in the setting of HER2-positive cancer.”

Aromatase inhibitors, including Femara, help block the growth of estrogen-sensitive breast tumors by lowering the amount of estrogen in the body. They block estrogen production in tissues other than the ovaries and are usually used in women who have reached menopause. Drugs, such as Tykerb, target tumors with too much HER2, a protein found in high levels in up to 25 percent of breast tumors. Tumors that overproduce HER2 tend to be more aggressive and more likely to recur than those that do not.

“We’ve had treatments targeting the estrogen receptor for a long time, and we’ve had treatments targeting HER2 for a long time. This particular trial is combining the two,” Johnston noted, in an interview with *CURE*.

The reason for combining treatments stems from the fact that cancer cells have many genes and proteins that may be abnormal, Perez explained. Researchers

think the best options for the future will be to combine therapies to address these various abnormalities.

In addition, Johnston explained in his presentation that “current therapies are limited by de novo or acquired resistance” and “dual therapies are a rational approach for overcoming endocrine resistance.”

Safety is clearly an important consideration when adding a drug, such as Tykerb, to a well-tolerated endocrine agent, Johnston said in the presentation, “but the combination was well-tolerated and predictable, and there were no new unexpected toxicities.”

Findings in addition to the main result may have implications for future trials. There was “tantalizing evidence,” according to Johnston, that the combination of Tykerb and Femara may benefit patients who had previously received tamoxifen and relapsed on it.

“That was exploratory and we need to understand that more, but it gets to the point that if you can work out what’s happening in a patient’s cancer when it relapses, you can develop much more effective combinations to treat it.”

Perez said she found it fascinating that there was a trend for improvement in patients with HER2-normal cancer. “This is something that we want to help explore, because it could be potentially very important,” she said.

The results of the EGF30008 study bolster the rationale for conducting adjuvant trials addressing multiple-targeted therapies in breast cancer, according to Perez.

She is the principal investigator of one such trial, the Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation study (ALTTO). This is an international, phase III clinical trial of two targeted therapies for HER2-positive breast cancer, Tykerb and Herceptin (trastuzumab).

These two drugs target HER2 in different ways. The ALTTO study will try to find out whether one of these drugs works better than the other at preventing recurrence, and whether the two drugs work better together than either does separately. If the ALTTO patients have estrogen receptor-positive breast cancer, they will also receive an anti-estrogen drug, such as Femara, in combination with the anti-HER2 treatments, Perez explained. “ALTTO started several months ago and enrollment is already ahead of projections,” she reported.

In the interview with *CURE*, Johnston said the next part of his group’s work will be a very detailed analysis of tumors collected from about 1,000 participants in the trial.

“We are now going to set up a whole load of studies to analyze these tumors in detail and see if we can identify tumor attributes other than HER2 and the estrogen receptor that can help us identify the patients who can benefit” from this combination treatment.

“The bottom line is that we are making progress on the hormone treatments we’ve currently got,” Johnston said. “We know that these tumors are a little more resistant: we know that they have these various pathways that regulate things. We have to develop combinations that make the hormone drugs work better.”

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