Early-stage, HER2-positive breast cancer patients at increased risk of recurrence

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Early-stage breast cancer patients with HER2 positive tumors one centimeter or smaller are at significant risk of recurrence of their disease, compared to those with early-stage disease who do not express the aggressive protein, according to a study led by researchers at The University of Texas M. D. Anderson Cancer Center.

The findings, published today online in the Journal of Clinical Oncology, is the first large study to analyze this cohort and represents a shift in the way women with early-stage HER2 positive breast cancer should be assessed for risk of recurrence and considered for treatment, said the study's senior author, Ana M. Gonzalez-Angulo, M.D, associate professor in M. D. Anderson's Departments of Breast Medical Oncology and Systems Biology.

The research was first presented at the CRTC-AACR San Antonio Breast Cancer Symposium in December, 2008.

Herceptin, also known as trastuzumab, was approved for use in 1998 for women whose advanced breast cancer expresses Human Epidermal growth factor Receptor 2, or HER2. Approximately 15-20 percent of breast cancer cells produce an excess amount of the HER2 growth protein on their surface, which makes the cancer more aggressive. Herceptin is a monoclonal antibody that latches on to these proteins and inhibits tumor growth.

"This study represents a current debate within clinical practice - the risk

of recurrence for early-stage breast cancer patients with HER2 positive tumors one centimeter or smaller," said Gonzalez-Angulo. "Our findings show that women with early stage HER2 positive breast cancer have a 23 percent chance of recurrence. In contrast, the five-year survival rate of all women with such early-stage breast cancer is more than 90 percent.

"The findings indicate that physicians need to consider offering these women Herceptin-based therapy in the post-operative, or adjuvant setting," Gonzalez-Angulo continued.

Current guidelines call for no additional therapy after surgery and radiation if tumors are less than five millimeters and Herceptin-based adjuvant therapy should be discussed with patients if the tumors are from six to 10 millimeters, Gonzalez-Angulo explained.

According to Gonzalez-Angulo, the number of patients with HER2 positive tumors smaller than one centimeter continues to increase as breast cancer surveillance and early detection become increasingly sophisticated.

"Before now, there's been no data regarding how to treat these women because they were excluded from all the definitive trials confirming Herceptin's benefit. This data strongly suggests that we need to rethink how we treat early-stage breast cancer patients with HER2 positive tumors and likely offer anti-HER2 therapy in the adjuvant setting."

For the retrospective study, Gonzalez-Angulo, and her team used M. D. Anderson's Breast Cancer Research Database to analyze 965 patients treated between 1990 and 2002. All of the patients' tumors were smaller than one centimeter; patients whose receptor status could not be analyzed and/or had received adjuvant chemotherapy or Herceptin at any time were excluded. The median age of the women at diagnosis was 57 years. To validate the findings, a second cohort of 350 patients from European

institutions was also analyzed.

Of the M. D. Anderson patient population, more than 10 percent, or 98 patients, had HER2 positive tumors. In addition, 77 percent were hormone-receptor positive and 13 percent were triple receptor-negative.

In those analyzed with HER2 positive tumors, the five-year, recurrence-free survival was 77.1 percent; in contrast, HER2 negative patients' recurrence-free survival was 93.7 percent. Five-year distant recurrence-free survival was 86.4 percent in women with HER2 positive tumors compared to 97.2 percent in women with HER2-negative tumors. Patients with HER2-positive tumors had 2.68 times higher risk of recurrence and 5.3 times higher risk of distant recurrence than those with HER2-negative tumors.

In addition, women with HER2-positive tumors had 5.09 times the risk of recurrence and 7.81 times risk of distant recurrence than women with hormone receptor-positive tumors.

The European subset confirmed the M. D. Anderson findings and showed reproducibility, said Gonzalez-Angulo.

"The risk of recurrence was much higher than we suspected. With this study, we now have concrete evidence to discuss with our HER2 positive patients with even the smallest of tumors, and Herceptin alone or combined with chemotherapy should be strongly considered as adjuvant therapy," said Jennifer Litton, M.D., assistant professor in M. D. Anderson Department of Breast Medical Oncology, and also an author on the study. "This data should also encourage this subset of patients to be included in ongoing clinical trials with HER2-targeted therapies."

Gonzalez-Angulo and Litton hope that a specific, three-arm clinical trial can be designed comparing observation, Herceptin, and Herceptin

combined with chemotherapy.

Currently, M. D. Anderson is a study site for BETH (BEvacizumab and Trastuzumab Adjuvant Therapy in HER2-positive Breast Cancer), an international Phase III trial investigating the benefits of combining Avastin and Herceptin, together with chemotherapy for early stage HER2-positive breast cancer. Vincente Valero, M.D., professor in the Department of Breast Medical Oncology and also an author on the JCO research, is the study's institutional PI.

Source: University of Texas M. D. Anderson Cancer Center (news : web)