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TWO STUDIES REPORT WOMEN WITH SMALL HER2-POSITIVE BREAST CANCERS HAVE AN INCREASED RISK OF CANCER RECURRENCE AND METASTASIS AND MAY BENEFIT FROM ADJUVANT TRASTUZUMAB THERAPY

Researchers say patients may want to consider adjuvant trastuzumab (Herceptin) therapy

Two retrospective studies led by researchers in the United States and Italy report that women with HER2-positive breast cancers 1 cm or less in diameter that have not spread to the lymph nodes ("node-negative" tumors) have a risk of recurrence that is two to five times greater than that of women with HER2-negative breast cancers. The U.S. study also identified an increased risk of metastasis among women with small HER2-positive tumors, compared to those with HER2-negative tumors.

HER2-positive disease (in which tumors over-express the HER2 protein) is relatively uncommon in women with small, early-stage breast cancers, accounting for approximately 7 to 10 percent of the cases in these two studies. Although women who successfully complete treatment for early-stage HER2-positive breast cancer are less likely to experience a cancer recurrence than those diagnosed at a later stage, the authors of both studies recommended that anti-HER2 therapy with trastuzumab (Herceptin) be considered to reduce this risk following successful surgery.

U.S. study finds that HER2 status strongly predicts risk of breast cancer recurrence and metastasis

Researchers from M. D. Anderson Cancer Center in Houston reported that women with HER2-positive breast cancers 1 cm or less in diameter that have not spread to the lymph nodes have nearly three times the risk of recurrence and more than five times the risk of metastasis five years after diagnosis compared with women with similar-sized HER2-negative tumors.

The investigators reviewed records from 965 women

diagnosed between 1990 and 2002 at their institution with breast cancers 1 cm or less in size that had not spread to nearby lymph nodes. They compared the rates of recurrence and metastasis among women with HER2-positive and HER2-negative breast cancers after a median follow-up of six years. In addition, samples from an additional 350 women with breast cancer from two other institutions were analyzed to validate their findings.

They found that five years after diagnosis, 77.1 percent of the HER2-positive patients were free of recurrence and 86.4 percent were free of metastasis, compared with 93.7 percent and 97.2 percent of the HER2-negative patients, respectively. Compared with women who had HER2-negative tumors, women with HER2-positive tumors were 2.68 times more likely to experience a recurrence and 5.3 times more likely to experience metastasis. The results of the analysis of the breast cancers from other institutions were consistent with these findings.

Italian study reports small HER2-positive breast tumors have higher risk of recurrence, but to a lesser degree than U.S. study, and poor disease-free survival

In the second study, researchers from the Istituto Europeo di Oncologia in Milan found that women with HER2-positive node-negative breast tumors 1 cm or less in diameter have a 2.4-fold risk of recurrence compared to those with HER2-negative disease. Additionally, women whose tumors also had receptors for progesterone and/or estrogen had less favorable disease-free survival (the length of time after treatment during which a patient lives with no sign of the disease), with a 5.1-fold risk of recurrence compared with the endocrine unresponsive tumors.

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The investigators reviewed records from 2,130 women who were surgically treated between 1999 and 2006 for tumors 1 cm or less in diameter that had not spread to the lymph nodes. Of these women, 150 (7 percent) had HER2-positive disease. Researchers examined the risk of recurrence and disease-free survival among women with both HER2-positive and HER2-negative disease, and further stratified patients according to hormone receptor status (the presence or absence of receptors for estrogen or progesterone).

After a median follow-up of 4.6 years, they found that all subjects had high-rates of disease-free survival but that HER2-positive disease was associated with worse disease-free survival, regardless of hormone receptor status. Among women with hormone receptor positive disease, 5-year disease-free survival was 92 percent for patients with HER2-positive tumors and 99 percent for patients with HER2-negative tumors. In patients with hormone receptor-negative disease, disease-free survival was 91 percent and 92 percent, respectively.

About Small, HER2-Positive Breast Cancers

To date, very little data exist on the adjuvant treatment of small, node-negative breast tumors. While patients with this stage of disease generally have a favorable diagnosis, clinicians continue to explore strategies for improving outcomes.

Women with small HER2-positive tumors are currently treated with mastectomy or with lumpectomy followed by radiation. Some 25 percent of all breast cancers over-express the HER2 protein, which is known to be associated with a higher risk of recurrence and worse overall survival. In the U.S., trastuzumab is FDA-approved for the treatment of node-positive disease and for women with node-negative disease with hormone (estrogen or progesterone) receptor-positive tumors who have another high-risk feature (size 2 cm or more, age under 35, or tumor grade 2 or 3). Consensus guidelines, such as those from the National Comprehensive Cancer Network, do not recommend trastuzumab therapy for tumors less than 1 cm, due to a lack of prior supporting evidence.

What This Means for Patients

Advances in screening have enabled the detection of breast cancers at an earlier, and generally more treatable stage. In the United States, it is not uncommon for clinicians to offer trastuzumab as part of adjuvant therapy to women with small, HER2-positive tumors whose cancer has not spread to the lymph nodes. The findings of this study indicate that many more women may be candidates for this therapy, and that they should be offered participation in clinical trials assessing the effectiveness of trastuzumab in women with small, node-negative tumors. Women may want to discuss adjuvant treatment with their doctors.



Helpful Links

- [Cancer.Net Guide to Breast Cancer \(www.cancer.net/breast\)](http://www.cancer.net/breast)
- [What to Know: ASCO's Guideline on HER2 Testing for Breast Cancer \(www.cancer.net/whattoknow\)](http://www.cancer.net/whattoknow)