

## Even tiny breast tumors can be aggressive and may require maximum therapy

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Breast tumors that are 1 centimeter in size or smaller — no more than 0.4 inch in length — can still be very aggressive and may require more intensive therapy than is routinely offered today, say researchers at Mayo Clinic in Jacksonville, Fla.

The study, which is being presented at the San Antonio Breast Cancer Symposium, is one of the few that has looked at outcomes of women who have tiny tumors that have not spread to the lymph nodes. The findings suggest that outcome of two types of breast cancer — those classified as HER2 positive (HER2+) and triple negative — may not depend on size alone.

“This is a small study and so we can’t make treatment recommendations from it, but it appears that biology and not only size matters when it comes to selecting therapy for small, invasive tumors,” says the study’s lead researcher, Surabhi Amar, M.D., a fellow in Hematology/Oncology at Mayo Clinic in Jacksonville.

Currently, there are no definitive treatment guidelines for tumors less than 1 centimeter in size because clinical trials are usually conducted on women whose tumors are larger or are associated with lymph node involvement, Dr. Amar says. “We just don’t have extensive data on tumors this small, so treatment becomes a matter of physician discretion.”

Researchers at all three Mayo sites — Jacksonville; Scottsdale, Ariz.;

and Rochester, Minn. — participated in the study, which examined 401 women who were treated for breast cancer between 2001 and 2005 at the breast cancer clinics in Jacksonville and Scottsdale.

The vast majority (87 percent, or 350 women) had tumors that were classified as ER/PR positive and HER2 negative (in short, HER2 negative/ER/PR+). Twenty-seven women (6.7 percent) had tumors that were HER2+ and 24 patients (5.9 percent) were diagnosed with triple negative cancer — that is, ER/PR negative and HER2 negative. These classifications refer to receptors present on the outside of the tumor cell that are fueling growth, and cancer that is ER/PR+ is considered the least aggressive of the three categories. Generally, studies have shown that in all patients diagnosed with breast cancer, 15 to 20 percent of breast cancers are HER2+ and about 10 to 15 percent are triple negative.

Patients were followed for an average of almost three years, and so far researchers have data on all patients with HER2+ and triple negative cancers and on 219 women with HER2 negative/ER/PR+ cancer.

Researchers found that:

-- There were many more grade 2 and grade 3 tumors in women with the two rarer subtypes — 92 percent in HER2+ cancer and 91 percent in triple negative cancer — compared to HER2 negative/ER/PR+ cancer (36 percent). Tumors are graded 1-3, and higher grade tumors are more likely to grow faster and be more difficult to treat than lower grade tumors.

-- Cancer came back more frequently in HER2+ tumors (7.4 percent of patients relapsed) and triple negative cancers (12.5 percent), compared to HER2 negative/ER/PR+ cancer (1.3 percent).

-- Although the overall outcome of these small, lymph-node-negative tumors was excellent (overall survival 97.4 percent, disease free survival

95.1 percent), these outcomes were different in the three subgroups studied. The death rate was higher in triple negative breast cancer: there was one death in the 24 patients with triple negative tumors, none in the HER2+ group of 27 women, and one death related to relapse in 219 women with HER2 negative/ER/PR+ cancer.

Although only small numbers of women have the rarer cancer subtypes included in this study, the findings suggest that women with HER2+ and triple negative tumors should receive as much treatment as possible in order to prevent cancer relapse, Dr. Amar says. Researchers found that only 35 percent of women with triple negative cancer were treated with adjuvant chemotherapy (chemotherapy after surgery) despite the higher grade of the tumors. “Chemotherapy may not work as well as we would like in these tumors, but, still, physicians who treat patients with triple negative cancer should be aware of the higher risk of relapse, even if tumors are quite small,” she says.

Adjuvant chemotherapy was offered to 28 percent of patients with HER2+ tumors, and only 4 percent received the targeted therapy Herceptin, which has been designed specifically to treat this class of tumors. “Should Herceptin be offered to such small node-negative tumors” There is not enough data currently to answer this question,” Dr. Amar says. “But this study definitely highlights the fact that HER2 positive tumors, even if very small, may warrant more aggressive therapy.”

Only 3.9 percent of patients with HER2 neg/ER/PR+ cancer were treated with chemotherapy. “So although the rates of adjuvant chemotherapy use were significantly higher in the HER2+ and triple negative subgroups, these groups still showed a higher relapse rate,” she says.

Source: Mayo Clinic

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