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## **Breast Surgery May be Unnecessary for Appropriately Selected HER2+ Patients in the Future**

### ***Abstract: Patient Selection for Non-Operative Management of HER2+ Invasive Breast Cancer after Neoadjuvant Systemic Therapy***

Dallas, May 2, 2019--Tumor hormone status, possible DCIS on initial biopsy and imaging results following neoadjuvant chemotherapy (NCT) may help physicians predict whether surgery may be safely eliminated for traditionally aggressively treated HER2+ breast cancer in the future.

These were the findings of a new study comparing the clinicopathologic characteristics of HER2+ patients who had no evidence of residual cancer on a pathology report following NCT with those who did. NCT is chemotherapy delivered prior to primary traditional surgical treatment to help optimize the intervention. The study was presented here at the annual meeting of the American Society of Breast Surgeons.

“More than 56,000 cases of HER2+ breast cancer, a comparatively aggressive tumor, are diagnosed in the U.S. annually,” says lead researcher Susie Sun, MD, University of Texas MD Anderson Cancer Center. “Evidence is growing that certain patients are exceptional NCT responders, suggesting that when properly identified someday certain of these women may be candidates for non-operative treatment.”

Dr. Sun points out, however, that confirmation of NCT response using traditional medical imaging is often inconclusive, with a high rate of false negatives, making identification of appropriate patients difficult. “Our study shows that hormone receptor positive disease, presence of DCIS at diagnosis and inconclusive imaging results following neoadjuvant chemotherapy correlated with an incomplete response to NCT, suggesting these women must go on to surgical treatment,” she explains.

The study examined 280 patients with HER2+ breast cancer treated with NCT followed by surgical resection. Multivariate analyses were performed to determine predictors of residual disease. Of the 280 patients, 102 (36.4%) had a pathologic complete response (pCR) to NCT in both the breast and lymph node.

Patients with incomplete pathologic response were more likely to have hormone receptor positive compared with negative tumors (73.4% vs. 50.8%; respectively,  $p < 0.0001$ ). Also correlating with residual disease in the breast and nodes was incomplete radiologic response (OR 5.62,  $p = 0.002$ ), meaning that radiologists were unable to rule out residual disease.

DCIS was found in 129 (46.1%) patients on initial biopsy. Of these, 32 (24.8%) had residual DCIS only following NST. The therapy failed to eradicate in situ disease in 64.3% of patients. Women with both invasive disease and DCIS on initial biopsy were less likely than those without DCIS to achieve pCR in the breast (31% vs. 43%,  $p = 0.038$ ). Post-NCT imaging had a sensitivity of 97.1% and negative predictive value of 70.6% for residual cancer.

“This study is particularly important right now because it may help identify optimal patients for ongoing clinical trials omitting surgery for carefully selected HER2+ patients,” comments the study’s principal investigator, Henry Kuerer, MD, PhD, FACS, University of Texas MD Anderson Cancer Center. “Findings are extremely important because of the inability of medical imaging to reliably confirm the absence of cancer following initial NCT. They help delineate the types of HER2+ tumors that should not be included in our trials.”

“No one wants to have surgery unnecessarily,” says Dr. Sun. “This study and the clinical trial may help us delineate in the future which patients may be effectively treated non-operatively, while allowing us to provide more aggressive surgical intervention to the women with HER2+ breast cancer who need it.”

### **Expert Commentary:**

As we look to the future of treatment for patients with breast cancer, it is clear that a better understanding of tumor biology will guide us in omitting unnecessary treatments for some tumor types while remaining appropriately aggressive for others. This study by Dr. Sun and colleagues highlights clinical and radiologic characteristics of the aggressive HER2+ breast cancers that help predict a complete response to chemotherapy, thereby setting up opportunities to avoid surgery for these patients in the future. While still in the early stages of discovery, we look forward to additional research in this area to improve outcomes for our patients with breast cancer.

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**Abstract, Official Proceedings**

**Patient Selection for Non-Operative Management of HER2+ Invasive Breast Cancer after Neoadjuvant Systemic Therapy**

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**Objective:** With recent advances in neoadjuvant systemic therapy (NST), patients with HER2-positive breast cancer and pathologic complete response (pCR) following NST may be candidates for non-operative management clinical trials. For patients to be eligible for these trials, they must have a pCR in both the invasive and DCIS components to ensure no nidus for recurrence remains. The purpose of this study was to identify unique clinicopathologic characteristics that are associated with finding residual disease after NST. A secondary outcome was to assess the effect of NST on the invasive and DCIS components of HER2-positive breast cancer.

**Methods:** Two hundred eighty patients with clinical T1-2N0-1 HER2-positive breast cancer treated with NST followed by surgical resection were identified. Clinicopathologic characteristics of those who achieved pCR in the breast and lymph nodes were compared with those who had residual disease. Multivariate analyses were performed to evaluate for predictors of residual disease.

**Results:** Of the 280 patients, 102 (36.4%) had pCR in the breast and lymph nodes after NST, and 50 (17.9%) had residual DCIS in the breast only. DCIS was a component on initial biopsy in 129 (46.1%) of patients. Patients with residual disease in the breast and nodes were more likely to have hormone receptor-positive tumors compared with negative tumors (73.4% vs. 50.8%; respectively,  $p < 0.0001$ ). Variables that were predictive of residual disease in the breast and nodes included incomplete radiologic response (OR 5.62,  $p = 0.002$ ) and hormone-positive status (OR 2.56,  $p < 0.0001$ ). Combined imaging modalities (MRI, mammogram, ultrasound) after NST had a sensitivity of 97.1% and negative predictive value of 70.6% in the detection of residual disease in the breast and lymph nodes. NST failed to eradicate the DCIS component in 64.3% of patients with in situ disease on initial core biopsy. Patients with invasive disease with DCIS on initial core biopsy were less likely than those without DCIS on initial core biopsy to achieve pCR in the breast (31% vs. 43%,  $p = 0.038$ ).

**Conclusions:** Hormone receptor-positive tumors, radiologic evidence of residual disease, and DCIS on initial biopsy are associated with incomplete pathologic response after NST in HER2-positive breast cancer. The low negative predictive value of imaging after NST mandates the need for image-guided biopsy confirmation to rule out residual disease. These results help to delineate and identify unique characteristics associated with HER2-positive cancers for patients who may become eligible for inclusion in trials assessing non-operative management of exceptional responders after NST.