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To interview Louis Fehrenbacher, contact Julia Gunther at julia.gunther@aacr.org or 770-403-7690. For a photo of Fehrenbacher, click here.

Adjuvant Trastuzumab Did Not Improve Outcomes for Patients With HER2-low Breast Cancer

Current guidelines for defining HER2-positive status remain valid

SAN ANTONIO — Adding trastuzumab (Herceptin) to standard adjuvant chemotherapy did not improve invasive disease–free survival for patients with early-stage breast cancer found to have low levels of HER2, as defined as immunohistochemistry (IHC) 1+ or 2+ and/or in situ hybridization (ISH) negative, according to data from the randomized, phase III NSABP-B-47 clinical trial presented at the 2017 San Antonio Breast Cancer Symposium, held Dec. 5–9.

"Current guidelines classify a breast cancer as HER2 positive if immunohistochemistry testing shows it has high levels of HER2 protein, defined as IHC 3+, or in situ hybridization shows it has increased numbers of copies of the HER2 gene, defined as ISH positive" said Louis Fehrenbacher, MD, medical director of Kaiser Permanente Oncology Clinical Trials and an oncologist with the Kaiser Permanente Vallejo Medical Center, California. "Adding one year of treatment with trastuzumab to standard adjuvant chemotherapy significantly reduces cancer recurrence and improves survival for patients with early-stage HER2-positive breast cancer.

"About 15 percent of breast cancers are HER2 positive, but another 45 percent have low levels of HER2, and these patients are not currently treated with adjuvant trastuzumab," continued Fehrenbacher. "In some of the early trastuzumab clinical trials, there was a signal that patients with HER2-low breast cancer may benefit from the HER2-targeted therapeutic. We designed and conducted NSABP-B-47 to test in a large, rigorous clinical trial whether this was indeed the case."

Fehrenbacher explained that although the data show that adding trastuzumab to standard adjuvant chemotherapy did not improve outcomes for patients with early-stage HER2-low breast cancer, it was vital to have conducted the study so that patients with this form of the disease can unequivocally know that trastuzumab is not a beneficial treatment for them. Trastuzumab treatment can cause serious adverse effects, including cardiotoxicity, so it is important to know that current guidelines defining HER2-positive status are valid and ensure that no patients are under- or overtreated, he said.

Fehrenbacher and colleagues enrolled 3,270 patients with early-stage breast cancer that was either IHC 1+, IHC 2+, and/or ISH negative in the trial. The patients were randomized 1:1 to standard adjuvant chemotherapy with or without a year of trastuzumab.

After a median follow-up of 46.1 months, 264 patients had either recurrence of their original breast cancer, a diagnosis of a new breast cancer, a diagnosis of new cancer outside the breast, or had died. These 264 events triggered analysis of the primary endpoint of the trial, invasive disease–free survival.

Among the 1,640 patients receiving trastuzumab, five-year invasive disease–free survival was 89.6 percent. It was 89.2 percent among the 1,630 patients who did not receive the HER2-targeted therapeutic. The findings did not differ if the patients were subdivided by HER2 IHC level, extent of lymph node involvement, or hormone receptor status.

In addition, five-year estimates for recurrence-free interval, distant recurrence–free interval, and overall survival were not statistically different for patients receiving trastuzumab compared with those not receiving trastuzumab.

This study was supported by funds from the National Cancer Institute and Genentech. Fehrenbacher declares no conflicts of interest.

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The mission of the 2017 San Antonio Breast Cancer Symposium is to produce a unique and comprehensive scientific meeting that encompasses the full spectrum of breast cancer research, facilitating the rapid translation of new knowledge into better care for patients with breast cancer. The UT Health San Antonio Cancer Center, the American Association for Cancer Research (AACR), and Baylor College of Medicine are joint sponsors of the San Antonio Breast Cancer Symposium. This collaboration utilizes the clinical strengths of the UT Health San Antonio Cancer Center and Baylor and the AACR's scientific prestige in basic, translational, and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. For more information about the symposium, please visit www.sabcs.org.