Dual HER2 Blockade Significantly Extends Progression-Free Survival

AACR

- Two agents blocking HER2 led to an additional six months of progression-free survival.
- Side effects were minimal with the addition of pertuzumab.
- Results published in the *New England Journal of Medicine*.

SAN ANTONIO - Adding pertuzumab to a combination of trastuzumab and docetaxel chemotherapy extended progression-free survival by a median of 6.1 months in patients with metastatic HER2-positive breast cancer compared with patients who received the combination therapy with placebo.

Researchers conducted an international phase 3, double-blind, randomized trial, known as CLEOPATRA (CLinical Evaluation Of Pertuzumab And TRAstuzumab), in which they randomly assigned 808 patients to receive trastuzumab and docetaxel chemotherapy with pertuzumab or placebo. Progression-free survival (PFS) was 18.5 months for patients who received pertuzumab compared with 12.4 months for patients who received placebo - a 38 percent reduction in risk for progression.

The findings, reported at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, held Dec. 6-10, 2011, represent a significant advance in the treatment of this advanced breast cancer, said senior researcher José Baselga, M.D., Ph.D., professor in the department of medicine at Harvard Medical School, associate director of the Massachusetts General Hospital Cancer Center and chief of hematology/oncology at Massachusetts General Hospital.

"This is huge. It is very uncommon to have a clinical trial show this level of improvement in PFS," said Baselga. "Most metastatic patients with HER2-positive breast cancer eventually stop responding to trastuzumab, so the fact that we now have an agent that can be added to current treatment to delay progression is very exciting. With the advent of trastuzumab and now pertuzumab, we have come a very long way in treating a type of breast cancer that once had a very poor prognosis."

The results were published in the *New England Journal of Medicine*.

Pertuzumab is designed to work in combination with trastuzumab as a dual blockade of the HER2 growth factor, which fuels about one third of all breast tumors. Both drugs are monoclonal antibodies that bind to the HER2 receptor protein in different locations. Pertuzumabs role is to prevent the receptor from linking to HER3 and therefore forming a "dimer" that further signals tumor growth - making pertuzumab the first in a new class of drugs called "dimerization inhibitors,"

Baselga said. "These two agents offer a dual HER2 blockade, shutting down different mechanisms responsible for HER2 signaling."

Adding pertuzumab to the combination therapy resulted in an objective response rate (tumor shrinkage of at least 30 percent) of 80.2 percent compared with 69.3 percent for the combination therapy alone.

Although survival outcomes are not mature, meaning not enough time has passed for a valid statistical analysis, Baselga reported 69 deaths among the 402 patients treated with the three-drug combination and 96 deaths among the 406 patients who received two drugs.

He added that the three-drug combination is "remarkably safe and well tolerated. Only minimal side effects were seen with the addition of pertuzumab." Some of those effects were grades 1 and 2 diarrhea and neutropenia, but no additional cardiac toxicity was seen, he said.

Enrollment is already under way in a new double-blind, randomized clinical trial, APHINITY, to test the use of pertuzumab as adjuvant treatment for early-stage HER2-positive breast cancer. "It is in that setting that you can really cure patients," Baselga said.

The mission of the CTRC-AACR 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 Cancer Therapy & Research Center (CTRC) at The University of Texas Health Science Center at San Antonio, 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 CTRC and Baylor and the AACRs scientific prestige in basic, translational and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. The 34th annual symposium is expected to draw nearly 8,000 participants from more than 90 countries.

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