Herceptin® Combined With Chemotherapy Improves Disease-Free Survival for Patients With Early-Stage Breast Cancer

Results from two large randomized clinical trials for patients with HER-2 positive invasive breast cancer show that those patients with early-stage breast cancer who received Herceptin® (trastuzumab) in combination with chemotherapy had a significant decrease in risk for breast cancer recurrence compared with patients who received the same chemotherapy without trastuzumab. Patients are considered “HER-2 positive” if their cancer cells "overexpress," or make too much of, a protein called HER–2, which is found on the surface of cancer cells. Trastuzumab slows or stops the growth of these cells, and it is only used to treat cancers that overexpress the HER–2 protein. Approximately 20 percent to 30 percent of breast cancers overexpress HER-2. These tumors tend to grow faster and are generally more likely to recur than tumors that do not overproduce HER-2.

The clinical trials were sponsored by the National Cancer Institute (NCI), part of the National Institutes of Health, and conducted by a network of researchers led by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the North Central Cancer Treatment Group (NCCTG), in collaboration with the Cancer and Leukemia Group B, the Eastern Cooperative Oncology Group, and the Southwest Oncology Group. Genentech, Inc., South San Francisco, Calif., which manufactures trastuzumab, provided the drug for the trials under the Cooperative Research and Development Agreement (CRADA) with NCI for the clinical development of trastuzumab.

The Data Monitoring Committees overseeing the combined analysis of these trials (known as NSABP-B-31 and NCCTG-N9831) recommended that the results of a recent combined interim analysis be made public because the studies had met their primary endpoints of
increasing disease-free survival (the amount of time patients live without return of the cancer) in patients receiving trastuzumab in combination with chemotherapy. The improvement in overall survival also was statistically significant for women receiving a combination of chemotherapy and trastuzumab.

Patients in the clinical trials who received trastuzumab in combination with standard combination chemotherapy had a 52 percent decrease in disease recurrence compared to patients treated with chemotherapy alone. This difference is highly statistically significant. “This is a major advance for many thousands of women with breast cancer,” said NCI Director Andrew C. von Eschenbach, M.D. “These results are one more example that we are at a major turning point in the use of targeted therapies to eliminate suffering and death from cancer,” he added.

The leaders of the studies underscored the significance of these results and cited the collaborative efforts involved. “These findings confirm that we now have a very potent weapon against the recurrence of cancer cells that overexpress HER-2,” said Edith A. Perez, M.D., who chaired the NCCTG trial and is a medical oncologist at the Mayo Clinic in Jacksonville, Fla. “We gratefully acknowledge the contribution of our co-investigators and, most importantly, our courageous patients in helping to achieve these unprecedented results.”

Edward Romond, M.D., study chair for the NSABP and professor of oncology at the University of Kentucky, in Lexington, Ky., noted, “For women with this type of aggressive breast cancer, the addition of trastuzumab to chemotherapy appears to virtually reverse prognosis from unfavorable to good.”

“These are truly life-saving results in a major disease,” said JoAnne Zujewski, M.D., who oversees breast cancer trials for NCI’s Cancer Therapy Evaluation Program. More detailed results from these studies will be presented at the American Society of Clinical Oncology (ASCO) annual meeting on May 16, 2005, in Orlando, Fla.

Information from over 3,300 patients enrolled in these studies was used for analysis. Patients with operable breast cancer whose tumors over-expressed HER-2 were enrolled in these studies between February 2000 and April 2005. Patients were randomized to receive chemotherapy with doxorubicin and cyclophosphamide followed by paclitaxel, or doxorubicin and cyclophosphamide followed by paclitaxel and trastuzumab. Most patients had lymph node-positive breast cancer, or breast cancer that had spread to the lymph nodes, with only a minority having lymph node-negative disease. The limited information in the node-negative group did not allow for a separate analysis of this group.
Chemotherapy of the type given in these studies has a risk of congestive heart failure (weakening of the heart muscle) of less than 1 percent. In these studies, the likelihood of congestive heart failure in women receiving the combination of chemotherapy and trastuzumab was increased by 3 percent to 4 percent. Patients in these studies will continue to be followed for any additional side effects. Additional safety data will be presented at ASCO.

Trastuzumab is an example of a “targeted” therapy -- an agent that is directed against a specific change in the cancer cell. Trastuzumab was approved for the treatment of advanced breast cancer in 1998.

An estimated 211,240 women will be diagnosed with breast cancer in the United States in 2005. Of these, about 30 percent have lymph node-positive breast cancer, and about 20 percent to 30 percent of these tumors overexpress the HER-2 protein, the target for trastuzumab. Breast cancer is the most commonly diagnosed cancer in women and the second leading cause of cancer-related death in women in this country. An estimated 40,110 deaths from female breast cancer will occur in 2005 in the United States, accounting for about 15 percent of all cancer-related deaths in women in the nation.

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*NSABP-B-31*: Phase III Randomized Study of Doxorubicin and Cyclophosphamide Followed By Paclitaxel With or Without Trastuzumab (Herceptin) in Women With Node-Positive Breast Cancer That Overexpresses HER2

*NCCTG-N9831*: Phase III Randomized Study of Doxorubicin Plus Cyclophosphamide Followed By Paclitaxel With or Without Trastuzumab (Herceptin®) in Women With HER-2-Overexpressing Node-Positive or High-Risk Node-Negative Breast Cancer