Women with Early Stage Breast Cancer Sought to Evaluate the Benefit of Herceptin Therapy

Pittsburgh, PA -- The National Surgical Adjuvant Breast and Bowel Project (NSABP) has launched a new phase III clinical trial that will evaluate Herceptin® (Trastuzumab) in the adjuvant setting. Conducted in more than 100 sites across the United States and Canada, Protocol B-31 will assess the safety and efficacy of the combination of Herceptin and chemotherapy in the treatment of 2700 node-positive breast cancer patients whose tumors overexpress the HER2 (human epidermal growth factor receptor-2) protein or demonstrate evidence of HER2 gene-amplification.

The HER2 gene (also referred to as erbB-2 or HER2/ neu) produces a protein that stimulates normal cell growth, however, it also seems to play a significant role in the biology of breast cancer. Overexpression, or an abundance, of the HER2 protein is found in about 25%-30% of malignant breast tumors and is associated with more aggressive cancer growth and shortened patient survival. Based on this knowledge, researchers are now testing therapies that are aimed at tumors with HER2 overexpression.

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Herceptin, a humanized monoclonal antibody, was approved by the U.S. Food and Drug Administration (FDA) to treat women with metastatic breast cancer whose tumors are known to have an overexpression of HER2. Previous research has proven Herceptin’s ability to target the HER2 receptor in metastatic breast cancer, which tends to decrease the spread of the disease and prolongs patient survival. In a pivotal clinical trial, women with HER2 positive metastatic breast cancer who received Herceptin in combination with chemotherapy achieved a 50 percent response rate compared to 32 percent for women receiving chemotherapy alone. Women who received Herceptin in addition to chemotherapy lived longer than those who received chemotherapy alone. Few therapies have demonstrated this type of survival benefit in this patient population. In the NSABP B-31 trial, the role of Herceptin will be tested in women with breast cancers having HER2 overexpression and whose tumors have spread to the axillary (underarm) lymph nodes but not to other organs. They will be given either chemotherapy alone, or chemotherapy plus Herceptin.

“This trial is the first NSABP adjuvant phase III study to evaluate a biologic agent like Herceptin in patients with operable breast cancer,” says Elizabeth Tan-Chiu, MD, NSABP associate director of medical oversight and B-31’s protocol officer. We hope to learn whether the use of Herceptin in this group of breast cancer patients can provide a major advancement when added to the standard therapy of surgery, chemotherapy, and radiation therapy.”

“Herceptin has demonstrated a survival advantage in women with HER2 positive metastatic breast cancer, a particularly aggressive form of the disease, when combined with chemotherapy considered standard of care,” said Gwen Fyfe, MD, Senior Director of Oncology at Genentech. “We believe that the response seen with Herceptin in metastatic disease warrants further study in the adjuvant breast cancer setting. We are pleased to be working with the NSABP on protocol B-31 to evaluate the potential safety and efficacy of adding Herceptin to chemotherapy for women with HER2 positive early stage breast cancer.”

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The side effects most commonly associated with Herceptin include fever and chills, which are “infusion-related” reactions. They are generally mild to moderate, and treatable. These side effects usually occur shortly after the drug’s first administration and tend to disappear as therapy continues. In some patients, previous research has shown that Herceptin alone, or in combination with standard chemotherapy, can increase a patient’s risk for developing serious heart problems. As a result, B-31 was designed to closely monitor patients for serious heart problems.

NSABP Protocol B-31 will be conducted in two stages. Stage 1 will evaluate 1000 patients for cardiac safety and compare the toxicities of adding weekly Herceptin to adjuvant Taxol following Adriamycin and cyclophosphamide (AC). If researchers determine that the potential benefits of Herceptin therapy are greater than the drug-related side effects, the study will proceed to Stage 2. This second stage will accrue an additional 1700 patients to study the efficacy of adding Herceptin to the standard chemotherapy regimen (AC followed by Taxol) in prolonging patient survival and disease-free survival.

In women with metastatic breast cancer, Herceptin may also be associated with increased shortness of breath, or reactions that are pulmonary in nature. Rarely, these reactions can be severe or life threatening. Patients with pre-existing lung disease or breast cancer that had spread to their lungs may be more susceptible to these reactions. Since B-31 is designed to evaluate the potential safety and efficacy of Herceptin in women with early stage breast cancer, these pulmonary reactions are rarely expected to occur.

In B-31, patients will be randomly divided into two therapy groups after balancing for the number of positive nodes, type of surgery (lumpectomy, mastectomy), tamoxifen administration, and choice of radiotherapy. Both groups will receive a total of eight cycles (1 cycle = 1 treatment every 3 weeks) of therapy. Group 1, the control group, will receive four cycles of 60 mg of Adriamycin (doxorubicin) and 600 mg of cyclophosphamide (AC) followed by four cycles of 175 mg of Taxol (paclitaxel). Group 2 will receive the same AC and Taxol therapy schedule plus a weekly dose of

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Herceptin. Women in both groups whose tumors are estrogen-receptor-positive (ER+) or progesterone-receptor-positive (PgR+) will also receive tamoxifen (20 mg/day) for 5 years. Tamoxifen is optional for women whose tumors are ER-negative or PgR-negative.

In B-31, 2700 women will be enrolled over five years; as of October 5, 2000, 167 women have enrolled in the trial. To participate, a woman must meet the following criteria: 1) operable breast cancer treated either with lumpectomy plus irradiation or mastectomy; 2) histologically positive axillary nodes; 3) breast cancer with strong HER2 protein overexpression determined either by immunohistochemistry (IHC) or HER2 gene amplification by fluorescent in situ hybridization (FISH); and 4) no evidence of metastatic disease. Women with existing heart disease are not eligible to participate.

Herceptin was discovered and developed and is manufactured and marketed in the U.S. by Genentech. It is currently indicated as a first line therapy in combination with Taxol and alone as a second and third line therapy for women with metastatic breast cancer who have tumors that overexpress the HER2 protein.

For more information or to locate a participating hospital, in the United States call the National Cancer Institute’s (NCI) Cancer Information Service (CIS) at 1-800-4-CANCER or visit the NCI’s clinical trials Web site at http://cancertrials.nci.nih.gov.

The NSABP is a nonprofit, clinical trials cooperative group, which includes a network of over 300 professionals located in the U.S. and Canada. Research conducted by the NSABP is supported primarily by grants from the NCI. For more than 40 years, the NSABP has successfully conducted large-scale, randomized clinical trials in breast and colorectal cancer that have altered and improved the standard of care for women and men with these diseases. To learn more about the NSABP, please visit our Web site at http://www.nsabp.pitt.edu.

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