

IN EVERY ISSUE

# Herceptin Combinations Improve Survival, Lessen Heart Toxicity

BY LAURA BEIL

Two studies presented in December at the San Antonio Breast Cancer Symposium offer hope of enhancing both the effectiveness and safety of Herceptin (trastuzumab), the drug that helped introduce the era of targeted therapy a decade ago.

One experimental combination is Herceptin and Tykerb (lapatinib)—two drugs that target the HER2 protein overproduced in about 25 percent of breast tumors. Data presented in San Antonio suggest the combination may help women with advanced breast cancer live longer. It is one of the few studies to report a regimen that has the ability to prolong survival among women with metastatic disease.

In describing the results, Kimberly Blackwell, MD, of Duke University Medical Center, reported that women who received the two-drug combination lived an average of about 14 months, while women who took Tykerb alone lived about 9.5 months. She noted that the study took place among women whose disease had progressed despite an average of three prior chemotherapy regimens; some women had tried as many as six.

“These were patients for whom there were not a lot of good options,” she said. After taking the combination—which did not include a new round of chemotherapy—“15 more, out of 100 women, were alive a year later,” she said.

Herceptin, approved for both early-stage and metastatic breast cancer, targets only HER2, while Tykerb, approved for metastatic breast cancer, targets HER2 and a related gene called HER1. Herceptin targets HER2 from the outside of the cell, and Tykerb interferes with the cellular machinery inside. The hope is that the combination might give the tumor a double whammy.

The question of whether to use Herceptin, Tykerb, or a combination of the two in women with early-stage breast cancer will be answered with results of another study under way, called ALTTO (Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization), which is expected to produce its first results in approximately two years.

Researchers are also trying to determine which drug makes the best chemotherapy platform to use with Herceptin. Scientists have sought to reduce Herceptin’s most serious side effect—a dangerous toxicity to the heart—while still preserving its tumor-fighting effectiveness.

One of the largest ongoing studies of Herceptin is named BCIRG 006; results of

this study were first presented during the 2005 symposium, and it reported a risk of heart damage from Herceptin, especially when used in combination with anthracyclines, some of the most widely used chemotherapy drugs. But the study is still ongoing, as researchers try to determine whether using non-anthracycline drugs might reduce the cardiac danger from Herceptin. The BCIRG 006 trial compares three approaches, with about 1,000 women in each group: standard anthracycline-based chemotherapy without Herceptin, anthracycline-based chemotherapy with Herceptin, and Taxotere-based (non-anthracycline) chemotherapy with Herceptin.

Consistent with results presented previously, the latest update indicates that using Taxotere (docetaxel) can make Herceptin safer for the heart. After five years of follow-up, four patients with the Taxotere-based Herceptin therapy experienced heart failure, compared with 21 who took Herceptin with an anthracycline regimen. “The damage we’re doing to the heart is not transient,” said Dennis Slamon, MD, PhD, of the UCLA Women’s Cancer Research Program. Based on the study results so far, he prefers that most women receive treatment with Taxotere-based chemotherapy cocktails.

Not all doctors agree. “We cannot conclude that this is a better regimen,” said Edith Perez, MD, director of the breast program at the Mayo Clinic in Florida, of the Taxotere-based regimen. She pointed out that fewer women who received Herceptin with the anthracycline regimen died during the study than women who received either chemotherapy alone or Taxotere-based Herceptin treatment, although the difference in survival between the two Herceptin arms was not statistically significant. No woman in any treatment group so far has died from heart disease.

Given the new results, Perez said she will continue to recommend anthracycline-based chemotherapy with Herceptin. “At the same time,” she said, “I am open to alternatives.”