

Data from San Antonio Breast Cancer Symposium Offers Hope and Highlights Surprising Results

At the recent 2006 San Antonio Breast Cancer Symposium (SABCS) a myriad of new studies were revealed, offering some insights into the future direction of breast cancer research, diagnosis, prevention, and treatment. With thousands of abstracts shared at the conference, there is an almost overwhelming amount of new information and data for the advocate community to get a handle on. However, below we have highlighted a handful of the studies that seem particularly significant to breast cancer advocates and the patients that they serve.

- **Abstract #1:** A phase II combination study of lapatinib and paclitaxel as a neoadjuvant therapy in patients with newly diagnosed inflammatory breast cancer (IBC). This study evaluated the investigational therapy lapatinib – also known as Tykerb – to determine its efficacy in newly diagnosed patients with inflammatory breast cancer (IBC), a relatively rare form of the disease that comprises just 1-2% of all breast cancer diagnoses. According to the results of this Phase II study of 35 patients, lapatinib has shown activity both alone and when used in combination with paclitaxel.

Because IBC is a very aggressive cancer, it is typically treated with a combination of anthracyclines and taxanes. This regimen typically lasts for 24 weeks, with a clinical response rate of 60-75%, and progression in about 10% of patients. The new regimen of lapatinib and paclitaxel tested in this study was a much shorter treatment period lasting just 14 weeks. Patients in the clinical trial took lapatinib orally once daily as a monotherapy for two weeks, and then added weekly paclitaxel therapy to the daily lapatinib for an additional 12 weeks. The overall clinical response rate observed in this study was 80%.

Of the 35 patients in the study, 30 were HER2+ and none of those patients experienced disease progression. In the other cohort of five HER2- patients, none experienced a complete response, although four patients had a partial response (80%), and one patient progressed during therapy. Based on these results, lapatinib is one of the few agents that have shown any activity in IBC thus far. It will be interesting for the community to see whether additional clinical trials of lapatinib in IBC patients support these promising results.

- **Abstract #34:** Long term efficacy of tamoxifen for chemoprevention – results of the IBIS-I study. There is exciting data from a long-term, large study of tamoxifen and its role in the prevention of breast cancer. The study of 7,145 healthy women considered to be at high risk for breast cancer demonstrated that tamoxifen's protective effect continues for years after treatment is stopped. Specifically, the study showed that tamoxifen continues to provide benefit for these women even after ten years, which included five years on the drug and then five years off it.

The initial results of this study were released in 2002 after the women had undergone five years of therapy, and those results indicated that tamoxifen reduced breast cancer by about a third. The results of the study five years later – and five years after the therapy was stopped – support the initial findings with a 29% reduction in all cases of breast cancer and a 34% reduction in estrogen-receptor positive (ER+) tumors. Even more promising, the study authors concluded that the side effects associated with tamoxifen therapy stop once the therapy is discontinued, although the drug's benefit clearly continues. This finding significantly improves the risk/benefit profile for women considering undergoing tamoxifen treatment, and has important implications about improved quality of life for the patients who continue to benefit long after the treatment and its side effects are finished.

Interestingly, the study also revealed that treatment with tamoxifen does not provide protection from developing breast cancer due to taking hormone replacement therapy, as previously suggested. In addition, the study authors observed a four-fold increase in endometrial cancer among the women who were actively taking tamoxifen, although that increase disappeared once the therapy was halted. The overall mortality rate was higher in the group of women who took tamoxifen for ten years than those in the placebo arm, although the difference was not considered to be statistically significant.

- Abstract #45: Quantitative RT-PCR analysis of ER and PR by Oncotype DX indicates distinct and different associations with prognosis and prediction of tamoxifen benefit. This study used Oncotype DX to measure the association between progesterone-receptor (PR) and estrogen-receptor (ER) expression using RT-PCR technology to better understand the predictive and prognostic roles of these markers. The study evaluated tumor samples from more than 1,000 patients from two studies previously conducted by Kaiser Permanente and the National Surgical Adjuvant Breast and Bowel Program (NSABP).

The study findings showed PR to be a characteristic of disease progression – or an accurate prognostic measure – but it is not predictive of whether the patient will benefit from tamoxifen. Interestingly, the results also suggested that measuring ER by using the Oncotype DX assay is primarily predictive of whether tamoxifen will provide any benefit to the patient, but ER is not a useful prognostic marker.

By understanding the unique roles that ER and PR play, these results provide further evidence of how the Oncotype DX assay provides individualized insight into both the prognosis and prediction of treatment benefit for each patient.

- Abstract #52: BCIRG 006: 2nd interim analysis phase III randomized trial comparing doxorubicin and cyclophosphamide followed by docetaxel (AC→T) with doxorubicin and cyclophosphamide followed by docetaxel and trastuzumab (AC→TH) with docetaxel, carboplatin and trastuzumab (TCH) in Her2neu positive early breast cancer patients. For many physicians, anthracyclines have played a key role in the adjuvant treatment of breast cancer, but this study raises the controversial question of whether they are actually necessary. This abstract summarizes the second interim analysis of a large Phase III trial which demonstrates that the regimen of a taxane plus trastuzumab (also known as Herceptin) provides a similar survival benefit to a regimen containing an anthracycline plus trastuzumab, with significantly less toxicity.

This study of 3,233 women with early stage HER2+ breast cancer evaluated the patients in three study groups in order to compare the standard of care with two experimental arms:

- Group A, the control group — four cycles of doxorubicin (Adriamycin) and cyclophosphamide followed by four cycles of docetaxel (Taxotere).
- Group B — Trastuzumab added to the group A regimen.
- Group C, the group without an anthracycline — six cycles of docetaxel with carboplatin and trastuzumab.

According to the study authors, the results confirm the findings of the first interim analysis of this trial which were announced in April 2005. Both experimental groups (groups B and C) had significantly better outcomes than the control group in reducing the risk for death while also improving disease-free survival. Although the two experimental arms exhibited similar efficacy, patients in group B experienced five times more cardiotoxicity, due to potential cardiac damage from both the anthracycline and from trastuzumab. By comparison, group C received the therapeutic benefits while sparing the patients in that arm the significant cardiotoxicity risk experienced by group B.

Because this study suggests that the use of anthracyclines in the adjuvant setting may be more harmful than beneficial, it will be important to understand the final analysis of this study and see how physicians translate those learnings into clinical practice.

For additional information on the wealth of data that was presented at the conference, we encourage you to view the full abstracts at www.sabcs.org.