Update From the 2004 San Antonio Breast Cancer Symposium  
December 29, 2004

More than 6,000 physicians, oncologists, radiologists, epidemiologists, basic scientists, and breast cancer advocates from 80 countries attended the 2004 San Antonio Breast Cancer Symposium, a forum for the discussion of new advances in breast cancer treatment.

The symposium, which was held December 8–11, included more than 600 general presentations and poster presentations. Below is a summary of some of the presentations that have immediate effects on women recently diagnosed with breast cancer and those making treatment decisions.

Genetic Test Can Help Predict Which Women with Early Stage Breast Cancer Will Benefit Most from Chemotherapy

Researchers from the National Surgical Adjuvant Breast and Bowel Project (NSABP) and Genomic Health, a company based in Northern California, reported last year, at the 2003 San Antonio Symposium, that they had developed a new genetic test that could help predict the likelihood that a breast cancer would recur.

This year, the test, called the Oncotype DX, again made headlines. The same research group reported that a new study by the NSABP and Genomic Health showed that the test not only could predict which women with node-negative, estrogen receptor (ER)-positive breast cancer were most likely to have a distant recurrence (metastasis) but which women would benefit most from having chemotherapy in addition to tamoxifen.

Background
Oncologists currently use a woman’s age, tumor size, tumor grade, and estrogen receptor status to assess her risk for having her cancer metastasize. But it is still a “best guess” scenario. There’s no perfect way of determining which women will have their tumors metastasize and thus who will benefit from chemotherapy and who doesn’t really need it. As a result, many women receive chemotherapy who probably don’t need it, while others who could benefit don’t get it.

Genomic Health developed its new genetic test by analyzing tumor samples from nearly 700 women who had been involved in a 1980s NSABP study. The analysis identified 21 genes that appeared to be related to how likely a woman who was node-negative, ER-positive, and had been treated with tamoxifen was to have had her cancer recur outside the breast (metastasize) within 10 years.

The researchers then gauged the reliability of the test by testing tumor tissue stored from 668 women who had been enrolled in the NSABP B-14 trial from 1982–1988. The women’s outcomes had been tracked by the NSABP, which allowed the researchers to compare the test’s prediction with actual recurrences.

2003 Data
The data presented in 2003 indicated that the test was able to accurately assign women into low-, intermediate-, and high-risk groups. This research was published online in the New England
Journal of Medicine (NEJM) to coincide with the latest research presented at the 2004 San Antonio Symposium on the Oncotype DX test.

The genetic test divides women into three groups—low, medium, and high risk for recurrence. As the researchers reported in 2003 and in the NEJM article, 6.8 percent of the women who the test found to be low risk had a recurrence outside the breast within 10 years. In contrast, 14.3 percent of the women who the test found to be intermediate risk had a recurrence and 30.5 percent of the women who the test rated as high risk had a recurrence.

2004 Data
The data presented this year at San Antonio showed that not only could the test accurately divide women into three risk groups, but that it could predict who would benefit most from chemotherapy. In the latest study, the researchers looked at women who had been in the NSABP B-20 trial, which was designed to compare the benefits of tamoxifen alone to chemotherapy plus tamoxifen in women with ER-positive tumors that had not spread to their lymph nodes.

[The NSABP B-20 trial found that chemotherapy plus tamoxifen was a better combination. As a result, chemotherapy plus tamoxifen became the standard treatment recommendation for women with early stage breast cancer.]

The NSABP/Genomic Health study found that the Oncotype DX recurrence score was able to differentiate between which women benefited most from chemotherapy and which women only need tamoxifen. The researchers found that women who had a high recurrence score (a score greater than 31) had a large benefit from chemotherapy. In this group, 40 percent of the women who received tamoxifen alone had a recurrence of cancer within 10 years, compared with 12 percent of the women who received both tamoxifen and chemotherapy.

In contrast, those who had a low recurrence score (a score less than 18) derived little benefit from chemotherapy. In this group, both the women who received chemotherapy and tamoxifen and the women who received tamoxifen alone had a recurrence rate of roughly 5 percent.

The Oncotype DX test is already available for women with estrogen-sensitive tumors. The test can only be done at Genomic Health (tumor samples must be sent to Genomic Health); no test kit is being sold to other laboratories or private physicians. The test costs $3,460; it is not yet known when or if insurance companies will cover it.

If you have the test done, your result will be reported as a “recurrence score” from 0–100.

- A recurrence score less than 18 means a woman has a low risk of recurrence. For example, a woman with a recurrence score of 3 would have about a 4 percent chance of recurrence, while a woman with a score of 15 would have about a 9 percent chance of recurrence. It is this group of women who had a recurrence rate of about 5 percent whether they received tamoxifen alone or tamoxifen plus chemotherapy.
- A score between 18–30 signifies an intermediate risk of recurrence. For example, a woman with a recurrence score of 20 would have about a 12 percent chance of recurrence, while a woman with a score of 28 would have about an 18 percent risk of recurrence.
- A score of 31 or higher indicates a woman has a high risk of recurrence. For example, a woman with a recurrence score of 35 would have about a 22 percent risk for recurrence,
while a woman with a score of 45 would have about a 30 percent risk for recurrence. It is this group of women who derived the most benefit from chemotherapy.

Susan says:

Oncologists hope that one day we will be able to provide all women with breast cancer with individualized treatment that is determined by specific aspects of the breast tumor. Testing for HER2 status (also sometimes referred to as HER-2 or Her-2/neu or erb-b2) and hormone sensitivity has aided us in this process. The new genetic test, Oncotype DX, is another step in that direction. It can’t predict what will happen to each individual woman, but it does provide increased information about which women are more likely to benefit from chemotherapy.

There are, however, a few caveats. As Robert Bast Jr., MD, and Gabriel Hortobagyi, MD, of the University of Texas M.D. Anderson Cancer Center in Houston, point out in their editorial in the *NEJM*, all the women in these studies were given tamoxifen. Will the test be as accurate in women who are treated with aromatase inhibitors? It most likely will be. But we don’t know. Also, what about women who are ER-positive but choose not to take tamoxifen or an aromatase inhibitor? Can the test predict what their recurrence will be? We don’t know.

It is also important to remember that not all women with breast cancer will benefit from the test. It is specifically for women who have tumors that are node-negative and ER-positive. This does, however, represent about 50 percent of all women diagnosed with breast cancer.

I think that if a woman has the test done and finds that she has a high chance for recurrence and will most likely benefit from chemotherapy, it will help make her decision to have chemotherapy easier. For those who have an intermediate score, it will still be a personal decision about whether to have chemotherapy in addition to hormonal therapy. And for the 50 percent of women with early stage breast cancer who have a low risk of recurrence and who appear to obtain the same benefit from tamoxifen as from tamoxifen and chemotherapy, the decision to forgo chemotherapy may be easier. But this, too, will still remain a very personal and individual choice.

Arimidex (Anastrozole) Update

Hormonal therapies are used to treat women with estrogen receptor (ER)- or progesterone receptor (PR)-positive tumors. Tamoxifen and anastrazole (brand name Arimidex) are both hormonal therapies, but they work in different ways. Tamoxifen keeps estrogen from getting into the cancer cells, whereas Arimidex—a type of drug called an aromatase inhibitor—blocks aromatase, the enzyme that converts androgens into estrogen. Although pre- and postmenopausal women can use tamoxifen as hormonal therapy, only postmenopausal women can use an aromatase inhibitor like Arimidex.

In November, a committee the American Society of Clinical Oncology convened to assess the adjuvant (postsurgical) use of aromatase inhibitors, concluded that most postmenopausal women should be treated with an aromatase inhibitor to reduce their risk for a breast cancer recurrence.

Findings presented at the San Antonio Symposium from the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial, and published simultaneously in *The Lancet*, appear to support this assessment.

The ATAC trial was the first to put Arimidex and tamoxifen head-to-head, and while earlier results had been reported at previous San Antonio Symposia, many clinicians have been eagerly
waiting to see what the study would show after women had been on their treatment for five years—the standard treatment for hormonal therapy.

The trial included 9,366 postmenopausal women with early breast cancer from 21 countries. The women were initially divided into three treatment groups. One-third was given Arimidex, one-third was given tamoxifen, and one-third was given Arimidex and tamoxifen. Nearly three years into the study, the researchers stopped the combination arm when it was found to be no more effective than tamoxifen alone.

The researchers found that after five years of treatment, the women in the Arimidex group had fewer recurrences and a longer time before recurrence occurred than did women in the tamoxifen group. Specifically, 575 women in the Arimidex group had a recurrence, compared with 651 women in the tamoxifen group. Arimidex also reduced the risk of a woman developing contralateral breast cancer (cancer in the opposite breast), with 35 of the women on Arimidex developing contralateral cancer compared with 59 of the women on tamoxifen.

Preventing recurrence is significant, but an even more important question is whether Arimidex is better at extending overall survival. After five years, the study found that overall survival was similar for women in both the tamoxifen and Arimidex groups. But since most of the women in the trial had a good prognosis to begin with—61 percent were lymph node-negative and 64 percent had tumors that were less than 2cm in size—it is actually too early for the study to show a difference in overall survival. However, the researchers predict that because Arimidex has been found to be better at preventing local recurrences and distant recurrences (metastasis), a survival benefit ultimately will be seen as well. This remains to be seen.

Clinicians also have been concerned about the side effects associated with Arimidex. The study found that the women on Arimidex had fewer hot flashes, less vaginal discharge, and fewer incidents of blood clots or endometrial cancer than did the women on tamoxifen. However, the women on Arimidex did experience more fractures and experience more joint and bone pain. These side effects had been noted throughout the study.

Susan says:

Three aromatase inhibitors are now approved for use in the United States: Arimidex, letrozole (brand name Femara), and exemestane (brand name Aromasin). As more research is published about all of these drugs, more women are wondering if they should switch to Arimidex instead of staying on tamoxifen or if they should use Arimidex or another aromatase inhibitor instead of tamoxifen as their hormonal treatment.

With the five-year results of the ATAC trial in, and with the American Society of Clinical Oncology (ASCO) committee concluding that most women should be treated with an aromatase inhibitor. These drugs are going to gradually become the most widely used hormone therapy and tamoxifen will no longer be the standard of care.

What we don’t yet know, however, is whether it is better for a woman to be on an aromatase inhibitor, like Arimidex, for five years or to start on tamoxifen for two or three years, and then switch to an aromatase inhibitor for the remainder of her five years of hormonal therapy. Trials underway will soon provide that information.
It’s also important for women to remember that, as the ATAC trial showed, aromatase inhibitors like Arimidex are not problem-free. Women on aromatase inhibitors have a higher risk of developing fractures and bone and joint pain. In fact, for some women the bone and joint pain is too intense for them to stay on the drug. We also don’t yet know if any long-term side effects will surface in the next five to 10 years. Only time will tell.

It is important for any woman going on hormonal therapy to discuss with her clinician the risks and benefits of taking an aromatase inhibitor for five years as compared with starting on tamoxifen and then switching to an aromatase inhibitor after two or three years.

Also, women who cannot tolerate the side effects of an aromatase inhibitor should not worry about having to switch to tamoxifen. Tamoxifen is and remains an excellent hormonal treatment, and will always have an important place in breast cancer care.

**New Data on Sentinel Node Biopsy**

Breast cancer surgery typically includes an examination of the lymph nodes under the arm to determine if the cancer has spread beyond the breast. Only if the chance of finding cancer in the lymph nodes is extremely low—for example, when a woman has ductal carcinoma in situ (DCIS) or an invasive tumor less than 5mm in size—will a surgeon suggest that evaluation of the lymph nodes may not be necessary.

If cancer is found in the nodes, it will help guide decisions related to adjuvant chemotherapy. Also, removing nodes that contain cancer can help prevent a recurrence in the armpit. There is no evidence, however, that removing and examining lymph nodes affects survival.

The standard technique for removing lymph nodes has been axillary dissection. To perform an axillary dissection, the surgeon removes the fat tissue in the hollow of the armpit, which contains the lymph nodes. Usually 10 to 15 lymph nodes (about one-third of the lymph nodes that are under the arm) are removed.

A newer technique for examining the nodes is called sentinel node biopsy. To perform a sentinel node biopsy, the surgeon injects a small amount of blue dye and/or radioactivity into the breast near the tumor. This material will naturally move toward the lymph nodes and to the first draining node for that area of the breast. This is the node that is most likely to have drained any cancer cells spreading through the lymph system from the tumor. This node or nodes are then removed and studied. If this node is normal, then there’s a very low chance that the surgeon will have missed another positive node. If it contains cancer cells, then the cancer may have moved on to other nodes. Currently the standard of care is for a woman who has a positive sentinel node—meaning the node contains cancer cells—to go on to have a full axillary dissection.

One of the reasons that researchers are interested in learning more about the sentinel node biopsy is that it appears that women who undergo this procedure are less likely to develop arm problems, including lymphedema. Lymphedema, a condition characterized by swelling and pain in the arm, occurs when lymphatic fluid builds up because it cannot drain properly. Lymphedema is estimated to affect about 40 to 50 percent of women whose breast cancer treatment included extensive lymph node dissection or radiation.

This year at San Antonio, researchers presented preliminary results from the NSABP B-32 study, a prospective, randomized Phase III clinical trial looking at whether sentinel node biopsy provides the same information as axillary dissection of the lymph nodes with fewer side effects.
Although a number of surgeons now routinely perform sentinel node biopsies, more data is needed about how the benefits and risks of this procedure compare to the traditional axillary node dissection. The NSABP B-32 trial is one of the studies following women long-range to determine if sentinel node biopsy is as accurate a procedure for detecting if cancer has spread to the lymph nodes as axillary node dissection.

The study is following 5,210 women who had breast cancer surgery. None of the women showed signs that their cancer had spread to their lymph nodes when their doctors examined them. The women were randomized to two groups. One group had a sentinel node dissection immediately followed by axillary dissection. The second group had a sentinel node dissection. If the sentinel node was found to be positive, an axillary dissection was performed and more nodes were removed. If the sentinel node was negative, no axillary surgery was performed.

The study found that removing just one to three sentinel nodes is as good an indicator of whether cancer has spread to the lymph nodes as is removing the 12 to 15 that are removed during axillary dissection. Specifically, the study found that sentinel node biopsy was 97 percent accurate in determining whether cancer had spread beyond the breast.

Another group of researchers presented two studies from a similar trial taking place in the United Kingdom. The Axillary Lymphatic Mapping Against Nodal Axillary Clearance (ALMANAC) trial is a large, randomized study comparing sentinel node biopsy to axillary dissection. The trial found that women who had a sentinel node biopsy had fewer arm and shoulder problems—less arm swelling and numbness and fewer problems with arm movement—than did women who had an axillary node dissection. In terms of quality of life, the study found that at one, three, and six months after surgery, the women who had the sentinel node biopsy scored higher on a quality-of-life questionnaire than did the women who had the axillary node dissection.

Susan says:

Although the studies evaluating sentinel node biopsy are not complete, an increasing number of surgeons are now performing sentinel node biopsies with the aim of providing women with the information they need about whether cancer has spread beyond the breast while decreasing their chances of developing arm problems, including lymphedema. Because lymphedema is a chronic illness that affects quality of life, finding ways to reduce a woman’s risk of developing lymphedema due to breast cancer surgery is very important.

If you want to have a sentinel node biopsy, you should discuss with your surgeon how comfortable she/he is doing the procedure and how many she/he has already performed. You want to have a surgeon who has experience doing sentinel node biopsy, or is working under the supervision of someone who has this experience, because the procedure is difficult to learn—it’s been estimated that a surgeon must do between 20 to 30 sentinel node biopsies to become really good at it.

You should ask your surgeon how many times she/he has done the procedure and what percentage of the time she/he has been able to find the sentinel node. It should be at least 85 percent. Also ask about the surgeon’s false negative rate. (A false negative means the sentinel node tested negative for cancer cells but there was a positive node somewhere else.) The false negative rate should be under 5 percent. If the surgeon is unable or unwilling to give you this information, that’s a good sign that you should look for another surgeon. If the surgeon is learning
how to do the procedure and working with a supervising surgeon, you should find out the
supervising surgeon’s ability to find the sentinel node and false negative rate.

There are some situations in which a surgeon cannot perform a sentinel node biopsy, for example
if you have had a breast reduction or silicone implants. Also, if you have lymph nodes under the
arm that your clinician can feel are enlarged, then the procedure isn’t necessary; the doctor will
be able to find them without the dye. If you have two lumps in different places in your breast, the
sentinel nodes will be in two parts of the breast, so the procedure won’t work. Also, sentinel node
biopsy tends to be less successful in older women and in women with extensive DCIS.

You can learn more about the Annual San Antonio Breast Cancer Symposium on the conference
website: www.sabcs.org