Dr. Susan Love’s Update from the 26th Annual San Antonio Breast Cancer Symposium
December 3–6, 2003

More than 6,000 physicians, oncologists, radiologists, epidemiologists, basic scientists, and breast cancer advocates from 80 countries attended the 2003 San Antonio Breast Cancer Symposium, a forum for the discussion of new advances in breast cancer treatment.

The symposium, which was held December 3–6, 2003 included more than 55 general presentations and 550 poster presentations. Below is a summary of some of the key presentations and findings and what they mean for women diagnosed with breast cancer.

New Test to Help Women with Early Stage Breast Cancer Make Treatment Choices

Researchers from the National Surgical Adjuvant Breast and Bowel Project (NSABP) and Genomic Health reported that a new genetic test can help predict the likelihood that a breast cancer will recur, and, in turn, whether chemotherapy is necessary. Oncologists currently use a woman’s age, tumor size, tumor grade, and estrogen receptor status to assess her risk for distant recurrence (metastasis). But it is still a “best guess” scenario—we don’t have a perfect way of determining who will benefit from chemo and who doesn’t really need it.

Genomic Health developed the 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 a breast cancer recurrence.

The researchers then needed to test whether these 21 genes could actually predict who would have a recurrence. They did this by testing tumor tissue stored from 668 women who had been enrolled in the NSABP B-14 trial from 1982–1988. All of the women were node-negative, estrogen receptor (ER)-positive, and had been treated with tamoxifen. The women’s outcomes had been tracked by the NSABP, which allowed the researchers to compare the test's prediction with actual recurrences.

The study found that the genetic test was able to accurately assign women into low-, intermediate-, and high-risk groups. Further, the test was better at predicting recurrence than was age, tumor size, and tumor grade.

The test should be available in 2004. It is not yet known whether insurance will cover it or how much it will cost. 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.
- 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.
Susan says:

For some women the risk of a recurrence is so low that chemotherapy is unnecessary, especially when hormonal therapy (tamoxifen or an aromatase inhibitor) is given.

Women who are node-negative have the lowest risk for recurrence, and the majority of node-negative women—85 percent—would not have a distant recurrence even if they did not have chemotherapy. This means that many more women get chemotherapy than who actually need it. This new test by Genomic Health provides additional information about the tumor that may help oncologists and women with breast cancer determine if chemotherapy is the right choice for them.

It is important to understand that this new test cannot definitively say who needs chemo and who doesn't. In fact, another study presented at the conference found that the test was not an accurate predictor of recurrence in women who did not take tamoxifen. Also, 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, it will help make her decision to have chemotherapy easier. But for those who have a low score and thus a low risk for recurrence, it will still be a very individual and personal decision about whether to have chemotherapy.

Arimidex (Anastrozole) Update

Hormonal therapies are used to treat women with estrogen receptor (ER)- or progesterone receptor (PR)-positive tumors. Tamoxifen and anastrozole (brand name Arimidex) are both hormonal therapies, but they work in different ways. Tamoxifen keeps estrogen from getting into the cancer cells, whereas Arimidex—which is 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.

The IMPACT Trial

Researchers from the UK presented the results of the IMPACT trial, which evaluated different hormonal strategies in the neoadjuvant setting. (Neoadjuvant treatment is typically used to shrink large tumors. If the tumor gets small enough, a woman may be able to have a lumpectomy instead of a mastectomy.)

The 330 women in the study were postmenopausal and had estrogen receptor-positive tumors that were at least 2cm in size. They were randomized to receive Arimidex, tamoxifen, or Arimidex plus tamoxifen for three months prior to surgery.

The study found that the tumors responded equally well—response was measured as at least a 50 percent reduction in size—to Arimidex and tamoxifen or the combination of the two. The response rates were 37 percent for Arimidex, 36 percent for tamoxifen, and 39 percent for the combination.

Susan says:

Neoadjuvant treatment is typically used to try to reduce the size of large tumors so that women can have a lumpectomy instead of a mastectomy. It makes sense to use hormonal therapy for this purpose, and as this study found, both tamoxifen and Arimidex appear equally effective at shrinking tumor size.

Surgical assessments prior to the neoadjuvant treatment found that 56 percent of the women would probably have needed to have a mastectomy. The study found that twice as many women in the Arimidex group, compared with those in tamoxifen group, became eligible for a lumpectomy. This may make Arimidex sound like a better choice, but this number must be viewed skeptically. Surgical assessments were available for only 67 percent of the women enrolled in the study. Further, not only are tumors hard to measure before they are
removed, but the change in tumor size may have been easier to measure in the larger tumors than it was in the smaller ones.

The study also suggested that women with HER2-positive tumors may respond better to Arimidex than tamoxifen (HER2 is also sometimes referred to as HER-2 or Her-2/neu or erb-b2), as 58 percent of the HER2-positive women responded to Arimidex, compared with 22 percent of the women on tamoxifen and 31 percent of the women on the combination treatment. However, this analysis was based on only 34 patients, which is too small of a number to allow us to say one drug is better than the other. This finding does, however, support findings from a letrozole trial (brand name Femara, another type of aromatase inhibitor) that found that women who were HER2-positive did better on femara than on tamoxifen.

The bottom line: This study supports the use of hormonal therapy and not just chemotherapy as neoadjuvant treatment for women with large tumors, and it is something women who would prefer to have a lumpectomy and radiation instead of a mastectomy should consider. In addition, it appears that Arimidex or another aromatase inhibitor may be a better option for women who are HER2-positive, but more research is still needed.

**Tamoxifen and Arimidex for Hormonal Treatment**

Italian researchers presented the results of a study that explored whether it was better for women to stay on tamoxifen for five years or to switch to Arimidex about halfway through their treatment.

The researchers' hypothesis was that switching would reduce side effects associated with tamoxifen and decrease the chance of tamoxifen resistance (resistance is when tumors no longer respond to a drug) as well as reduce the side effects and costs associated with Arimidex.

The study enrolled 448 node-positive, estrogen receptor-positive women who had been on tamoxifen for two to three years. They were randomly assigned to either continue on tamoxifen or to switch to Arimidex for the remainder of their time on hormonal treatment.

The study found that there were 19 recurrences and 5 second primary tumors in the tamoxifen group and 8 recurrences and 2 second primary tumors in the Arimidex group.

In terms of side effects, the women on Arimidex had higher rates of gastrointestinal symptoms and rising cholesterol but lower rates of gynecological symptoms, including endometrial cancer.

**Susan says:**

As more research is published about Arimidex and other aromatase inhibitors, 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.

Staying on tamoxifen for five years puts one at risk (albeit a low risk) for developing endometrial cancer. Switching to an aromatase inhibitor may increase cholesterol as well as increase the risk of experiencing bone and joint pain as well as developing osteoporosis.

Right now, we know more about tamoxifen than we do about aromatase inhibitors, like Arimidex, especially in terms of long-term side effects. And although Arimidex is being used more frequently, tamoxifen still remains the standard of care.

That said, doing 2.5 years of tamoxifen followed by 2.5 years of Arimidex might make sense for some women. Even so, the question remains whether doing so will balance out the side effects or compound them.
DCIS Update

Ductal carcinoma in situ (DCIS) is considered a pre-cancer because it is not able to spread to other parts of the body—the hallmark of cancer. However, if left untreated, about 30 percent of women with DCIS would develop invasive breast cancer. Because we don't yet know how to tell which DCIS will become invasive and which won't, we treat all women who are found to have DCIS.

Micrometastases in Women with DCIS

Even though DCIS is by definition noninvasive, there are times when solitary cancer cells or micrometastases (small clusters of 10–20 cells) are found in the sentinel nodes of women with DCIS. To determine the significance of these findings, researchers from the Netherlands conducted a retrospective study of women with DCIS, or with invasive ductal or lobular carcinoma that was 5mm or less in size, who had an axillary lymph node dissection as part of their surgery.

The study found it was not uncommon to detect lymph node metastases in women who have DCIS or very small invasive low-risk tumors. These cells were found in 11 percent (7/66) of the women with DCIS, 27 percent (3/11) of the women with DCIS and microinvasion, and 12 percent (2/17) of the women with invasive ductal or lobular carcinoma.

However—and importantly—these solitary cells or micrometastases did not have any impact on survival. After 8.5 years of follow-up, all of the women remained disease-free, without having chemotherapy.

Based on these findings the researchers concluded that it is not necessary to perform a full axillary node dissection when micrometastases are found in the sentinel node in women with DCIS or in women with T1a tumors who have no other negative prognostic factors.

Susan says:

This study confirms what many of us have thought for some time: The presence of micrometastases doesn't actually signify that the cancer has spread. In fact, the cells found in micrometastases are probably spread by the surgery and do not appear to have the potential to become malignant. These findings underscore that the presence of micrometastases in women with DCIS or small tumors does not signify that the cancer has spread to the lymph nodes or that an axillary lymph node dissection, a procedure that can put a woman at higher risk for developing lymphedema (painful swelling of the arm), is necessary.

The bottom line: Women with DCIS or small tumors who have micrometastases can be treated as node-negative. This means that as long as no other negative prognostic factors are present, they do not need to be treated with chemotherapy.

Wide Excision Alone for DCIS

Because DCIS is, by definition, a pre-cancer, surgeons have hypothesized that there may be some instances, such as if the DCIS is small and Grade 1 or 2, that radiation might not be necessary if the tumor is removed with wide margins.

(DCIS is graded based on how the breast cells look. In low-grade DCIS, the cells look more like regular cells than do the cells in high-grade DCIS. Both high-grade DCIS and low-grade DCIS have a 30 percent chance of developing into an invasive cancer if left untreated. The difference is that high-grade DCIS does it faster and becomes a more aggressive invasive cancer while the low-grade DCIS does it slower and becomes a less aggressive invasive cancer.)
To test this hypothesis, researchers at the Dana-Farber/Harvard Cancer Center in Boston followed 157 women with low-grade DCIS with surgical margins (the area surrounding the tumor) of at least 1cm who had surgery as their only treatment.

They found that even in this highly selected group of patients with DCIS there was still a substantial local recurrence rate. Thirteen women developed a local recurrence, 9 with DCIS and 4 with invasive disease. Based on this finding the researchers concluded that until there are better ways of identifying subgroups of women with DCIS who are at low risk for recurrence, DCIS is more effectively treated with surgery followed by radiation than with surgery alone.

Susan says:

It is not uncommon for women with DCIS to question whether they really need to have radiation. And while there are undoubtedly many women with DCIS who would be fine if they had surgery alone, as this study shows, we still aren't very good at determining which women those are. One day we will have tests that allow us to determine which women with DCIS are at the highest risk for developing invasive cancer. Until then, it makes sense for women with DCIS to have radiation after their lumpectomy.

Taxol and Taxotere Update

Docetaxel (brand name Taxotere) and paclitaxel (brand name Taxol) are both taxanes. Originally made from the bark of the Pacific yew tree, both Taxotere and Taxol are now a semi-synthetic product that comes from the needles and twigs of the Himalayan yew tree. Taxanes prevent the growth of cancer cells by affecting an important part of the cell structure called microtubules. Microtubules are formed when a cell starts dividing. Once the cell stops dividing, the microtubules are broken down or destroyed. Taxanes stop the microtubules from breaking down. As a result, the cancer cells become so clogged with microtubules that they cannot grow and divide.

A Comparison of Taxotere and Taxol in Women with Metastatic Breast Cancer

This trial randomized 449 women with metastatic breast cancer to either Taxotere or Taxol. The study found an overall response rate of 32 percent for the Taxotere and 25 percent for the Taxol. Length of response was longer on Taxotere: 7.5 months compared with 4.6 months for those on Taxol. So was time to progression: 4.6 months with Taxotere and 3.1 months with Taxol. Overall survival was longer for women on Taxotere as well: 15.4 months compared with 12.7 months for those on Taxol.

This study also incorporated a quality-of-life analysis. The women in both groups reported similar quality-of-life levels. However, there was more significant toxicity experienced by the women on Taxotere. In these women, neutropenia (an infection that can occur when a person's white blood cell count is too low), asthma, and neuromotor and neurosensory problems were all more common.

Susan says:

Although a survival difference of about three months does not seem like much, it is important to note that very few trials—only 10 found by the researchers—have ever demonstrated a statistically significant survival difference in metastatic breast cancer. Even though the quality-of-life analysis found that women felt about the same on both drugs, each woman will need to weigh for herself the benefit of possibly extending her life for a few more months with the potential for experiencing increased levels of toxicity.
Adjuvant Chemotherapy Combinations: FAC Compared with TAC

The Breast Cancer International Research Group (BCIRG) 001 trial compared the effectiveness of six 21-day cycles of FAC (5-fluorouracil, doxorubicin, and cyclophosphamide) with six 21-day cycles of TAC (Taxotere, doxorubicin, and cyclophosphamide).

The study randomized 1,491 pre- and postmenopausal, node-positive women to either FAC or TAC. After five years of follow-up, 75 percent of the women on TAC were disease-free, compared to 68 percent of the women on FAC. The study also found a survival advantage, with 87 percent of the women on TAC and 81 percent of the women on FAC alive after five years. The benefit was seen in both hormone receptor-positive and hormone receptor-negative women as well as in both HER2-positive and HER2-negative women.

There were no toxic deaths and no long-lasting toxicities in either group of women, although the women who received TAC did have a higher incidence of febrile neutropenia. (Febrile neutropenia is a fever related to a low white blood cell count. It can occur during chemotherapy because chemotherapy often kills good white blood cells along with cancer cells.)

Susan says:

Oncologists are continually trying to come up with "the best" chemotherapy regimen. The fact that this study found a survival advantage to using TAC over FAC is significant, and it makes TAC a combination more women may want to consider.

Abraxane: A New Way to Give Taxol

Taxanes like Taxol and Taxotere are strong cancer fighters. The problem with them is that they are harder to administer than other cancer drugs because they cannot be dissolved in water. Instead, they must be dissolved in a special type of solution, and these solutions have their own toxicities. Taxol is dissolved in Cremophor. Cremophor's toxicity limits how much Taxol can be given. It is also the reason why every patient who gets Taxol must receive a steroid premedication, why Taxol has a long infusion time, and why Taxol is more likely to damage the bone marrow, making neutropenia (an infection that can occur when a person's white blood cell count is too low) and other infections more likely to occur.

Abraxane is a new delivery method for Taxol. This new preparation contains no toxic solvents. Instead, the Taxol is contained in tiny nanoparticles and coated in a shell of human albumin protein, the body's natural transport system. Abraxane was also designed to bring the Taxol more directly to the tumor and to limit how much is absorbed by normal, healthy tissue.

To test the new delivery method, researchers from the US randomized 454 women with metastatic breast cancer to either Abraxane administered over 30 minutes once every three weeks without premedication or Taxol dissolved in Cremophor and administered over three hours once every three weeks with steroid and antihistamine premedication.

The study found that 33 percent of the women responded to Abraxane, compared with 19 percent who responded to Taxol. There was also a longer time to progression for women on Abraxane—21.9 weeks—compared with 16.1 weeks for women on Taxol. The women in the Abraxane group received a higher dose of Taxol, yet they had a lower incidence of neutropenia than did the women on the traditional Taxol regimen. Women in both groups experienced neuropathy—a pins-and-needles sensation, often in the hands and feet—but it resolved more quickly in those
on Abraxane. Based on these findings the researchers concluded it may be the Cremophor that is responsible for the high toxicity associated with Taxol.

Abraxane is being submitted to the US Food and Drug Administration for marketing approval.

**Susan says:**

The toxicities associated with Taxol and Taxotere have been a problem since they first began to be used for cancer treatment. Abraxane appears to have the potential to overcome these toxicities, and to allow Taxol to be given at a higher dose. This is significant, and it will undoubtedly encourage greater use of Taxol in the adjuvant and metastatic settings.

**Breast Cancer in Young Women**

**Web-Based Survey of Fertility Issues in Young Women with Breast Cancer**

More than 11,000 women under 40 are diagnosed with breast cancer each year, and many of these young women are concerned about how their breast cancer treatment will affect their fertility.

Young Survival Coalition and researchers from Brigham and Women's Hospital in Boston teamed up to study how fertility concerns affect young women's breast cancer decision-making. They developed a survey about fertility issues and emailed it to more than 1,700 Young Survival Coalition members.

The majority of the 732 women who completed the survey were about two years from their diagnosis. Most were white, college graduates, and married. At the time of their diagnosis, 60 percent were Stage II or Stage III and 56 percent had a desire to have a child.

The study found a high level of concern about fertility: 39 percent were very concerned; 18 percent were somewhat concerned; 16 percent were a little concerned; and 27 percent were not concerned. Further, 29 percent of the women surveyed said fertility concerns influenced their treatment decisions.

Seventy percent of the women surveyed discussed fertility concerns with their doctor, 17 percent with a fertility specialist. About 50 percent thought that their concerns were addressed adequately; 27 percent did not; and 20 percent were unsure about this.

The researchers noted that there were limitations to their study. For example, those who returned the survey may have been more likely to have fertility concerns, women's perceptions about how they felt at the time may differ from how they really did (recall bias), and the members of a young women's breast cancer advocacy organization may not be representative of all young women with breast cancer.

**Susan says:**

One of the problems young women with estrogen receptor-positive tumors face is that the chemotherapy treatments that are thought to be most effective for them are those that put them into menopause. What exactly is happening in chemotherapy-induced menopause is not clear. It is often talked about as "shutting the ovaries down," but that's not really what occurs, since menopause shifts the ovaries from being an egg-producing organ to a stromal organ that still produces small amounts of hormones.

Another problem, especially for women diagnosed in their 30s, is that the five years of hormonal treatment recommended for women with ER-positive tumors is going to delay when childbearing can begin. This, too, will impact fertility, because fertility decreases with age.
It clearly is important for oncologists to talk to young women about their fertility concerns. But it also must be remembered that the primary focus has to be on deciding what treatments will give a young woman the best chance of survival.

Leuprolide Acetate (Lupron) Three-Month Depot Offers Similar Efficacy to CMF

Pre- and perimenopausal women with breast cancer are typically treated with adjuvant chemotherapy. In Europe, however, researchers have taken the lead in exploring the effectiveness of hormonal therapies as an alternative to chemotherapy.

German researchers reported the results of a trial that randomized 599 pre- and perimenopausal women with T1-3, node-positive, estrogen receptor- and/or progesterone receptor-positive tumors to six cycles of CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) or leuprolide acetate (brand name Lupron) every three months for two years. Lupron stops estrogen production by inducing temporary menopause. The medicine is in depot form, which means that it is released slowly over the three months. The shots are given deep into a muscle.

The study found that 49 (19 percent) of the women on CMF and 46 (17 percent) of the women on Lupron progressed during their treatment.

The most common side effects in the women on Lupron were hot flashes, sweating, mood swings, insomnia, and weight gain. (If these sound like menopausal symptoms, it's because they are.)

The most common side effects in the women on CMF were those typically associated with chemotherapy: nausea, vomiting, diarrhea, and tiredness.

Based on these findings the researchers concluded that treatment with Lupron is at least as good as adjuvant treatment with CMF in pre- and perimenopausal patients with ER-positive, node-positive breast cancer.

Susan says:

Hormonal therapy for premenopausal women is more widely accepted in Europe, and this is another in a series of studies that supports it use.

These studies have reopened an old debate about the role of amenorrhea—having your period stop—in breast cancer treatment. Chemotherapy often causes amenorrhea and studies have found that women whose periods permanently stop have a better prognosis than do those women who get their periods back. (This is also directly linked to a woman's age. Older women are less likely to have their periods return than are younger women.)

This study found that about 50 percent of the women in the CMF group became premenopausal again, and the researchers are continuing to study differences between these two groups to see what role amenorrhea played in outcome. Also, the women in this study were given Lupron for two years. But it is not clear that that is the optimal amount of time, and there are studies now underway that are looking at whether three or four years of Lupron is better than two.

I believe it is long past time for doctors in the US to be more open to endocrine therapies, and to begin discussing these studies and these options with their premenopausal patients.
Komen Foundation Award Lecture

Dr. Walter Willett, chairman of the department of nutrition at the Harvard School of Public Health was one of two recipients of this year's Komen Foundation Brinker Award for Scientific Distinction. (The other winner was Mina J. Bissell, PhD, a distinguished scientist in the Life Sciences Division at Lawrence Berkeley National Laboratory and a member of the Scientific Advisory Board of the Susan Love MD Breast Cancer Research Foundation.) Dr. Willett conducts research on whether things that we can control—such as diet and exercise—can help prevent disease.

Dr. Willett noted that although increases in dietary fat consumption have been repeatedly mentioned as a possible factor in breast cancer risk, research has not shown a clear association between total dietary fat intake and breast cancer. But all fat is not the same, and it is possible, he said, that animal fat is actually more of a problem than other types of fat. He noted that on large dairy farms cows are continuously fed hormones to keep them producing milk. And this means that the milk they produce contains large amounts of hormones. These high hormone levels are present in whole, low-fat, and non-fat milk.

Dr. Willett also discussed alcohol and breast cancer risk. He noted that although alcohol has been shown to increase breast cancer risk, this only appears to be true in women with low folate levels.

Susan says:

Dr. Willett recommended that young girls and women reduce their milk consumption, and I am not sure. It is important for girls to build bone while they are growing. A solution may be organic low-fat milk which does not have additional hormones added. Adult women also should be taking calcium and vitamin D supplements.

Dr. Willett's comments about alcohol and breast cancer risk are also significant. Folate is a B vitamin that is found in a variety of foods; it is also added to many vitamin and mineral supplements. In its synthetic form it is referred to as folic acid.

If you are someone who enjoys a glass of wine with dinner, you may want to consider taking a folate supplement or a multivitamin that includes folate. The recommended daily dose of folate is 400mcg. The maximum safe level of folate is 1mg, or 1,000mcg of folate daily.

You can read more about alcohol and breast cancer risk here. (goes to FAQ's/ Alcohol)