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To each of you, happy Thanksgiving.

Dr. Silvana Martino



Breast Cancer Advisor

BY DR. SILVANA MARTINO • NOVEMBER 2011

BIOLOGY BASICS

In this issue I want to discuss the recurrence patterns of invasive breast cancer. Most breast cancers do not recur! Some do. To some degree, we can predict who is more likely to have a recurrence based on certain parameters available about the tumor at time of initial diagnosis. The most informative features are (1) the number of lymph nodes involved with tumor, (2) the size of the tumor in the breast, (3) whether the tumor is hormone positive or negative, (4) the Her2/neu status of the tumor, and (5) the grade of the tumor. Additional lab tests such as KI67 and the Oncotype Dx test can also be helpful in certain tumors.

A recurrence can become apparent at any time following the diagnosis of breast cancer. In general, recurrences are more common about two to three years after the diagnosis. Thereafter, the probability of recurring decreases with time. This pattern is most clearly seen with hormone negative breast cancers. Hormone positive breast cancers also have a peak during years two to three, with a subsequent

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Biology Basics continued

decrease; but, they have more of a tendency to continue to recur over many years.

Though it is true that most breast cancers that will ever recur will do so during the first five years, tumors can recur even many years later. It is for this reason that we continue to watch breast cancer patients for life.

Breast cancers can recur in any part of the body. However, there are certain organs that are more common and are watched more closely. The more common sites are bones, lymph nodes, skin, lungs, liver and the brain. Her2/neu positive tumors and triple negative tumors (hormone negative and Her2/neu negative) are somewhat more likely to travel to the brain. Hormone positive tumors are more likely to first appear in bones, lymph nodes and skin. Lobular invasive breast cancers are a bit more likely to recur in certain internal surfaces of the body (serosal surfaces), and can cause intestinal obstruction, obstruction to the flow of urine and a pattern that suggests meningitis (meningeal carcinomatosis).

Based on these patterns, your doctor has expectations of what your tumor is more likely to do. That is why it may seem at times that your oncologist is more interested in certain aspects of your health and not others.

In the next issue, I will discuss the order in which treatment decisions are made once there is a diagnosis of breast cancer.

WHAT'S NEW

1. Adjuvant therapy with zoledronic acid (zometa)

It has been recognized for many years that the bone marrow (the center part of bones) is a very active area and serves many functions. It produces blood cells and elements of our immune system. More recently, it has been noted that it also has the ability to serve as a resting or perhaps nesting place for breast cancer cells. Studies suggest that if we can influence the bone marrow space, we may be able to prevent not only metastases to bone but to other parts of the body as well. Several studies have tried to do this with the use of drugs called bisphosphonates.

As a natural and continuous process, bones are constantly being broken down and rebuilt. Cells called osteoclast have the function of breaking the bone down, and cells called osteoblast have the function of rebuilding bones. Bisphosphonate drugs are able to interfere with osteoclast function, thus promoting

the bone building side of the process. These drugs are commonly used in the treatment of tumors that have spread to bones. Their use helps bones to heal and reduces subsequent bone damage by tumors.

The present question is whether these drugs can also be used as a way to prevent tumors from spreading to bones and also to other organs.

The present question is whether these drugs can also be used as a way to prevent tumors from spreading to bones and also to other organs. Both animal and human studies have suggested that this can be done. The results in humans have not been consistent, however. Some have shown a beneficial effect and others have not. The most recent study to be reported is the AZURE trial. It included 3360 women with stage II and III breast cancer. They all received standard treatments. Half also received zoledronic acid (every 3 to 4 weeks for 6 doses and then every 3 to 6 months to complete 5 years of treatment), and half did not. Forty five percent of the women were premenopausal and all

continued next page

What's New continued

others were postmenopausal. The group has been followed for about 5 years. Their results demonstrate that in this large group of women, the outcome was the same whether the bisphosphonate drug was added or not.

Interestingly, if one separates the women based on whether they are pre or postmenopausal, there does appear to be benefit in the postmenopausal group. This may turn out to be a key point, as this same finding has been noted in other studies.

A rare but important side effect of bisphosphonates is osteonecrosis of the jaw. It was noted in about 2% of the women on zoledronic acid in this study. I have had one patient with this complication. Though it is uncommon, it can be debilitating.

A large American study looking at this same issue but using a different drug from this same category will be reported at the San Antonio Breast Cancer Symposium

in December 2011. It is hoped that it will provide a final answer to this question.

Reference: Robert E. Coleman, et al, N ENGL J MED, 365; 15, October 13, 2011, 1396-1405

2. TAC versus AC—T chemotherapy

In the 1990's the chemotherapy drug paclitaxel (Taxol) and docetaxel (Taxotere) were recognized as effective drugs against both early and advanced breast cancer. Their degree of effectiveness was comparable if not superior to Adriamycin which for many years was considered the most effective drug available. How to combine these newer drugs with Adriamycin containing chemotherapy programs has been an important question both from the perspective of effectiveness as well as toxicity. Taxol and Taxotere are similar but not identical to each other, so each has required study. An issue that I believe has now been resolved is whether giving all drugs together is superior to giving them in sequence. There are biological reasons based on principles of drug resistance to suspect that each way of doing it might be superior.

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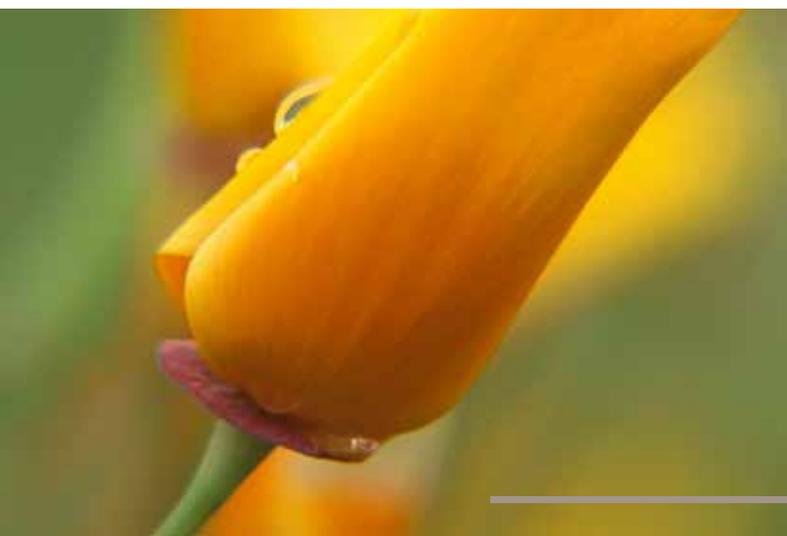
An international study involving 3,298 women from 335 centers in 37 countries was recently reported. The women had Her2/neu negative early breast cancer. They were randomized (similar to the flip of a coin) into two groups. One group received chemotherapy with Adriamycin, Cytoxan and docetaxel given every three weeks for 6 cycles. The other group received first Adriamycin and Cytoxan given every three weeks for 4 cycles and subsequently was give docetaxel every three weeks for 4 cycles. At five years of follow-up, the efficacy of both treatments was found to be the same.

I find this to be valuable information as it clearly demonstrates that neither way is superior and that one can choose between these two treatments based on preference and tolerability.

One caution. Though one can substitute Taxol for Taxotere if the drugs are used in sequence, Taxol cannot be substituted when all three

drugs are given together. This is due to an interaction between Taxol and Adriamycin that results in more potential heart toxicity.

Reference: Wolfgang Eiermann, et al, Phase III Study of Doxorubicin/ Cyclophosphamide With Concomitant Versus Sequential Docetaxel as Adjuvant Treatment in Patients With Human Epidermal Growth Factor Receptor 2-Normal, node-positive Breast Cancer:BCIRG-005 Trial, Journal of Clinical Oncology, vol.29(29), October 10, 2011, 3877-3884



QUESTIONS & ANSWERS

Q Dr. Martino, I have received chemotherapy and I am now on Femara that I have been told I need to take for five years. I have developed a lot of vaginal dryness and discomfort. I have tried a lot of lubricants but they don't help me very much. My gynecologist has given me vaginal estrogen cream but my oncologist has said that this is bad for breast cancer. What should I do?

A Vaginal dryness and discomfort is a common problem in women being treated for breast cancer. For some it is a relatively minor problem and for others it can be a major issue. The underlying cause of this problem is a decrease in estrogen production. This occurs naturally as women go through the menopause. Consequently, it is a problem experienced by many women who do not have breast cancer. Many of the therapies used for breast cancer also reduce estrogen and either cause, mimic, or accentuate the menopause. As part of this process, vaginal dryness and discomfort are a consequence. Libido is often also decreased.

In women who do not have breast cancer, the solution is the administration of estrogen which is available in several forms. In women with a history of breast cancer, the administration of any form of estrogen is considered to place them at potentially higher risk of breast cancer recurrence. Consequently, most

oncologists instruct their patients to not use any form of estrogen. Even when estrogen is applied vaginally, there does appear to be some internal absorption. Additionally, there is concern that if one is taking an anti estrogen hormone such as tamoxifen or an aromatase inhibitor, the use of estrogen will reduce the effectiveness of these agents.

Through one of my patients, I have recently been introduced to the use of the hormone DHEA as a way to treat vaginal symptoms. It is available in a vaginal form. There are studies demonstrating that it does reverse vaginal discomforts in postmenopausal women by producing local estrogen and androgen hormones. Measurements of blood levels of estrogen demonstrate that these levels are minimally elevated. Again, the safety of this minimal elevation in someone with breast cancer is unclear.

My personal practice has been to first determine if an individual woman has this problem or not. If she does, I favor the use of non estrogen vaginal lubricants. These should be used on a regular, daily basis very much as you might moisturize your skin daily and not only prior to sexual behavior. For many women this is adequate. Only when this approach is not adequate do I then advise an estrogen preparation. I prefer products that have a specific and low dose estrogen content such as Estring or Vagifem rather than estrogen creams. I have no experience prescribing DHEA.

To what degree, if any, these products increase the risk of breast cancer recurrence is not known, and this is the real issue. Consequently, if you chose to use them you have to accept a certain degree of risk. But it is a degree that we cannot quantify.

E-mail your questions to:
smartino@theangelesclinicfoundation.org

Disclosure: The information contained in this newsletter is for educational purposes only. It is not designed to diagnose or provide treatment recommendations. Please consult your own physicians for all decisions about your care.



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Reconstructing the breast: A choice of techniques following mastectomy

Historically, following mastectomy, the breast was not reconstructed. Patients were encouraged to accept their new body image and find mechanisms to cope with the physical mutilation. Fortunately, this view has given way to the idea that cancer surgery should involve as little mutilation as possible and to that end, plastic surgeons are more often consulted prior to mastectomy. All patients considering mastectomy should be made aware of various options now available for reconstruction.

Two major points are worth emphasizing: (1) immediate reconstruction (reconstruction started at the time of mastectomy) produces a better long term cosmetic outcome than reconstruction started months or years after the mastectomy; and (2) in most cases



Mastectomy without reconstruction.

of breast cancer, the skin of the breast does not need to be removed as part of the mastectomy. By starting the reconstruction at the time of mastectomy and having the cancer surgeon leave the skin not involved with tumor, almost natural reconstructions are often possible.

If the skin envelope is spared at the time of mastectomy, the challenge for the reconstructive team is how to safely “fill” the skin envelope of the breast. This can be done using implant technology (a combination of temporary tissue expanders and more permanent implants) or flap technology (the patient’s own tissues taken from the abdomen or the back). Sometimes these approaches are combined with the uses of a flap from the back and an underlying implant. If tissue from the lower abdomen is used (the TRAM flap), an implant can usually be avoided.

Patients and surgeons starting the process of breast reconstruction should remain aware that the priority of cancer surgery is to treat the cancer. Cosmetic outcome can be considered but sometimes must be compromised for other treatments including chemotherapy and radiation therapy. However, usually the necessary treatments can be given in coordination so as to maximize the patient’s cancer treatment and preserve the cosmetic appearance.

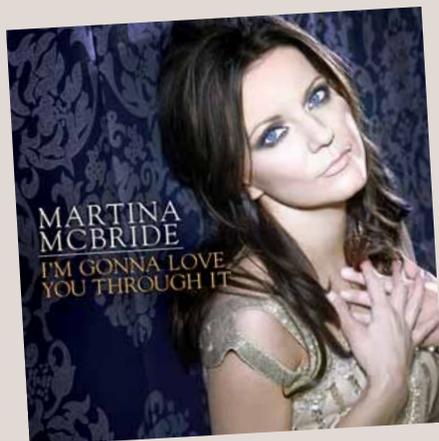


Reconstruction following skin sparing mastectomy.

MUSIC REVIEW

Well, reviewing a song is not something I anticipated doing but it seems right to do it nevertheless. Recently, I was watching the results of the TV show *Dancing With the Stars*. One of their guest performers was the noted singer Martina McBride. She sang a song titled *I'm Gonna Love You Through It*. The lyrics are about a 38 year old woman who has just received a phone call telling her the diagnosis is cancer and her husband's reaction to the news. It is a beautiful ballad with words full of meaning and experience. It brought many emotions to my mind. It reminded me of the many husbands, partners, friends and wives (yes, men get breast cancer too) that I have watched give love and strength to my patients, and how important they are in this journey.

I encourage all of you to listen to this song. It is beautiful.



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The Angeles Clinic Foundation is a nonprofit organization whose purpose is to sponsor and support programs, services, education, advocacy, and research related to cancer. Our goal is to make a difference in all aspects of the lives of people touched by cancer. Your support is important in the fight against cancer and the journey towards a cure.

Upcoming Foundation Events

For more information, please call us at
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Breast Cancer Education Seminar

November 13, 2011 • 3:00 - 5:00 PM
Community Room
Smith College Club of Los Angeles
Studio City, CA

Breast Cancer Education Seminar

November 16, 2011 • 11:45 AM - 1:30 PM
Temple Adat Ari El
Valley Village, CA



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