

Dear Readers,

October is National Breast Cancer Awareness Month. The purpose of this designation is to raise awareness of the magnitude of the breast cancer problem in this country and worldwide. There are still many women who for a multitude of reasons fail to obtain routine screening mammography and breast exams. Please take every opportunity to encourage all those around you to educate themselves about early detection.

Best Regards,
Dr. Silvana Martino



Breast Cancer Advisor

BY DR. SILVANA MARTINO • October 2012

INTRODUCING BREAST PALS

To celebrate National Breast Cancer Awareness Month, we at The Angeles Clinic Foundation are proud to introduce the BREAST PALS MENTOR PROGRAM. As many of you are personally aware, the diagnosis of breast cancer is a frightening experience. Having someone who has gone through the experience before you and who can provide you with personal guidance and answer your questions can be an invaluable asset. We have gathered a group of survivors with varied experiences who will serve as a personal pal to newly diagnosed patients. Because of the personal nature of this service, at present we can only serve those located in the Santa Monica/Los Angeles area. We anticipate expanding this service to a wider area in the future.

For those of you in other locations, please ask your own physicians about similar programs that may be available in your area.



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The Angeles Clinic FOUNDATION

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BIOLOGY BASICS

I will continue to discuss the management of metastatic breast cancer. The treatment goals of metastatic disease are: (1) to reduce symptoms from the disease and, (2) to preserve a person's functional capacity. Though we all recognize that all drugs have side effects, it is my opinion that the drugs given for the treatment of metastatic disease should not make a person feel worse than the disease itself does. The goal is not to eradicate the disease at the expense of the patient. Therefore, a person's preferences, and their tolerability must be a key part of treatment decisions.

In this issue, I will review hormonal therapies available for metastatic disease. These therapies are often also referred to as endocrine therapies. As a reminder, to use these therapies, one must have a tumor that is hormone receptor positive (estrogen and/or progesterone receptor positive). Even so, not all tumors that are hormone positive will respond. Hormonal positivity comes in degrees. The more hormonally positive a tumor is, the more likely it is to respond to hormonal therapy.

In choosing hormonal therapy, it is important to know a woman's menopausal status. Some hormonal therapies (the aromatase inhibitors) do not work when one is premenopausal. In such a situation, you must first make a woman postmenopausal by inactivating her ovaries.

To a reasonable degree, hormonal (or endocrine) therapies can be understood as working by reducing the amount of estrogen in the body and thereby reducing the amount of estrogen available for breast cancer cells to use to assist in their growth.

The earliest hormonal therapies were the surgical removal of the

endocrine organs of the body that influence the production of estrogen. These are the ovaries, the adrenal glands and the pituitary gland. Each of these was usually removed in succession. The ovaries make primarily estrogen. Their removal renders a woman postmenopausal. The adrenal and pituitary glands make many other vital hormones. Their removal requires that certain hormones that they influence must be replaced. There is no way to only remove the part that effects estrogen production. Removal of these glands renders patients very fragile and vulnerable to many other problems. Consequently, finding drugs that work against breast cancer and avoiding these surgical treatments became a major research focus. We now have several alternatives rendering these surgeries obsolete. There are, however, circumstances where surgical removal of the ovaries (oophorectomy) remains a good option.

Here is a list of modern hormonal therapies:

- Ovarian removal or ovarian suppression with LH-RH agonists (Lupron/Zoladex)
- Tamoxifen (Nolvadex)
- Toremifene citrate (Fareston)
- Aromatase Inhibitors (Arimidex/Femara/Aromasin)
- Fulvestrant (Faslodex)
- Megestrol acetate (Megace)
- Estrogen • Male hormones • Danazol

These therapies are used in succession keeping in mind a woman's menopausal status. The best clue that another hormonal treatment is likely to be effective is whether the tumor responded to prior hormonal treatment. The drug Afinitor that I have discussed in prior issues can be added to some hormonal therapies and prolongs the period of tumor control. There are times when one can use all of these treatments before a tumor develops hormonal resistance and chemotherapy must be introduced.

BIOGRAPHY

Dr. Silvana Martino

is the Director of Breast Cancer Research and Education at The Angeles Clinic Foundation in Santa Monica, California. She is board certified in internal medicine and medical oncology. Dr. Martino has specialized in the treatment and research of breast cancer for over three decades. She is a nationally recognized leader in the field of breast cancer. Her body of work has included research in breast cancer prevention, treatments for early breast cancer and metastatic disease. Dr. Martino has conducted and coordinated large national and international studies which have resulted in changing the standard of care worldwide.

DR. MARTINO'S
CURRICULUM VITAE

REVIEW OF META ANALYSIS

The Early Breast Cancer Trialists' Collaborative Group

I have recently returned from a planning meeting of the Early Breast Cancer Trialists' Collaborative Group held at the University of Oxford, in Oxford, England, and I want to review the purpose and process of this group for you.

Most of the information known about breast cancer treatments is the result of specific studies where a group of patients with similar disease is randomized (like the flip of a coin) and treated according to two different treatments. For example, women with hormone positive breast cancer are treated with either tamoxifen or Arimidex. Another example would be a study where they are treated with tamoxifen versus Femara. A third study compares tamoxifen versus Aromasin. Each study gives you a specific answer of whether one drug is better than the other in that particular group of women.

However, one can ask a different question. How does tamoxifen compare to the drugs collectively known as aromatase inhibitors (AIs) including Arimidex, Femara and Aromasin? This question allows you to compare two different classes of drugs (tamoxifen and AIs) that work in two separate ways against breast cancer cells. Different statistical methods and rules are necessary to answer a question when you are combining studies that are similar but not identical. This process is known as a meta-analysis.

This process was adopted in the 1980's by a statistical group from the University of Oxford in the United Kingdom. Its leader, Sir Richard Peto organized the Early Breast Cancer Trialists' Collaborative Group (EBCTCG). The purpose of this effort has been to collect data from all randomized research trials conducted worldwide on the treatments of early breast cancer. These data are periodically updated, analyzed, and the results published. Unlike some meta-analyses where one simply reviews the published articles about a topic and combines the published results, the EBCTCG obtains ongoing actual data about each patient in studies. Updates are obtained directly by contacting those conducting each study.

Every 5 years beginning in 1985, a group of researchers from around the world have gathered at the University of Oxford to discuss the process and the results from this large body of data on early breast cancer. Smaller meetings occur periodically as needed to assist this process. Multiple publications have resulted from this process which are collectively referred to as the "breast cancer meta-analysis." One of the most important aspects of this work is that it contains data on thousands of people. Another is that it tracks people for many years. These features are critical not only for observing the benefits of

various therapies, but also for observing side effects that are rare and side effects that occur many years after a therapy is given.

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The amount of data encompassed by this process is now so large, that the most recent meeting was actually a "planning meeting." About two hundred of us gathered to discuss what questions need to be addressed, and what new problems need to be resolved before we meet again next year to review new results. A major problem that needs a resolution is that in many studies there is insufficient funding to follow patients beyond a 5 or 10 year period. This is particularly an issue in countries like the U.S. where we lack a centralized insurance system that tracks patients, and where patient privacy laws are complex and vary from state to state. Nevertheless, obtaining long term data is a key feature of this project.

The next meeting of the EBCTCG will be in October, 2013. Results from that meeting will most likely be presented at the San Antonio Breast Cancer Symposium in December, 2013. I will review results in this newsletter as they become available.

WHAT'S NEW

1. Herceptin Update

Two important studies were presented at the 2012 European Society for Medical Oncology (ESMO) Congress in Vienna, Austria, providing guidance on how long to use trastuzumab (Herceptin) in patients with HER-2 positive, early breast cancer. Several studies already published have provided data on the value of using one year of Herceptin. The question that remained was whether one year was the ideal time or whether longer or shorter were better or as effective.

The HERA trial, conducted by the Breast International Group included 5102 women who, following completion of their chemotherapy, were randomized (like the flip of a coin) to either no Herceptin, one year of Herceptin, or two years of Herceptin. The initial results from this trial demonstrated that the groups given Herceptin did better than those not given Herceptin. An update on this comparison continues to demonstrate improved results with Herceptin treatment. In addition, Dr. Richard Gelber reported that at about 8 years of follow-up, it is now apparent that the one and two year Herceptin groups did equally as well. A bit more cardiac toxicity was seen in the group receiving two years of treatment. These long awaited results demonstrate that one year of Herceptin therapy should remain our standard. Longer therapy is not better.

There is however, another question. Is 6 months of

Herceptin just as good as one year? This question was addressed by the PHARE study conducted in France and presented by Dr. Xavier Pivot. This study included 3,380 women with HER-2 positive early breast cancer who in addition to chemotherapy received either 6 months or 12 months of Herceptin. At 42.5 months of follow-up, the results demonstrate that the two groups are doing about

the same. The 12 month group may be doing a bit better. The data is, at this point, considered to be statistically inconclusive, leaving some uncertainty on this question. Longer follow-up is needed to clarify whether 6 months is as good as one year of therapy. Several other ongoing trials are also addressing the issue of how long to give Herceptin. For now, one year appears to be best.

QUESTIONS & ANSWERS

(Q) Dr. Martino, I have been taking Arimidex for about 5 years. I have been pretty faithful about taking it each day but I have missed an occasional dose. Do I have to make that up at the end?

(A) I must say that this is a very common question. Even in studies where women are watched closely, it is apparent that most will forget to take their pill occasionally. Consequently, the data that we have on the benefits of these hormones does include women who have not taken every dose. The issue is, "how many tablets have you actually missed during the 5 year period?" If, it is truly as you state that you have missed an occasional dose, then I don't think you need to make them up at the end. If however, there have been months when you have not taken the drug, then I would favor that you make those up.

(Q) Dr. Martino, I have heard that getting pregnant increases the risk of getting breast cancer. Is this true?

(A) The answer to this question is a bit complex. In general, women who have had children and especially if they had their first full term pregnancy prior to about age 20, have a life time risk of breast cancer that is lower than women who have not had a full term pregnancy or have postponed their first pregnancy until they are older. However, there is also data that demonstrates that a woman's risk of breast cancer is increased for about 5 years after a pregnancy. The reason for this increase is not clear. It is presumed to be related to the hormones that are produced in the body as part of a pregnancy.

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GUEST WRITER

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Radiation Therapy After Lumpectomy and Its Role in Breast Conservation Therapy

Each year, more than 220,000 women are diagnosed with breast cancer in the United States. The vast majority of these women are found to have cancer that is localized to the breast or has spread only to the nearby lymph nodes. Most of these women are eligible for and do undergo breast conservation therapy (BCT). BCT refers to breast conserving surgery, which consists of a lumpectomy accompanied by surgery to remove axillary lymph nodes, followed by a moderate dose of radiation therapy to the breast. In some circumstances, the nearby lymph node regions may also be targeted with radiation therapy.

Post-lumpectomy radiation therapy is a critical component of successful breast conservation therapy. Even after a lumpectomy with negative surgical margins, approximately 40% of women have small amounts of microscopic residual cancer remaining in the breast. If left untreated, these residual cancer cells can grow into a recurrent tumor. Indeed, most studies of women who were treated with lumpectomy alone without radiation therapy have up to a 30-40% risk of having a cancer recurrence.



10-15%, and this risk is even further reduced with the incorporation of modern systemic therapy. A metaanalysis, or overview, of 17 clinical trials of BCT involving more than 10,000 women found that, by reducing the risk of cancer recurrence after lumpectomy, radiation therapy also significantly reduces the risk of death from breast cancer.

Although more than 2/3 of women with breast cancer undergo BCT, not all women are candidates for this type of therapy. Women who have diffuse disease that cannot be surgically removed with a negative margin by lumpectomy or who have multiple tumors in different quadrants of the breast are not good candidates for breast conservation surgery. In addition, women with large breast tumors relative to the size of their breast are unlikely to have acceptable cosmetic outcomes after lumpectomy. Finally, there are women who should not receive radiation therapy to the breast, including pregnant women, women who have received prior radiation to the breast, and women with certain collagen vascular diseases, such as scleroderma or active lupus. These women will typically be better served with a mastectomy with or without reconstruction. For patients with large

Post-lumpectomy radiation therapy aims to eradicate this microscopic residual cancer. As expected, the addition of radiation therapy after breast conservation surgery reduces the risk of recurrence by more than half to approximately

tumors relative to the size of their breast, though, it may be possible to administer chemotherapy before surgery to shrink the tumor, enable a breast conserving surgery, and proceed with BCT.

There are several options for post-lumpectomy radiation therapy. The standard method of delivering radiation therapy as part of BCT is to give many short daily treatments to the whole breast to an intermediate dose over the course of approximately 5 weeks. In many circumstances, this whole breast radiation therapy is followed by an additional “boost” of radiation dose delivered over the course of an additional 1-2 weeks to the surgical cavity left after the lumpectomy. The addition of this boost dose of radiation has been shown to further reduce the risk of a tumor recurrence, especially in younger patients and high-grade tumors. In select situations, women may be candidates to receive their radiation therapy to the whole breast in an accelerated course of approximately 3-4 weeks.

In women with smaller and more favorable tumors, there may also be the possibility of confining the radiation treatment volume to include only the tissue adjacent to the lumpectomy cavity. This technique is called accelerated partial breast irradiation (APBI) and is typically completed over the course of one week. APBI can be delivered using tightly focused external x-ray beams or brachytherapy, which involves the delivery of radiation directly into the surgical bed using temporarily-implanted catheters.

continued next page

Radiation Therapy continued

The radiation therapy process begins with a consultation with a radiation oncologist, who will review all relevant records, examine the patient, and help determine if the woman is a candidate for BCT and post-lumpectomy radiation therapy. Typically, radiation therapy should commence approximately 4-6 weeks after the breast conservation surgery. If chemotherapy is required, the post-lumpectomy radiation therapy often occurs 3-4 weeks after the completion of all chemotherapy cycles. The radiation oncologist develops a personalized radiation plan based on the anatomy of each woman. This process begins with a treatment planning CT scan. The radiation oncologist imports the images from this scan into a treatment planning computer and then generates a 3-dimensional model of the patient's chest. Using specialized treatment planning software, the radiation oncologist and physics team design multiple radiation beams that target the radiation dose to the breast while avoiding the adjacent normal tissues, such as the underlying heart and lungs. This treatment planning process typically takes several days. Once the treatment is approved by the radiation oncologist, the woman is ready to commence her course of radiation therapy.

Post-lumpectomy radiation therapy is a critical component of successful breast conservation therapy. As such, it plays an important role in the optimal management of breast cancer and is an exciting area in the field of breast oncology.

The Angeles Clinic FOUNDATION

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.

Recent Foundation Events

For more information, please call us at (310) 582-7909

Breast Cancer Seminars with Cathie Chung, MD, PhD

Location: Roth Staffing Companies, L.P., Orange, CA

Date: October 11, 2012

Topic: Breast Cancer Risk Assessment

Note: (Not open to the public)

Location: Cancer Support Community, VWSB

530 Hampshire Road, Westlake Village, CA

Phone: 805-379-4777

Date: October 18, 2012

Time: 6:30-8:00pm

Topic: Advanced Breast Cancer

Location: Temple Beth Am

1039 S. La Cienega Blvd., Los Angeles, CA

Phone: 310-652-7353

Date: October 22, 2012

Time: 7:30-9:00 pm

Topic: Breast Cancer: Awareness Is Our Greatest Tool

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