

Dear Readers,

With next month's issue, we will begin the third year of publishing the Breast Cancer Advisor. The audience that was first envisioned for this publication was my own patients. It was a way of keeping them up to date with medical information in the field of breast cancer that I considered important for their care. Over the past two years, others have found the Breast Cancer Advisor useful. Our audience now includes nurses, doctors and even some high school students. I am grateful to all who have contributed to making this publication successful. As always, feel free to copy or forward the Breast Cancer Advisor to others who may benefit from this information.

Best regards,
Dr. Silvana Martino



Breast Cancer Advisor

BY DR. SILVANA MARTINO • July 2013

BIOLOGY BASICS

Breast Cancer in Men

In this issue, I will review the management of metastatic breast cancer in men. As is true of breast cancer in general, the principles of treatment are similar to the manner in which breast cancer is treated in women. The sites of metastases in men are the same as in women. The most common sites are: (1) the chest wall, (2) the skin, (3) the bones, (4) the lungs, (5) the liver, (6) the brain and (7) all other sites.

If metastatic disease is suspected, a biopsy of the lesion should be done if at all technically possible. The biopsy material is sent to a pathologist for an accurate diagnosis and for performance of hormone receptor testing (estrogen and progesterone receptors) and HER2 testing. A history and physical exam of the patient needs to be performed to look for additional evidence of tumor and to determine if any symptoms exist that require immediate attention. A CT scan of the chest, abdomen and pelvis plus a bone scan should also be done to evaluate the

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Biology Basics continued

extent of disease. An MRI of the brain should be added if there are symptoms suggesting brain involvement. Some oncologists like to add a brain MRI even without symptoms in patients whose disease is HER2 positive or triple negative as these two groups are more prone to brain metastases. The sum of these investigations is to verify that one is dealing with a recurrent breast cancer and not some other diagnosis; to determine the extent of disease in the body; to clarify if there is a symptom that can be imminently life threatening and requires immediate attention and to clarify the hormonal and HER 2 status of the tumor. From these conclusions, one can then plan appropriate treatment.

It is important to keep in mind what the goals are in treating metastatic disease. Specifically, the goals are primarily to improve quality of life by reducing and preventing symptoms and secondarily to prolong life. Cure is rare when one is treating metastatic disease. Improving the quality of life and prolonging life are highly possible. It is in this setting that having a good relationship with your medical oncologist is most critical. It is in this setting where the practice of the art of medicine is most needed.

SURGERY

There are some occasions where surgery is needed. Obstructions of the intestinal or the renal (kidney/urine) system may require surgery. Some brain metastases may need surgery. Also, compression of the spinal cord by tumor may require prompt surgical intervention. Fluid accumulation around the lungs and heart (effusions) may need drainage.

RADIATION THERAPY

It is fairly common to include radiation therapy as part of the management of metastatic breast cancer. It is a method for

controlling disease in certain locations. It is useful in treating disease in the brain, spinal cord, skin, lymph nodes and bone metastases. It is not a good way to control lung or liver metastases. It is not a way to treat the entire body.

DRUG THERAPY

The primary modality for treating metastatic breast cancer is the use of various drugs. Unlike surgery and radiation, which are local therapies, drugs get into the blood stream and are carried in blood to most parts of the body. There are three classes of drugs in common use: hormones, chemotherapy and HER 2 directed therapies.

Most breast cancers in men are hormone positive. Consequently, hormonal therapy is often effective and used first. Orchiectomy (removal of the testes) was traditionally the first hormonal therapy used. It is an effective therapy, though often not favored by patients. It has been replaced by tamoxifen as the first hormonal therapy. When this agent fails, other hormones used include the aromatase inhibitors (Arimidex, Femara, and Aromasin) and megestrol acetate (Megace). Additionally, anti-androgens and luteinizing hormone-releasing hormone agonists (Lupron) have been shown to have activity. The drug Afinitor has been combined with hormones as a way to reverse resistance to hormonal therapy. Though there are no studies using this strategy specifically in men with breast cancer, it is reasonable to assume that it should work as it does in women.

Chemotherapy is used: (1) when the tumor has stopped responding to hormones, (2) the tumor is hormone receptor negative, (3) in conjunction with HER 2 directed therapies and (4) when the disease is growing rapidly, even if it is hormone positive. The choices of chemotherapy drugs in men are exactly

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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

Biology Basics continued

the same as in women. They can be used as single agents or in combinations. The commonly used drugs in this category are Adriamycin, Cytosan, methotrexate, fluorouracil, Taxol, Taxotere, Abraxane, Navelbine, gemcitabine (Gemzar), capecitabine (Xeloda), eribulin (Halaven) and ixabepilone (Ixempra).

For breast cancer which is HER2 positive, several options are now available: Herceptin, Tykerb, TDM-1 and Perjeta. These agents are generally combined with chemotherapy. They can also be used with some hormones, as single agents and combined with each other.

If part of the metastatic process involves bone metastases, as is often the case, an agent that specifically helps reduce bone damage from cancer (Aredia, Zometa and Xgeva) should be considered in addition to the treatments that have already been discussed.

Since the management of metastatic breast cancer in men is similar to the management of this process in women, you may wish to review this topic in the August-December, 2012, issues of this journal for additional details.

CLINICAL TRIALS

As I have previously stated, there are few studies in the field of breast cancer that are exclusive to men. Nevertheless, I believe that participation in clinical trials is critical. It is the only way that we will move our knowledge of this disease forward. I would urge all patients to participate and to seek opportunities to be included in clinical trials.

QUESTIONS & ANSWERS

(Q) Dr. Martino, I have finished my chemotherapy and my husband has planned a vacation for us. Is it OK for me to fly? How long should I wait?

(A) There is no specific rule that a certain number of days must pass between the end of chemotherapy and being on an airplane. It is a judgment that you should make with your doctor. The concern is primarily that of infection. Since an airplane is essentially a closed container where you are with a large number of strangers at least some of whom will be infected, some caution is prudent. At a minimum, you should wait until your blood counts are back to normal. I personally prefer that you let an additional few weeks go by to be sure that the counts remain normal since they can fluctuate as they recover. Your level of overall health is also important, as well as how your counts did during chemotherapy. For patients who are generally fragile or those whose blood counts did not recover easily or dropped very low during chemotherapy, I tend to restrict travel for a longer period. If you feel ill, I would not advise traveling. If your blood counts are not optimal, using a face mask may be helpful. As best as you can, avoid direct contact with people who are obviously infected. It may be possible to move to a different seat if someone near you is obviously ill. The other issue to consider is where you are going. Will there be good medical care available there should

you need it? If not, then I would postpone traveling. The bottom line is to allow your doctor to guide you as to when it is safe.

(Q) Dr. Martino, I have lobular carcinoma in situ. My doctor has advised me to have bilateral mastectomies. If the disease is only in one breast, why do I need to have both breasts removed? My sister had real breast cancer and she only had a lumpectomy. If all I have is pre cancer, why do I need so much surgery?

(A) Lobular carcinoma in situ is a type of change in the breast tissue that predicts that you are likely to develop invasive breast cancer in the future. It is a marker of future risk. The risk is shared by both breasts. If the lobular carcinoma in situ is found only in the right breast, it does not mean that only the right breast is at risk. It means that each breast is at risk. This is why your doctor has asked you to consider a mastectomy of each breast. Since you state that your sister had “real breast cancer,” this raises the possibility that members of your family may carry the breast cancer genes. Please discuss this issue with your doctor if that has not already been done. Though bilateral mastectomies will reduce your future risk of invasive breast cancer by about 90%, other non-surgical procedures are also available, though they are less effective. Your doctor may consider hormonal therapies such as bilateral oophorectomy, or prescribing hormonal therapy such as tamoxifen or Evista.

E-mail your questions to:

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WHAT'S NEW

Treatment of Early Breast Cancer

A primary goal of treating patients with early breast cancer is to identify how little therapy can be given and still lose none of the anticancer effect. In surgery, this concept has resulted in doing lumpectomy rather than mastectomy procedures and in doing sentinel node biopsies rather than axillary lymph node dissections.

In radiation therapy, this principle has led to shortened number of treatment days and the resurgence of radiation delivered only to the site of disease rather than radiating the entire breast following breast sparing surgery.

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Previous Issues

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This same goal is evident in the use of chemotherapy. During the 1970's and 1980's, adjuvant chemotherapy for early breast cancer was given for one to two years. Research looking at decreasingly shorter time spans led to the present day practice where adjuvant chemotherapy is given from three to six months only. There has also been a goal to identify therapies with less toxicity. One trial with both of these goals in mind has been reported by Dr. Lawrence Shulman from Dana-Farber Cancer Institute in Boston. I am proud to be a co-author of this work. This study was designed to answer two questions about the treatment for early breast cancer: (1) whether 6 cycles of chemotherapy were superior to 4 cycles and (2) whether a simpler and presumed less toxic treatment with Taxol only was equal to treatment with the combination of Adriamycin and Cytoxan.

The results to the first question were published in the November 20, 2012 issue of the Journal of Clinical Oncology and demonstrated that in women with up to 3 positive lymph nodes, 6 cycles of adjuvant therapy with Adriamycin/Cytoxan or with single agent Taxol were not superior to 4 cycles. Therefore, longer therapy with the same drugs was not more effective. It is important to recognize that these results apply only to patients with

not more than 3 lymph nodes involved with tumor since this was the category of participants in this study. For those with more lymph nodes involved, the results might be different.

The results to the second question were recently presented at the June 2013 meeting of the American Society of Clinical Oncology (ASCO) in Chicago. The study enrolled 3,871 patients with either node negative disease or, at most, 3 positive lymph nodes. The patients have been followed for a period of about 6 years. The data demonstrate that there were fewer side effects with Taxol therapy. This confirmed what we had anticipated. However, from these results, we cannot conclude that therapy with single agent Taxol is equal to the combination of Adriamycin/Cytoxan. Therefore, we cannot recommend the substitution of the less toxic therapy of

single agent Taxol for the more toxic, yet well recognized standard therapy of Adriamycin/Cytoxan.

Reference:

Shulman LN, Cirrincione CT, Berry DA, Becker HP, Pere EA, O'Reagan R, Martino S, et al. Six Cycles of Doxorubicin and Cyclophosphamide or Paclitaxel Are Not Superior to Four Cycles As Adjuvant Chemotherapy for Breast Cancer in Women With Zero to Three Positive Axillary Nodes: Cancer and Leukemia Group B 40101, Vol 30 (33), Nov 20, 2012, pp4071-4076.

Schulman LN, Berry DA, Cirrincione CT, Becker HP, Perez EA, O'Reagan R, Martino S, et al. Comparison of Doxorubicin and Cyclophosphamide (AC) versus Single Agent Paclitaxel (T) as Adjuvant Therapy for Breast Cancer in Women with 0-3 Positive Axillary Nodes: CALGB 40101, presented at ASCO, June, 2013.

Research looking at decreasingly shorter time spans led to the present day practice where adjuvant chemotherapy is given from three to six months only.

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Lymphedema

As the survival rates from breast cancer continue to improve, our attention must be increasingly focused on preventing and minimizing post treatment side effects. The goal of treatment must not only be a normal life span, but, also, normal function and quality of life. Lymphedema remains a dreaded sequelae from both surgery and radiation therapy.

Lymphedema is swelling of the soft tissue due to the accumulation of lymph fluid in the involved area. It may involve arms, legs, face, neck, genitals or any part of the body where the lymph vessels and or lymph nodes were interrupted, removed or are absent.

The body's lymph system is composed of a network of lymph vessels or channels that are connected to the lymph nodes. The main superficial lymph nodes that are connected to the lymph vessels are located in the neck, axillae (armpits) and the groin area. A deeper lymphatic system surrounds all internal organs.

The lymphatic system serves many critical functions. Its primary function is to collect and transport waste/



the lymph system plays an important role in the defense mechanism of the body and is thus part of our immune system. As is true of blood, lymph is primarily a liquid medium and continuously circulates throughout the body. If the lymph system fails to function properly, the lymph fluid accumulates in the tissue causing swelling called LYMPHEDEMA.

The most common cause of lymphedema of the upper extremity and upper quadrant is related to breast cancer surgery. The incidence of lymphedema after axillary lymph nodes dissection has been reported to be more than 50%. This problem led to a desire to identify ways to reduce the need for axillary dissection and was the impetus for the development of the sentinel node biopsy technique. The incidence of lymphedema following a sentinel lymph node procedure is less than 6%. The combination of surgery and radiation treatments increases the rate of lymphedema.

The onset of lymphedema after surgery and or radiation treatment is typically within the first year but it may occur even years later. One may experience tension, heaviness

and pressure of the arm, breast, armpit, hand and fingers followed by swelling. This may be followed by tightness from jewelry and clothing, with reduced flexibility in the hand, wrist and fingers.

and pressure of the arm, breast, armpit, hand and fingers followed by swelling. This may be followed by tightness from jewelry and clothing, with reduced flexibility in the hand, wrist and fingers.

In the early phase of lymphedema, the swelling is relieved by elevation of the affected arm. If the lymphedema is undiagnosed and or untreated, the swelling progresses and is not improved after rest or elevation.

Lymphedema increases the risk of infection in the affected area. Additionally, infection can worsen lymphedema.

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MILD LYMPHEDEMA OF THE RIGHT ARM

Guest Writer continued

Even though we do not yet have a cure for lymphedema, we can prevent the onset or progression of lymphedema with appropriate precautions and treatment. To protect the arm and upper quadrant after breast cancer surgery and or radiation treatments the following guidelines are advised. They are encouraged even in the absence of lymphedema.

1. Keep the arm clean and the skin moist. Avoid cuts, vigorous manicure, puncture wounds, etc.
2. Protect your hands with gloves when gardening, house cleaning, cooking or baking.
3. Avoid tight garments, tight bras, jewelry, IV's or blood pressure measurement on the involved arm.
4. Avoid heat (sunbathing, hot tubs, and direct application of hot packs or ice packs).
5. Do not over exercise. If you were athletic before surgery, start with about 50% of load and progress gradually to your body tolerance.
6. Maintain your body weight. Weight gain exacerbates lymphedema.
7. Restrict salty foods.
8. Treat cuts, insect bites with first aid measures. If you experience signs of infection such as redness, rash or heat of the involved area, associated with

fatigue, chills and fever, contact your doctor immediately for appropriate treatment.

Early diagnosis is the key to managing lymphedema and preventing its progression.

References for further information on Lymphedema:

1. National Lymphedema Network
2. American Cancer Society
3. Lymphedema Research Foundation
4. Academy of Lymphatic Studies
5. Lymphology

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.

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