

Breast Cancer Advisor

BY DR. SILVANA MARTINO

April 2014



Dear Readers,

Many of you have expressed an interest in learning more about the creation of TumorGrafts™ that I described in the last newsletter, and the process of drug testing that is available using that

system. Please contact Basmina Parmakhtiar, PhD either by calling (310) 582-7902 or e-mail her at bparmakhtiar@theangelesclinicfoundation.org.

Best regards,

Dr. Silvana Martino

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

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BIOLOGY BASICS

In this issue, I will continue to discuss sites of metastatic disease from breast cancer. Thus far, I have described the more common sites of disease such as bone, skin, lung, liver and brain. There are some less common locations that are encountered as part of this process. Because they are less common, it is important for both physicians and patients to be aware of them. The first of these are metastases to the eyes (ocular metastases). As with all other organs, one must distinguish between tumors that originate in the eyes versus those that have originated elsewhere in the body and spread to the eye region. Most tumors in this area fall in the second category; they are part of a metastatic process. Though metastases to the eyes can occur with any tumor, breast cancer and lung cancer are the more common. Other, less common tumors are melanoma and lymphomas.

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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.

BIOLOGY BASICS continued

In my experience, it is rare for the eyes to be the first place of metastases from breast cancer. I have only seen this on a few occasions. More often, it is a clinical situation that is part of a more generalized metastatic process.

Tumors from breast cancer that spread to the eye area can be located in several places in this region. The tumor can be located in the bones that surround the eye (the orbit). It can also be in bone at the site where the nerves that control vision and eye movement pass from their origin in the brain through the skull to the eye. The muscles and other soft tissues that surround the eyes can also be infiltrated with tumor. This process I have seen more often with invasive lobular carcinoma. The choroid layer of the inner eye is the most frequent area of involvement. In rare occasions, the eye lids are involved with metastatic cancer. It is more frequent to see multiple tumors in the eye rather than a single lesion. Though unilateral disease is more frequent, involvement of both eyes can also occur.

It is the patient who most often notices symptoms related to this metastatic process. On rare occasions, a routine eye exam may result in the first clue in an asymptomatic patient. The symptoms caused by tumor involvement of the eyes can be varied, and include a decrease in visual acuity, a “blind spot” in one’s visual field, distortion of the visual image, double vision (diplopia), inability to look in a particular direction, eye pain, sensitivity to light and headaches.

In evaluating a patient for the possibility of metastases to the eyes, it is important to keep in mind that the brain and the bone structures must also be evaluated as they are often also involved. An ophthalmologist, and if possible, one that has oncology experience or training is necessary for proper evaluation of

the patient. A retinal specialist may also be needed to assist in making the correct diagnosis. MRI or CT of the brain including the base of the skull is also needed.

The primary method for treating metastatic eye disease is radiation therapy. It is uncommon for surgery to be necessary. Though the patient will also be receiving systemic therapy, systemic modalities alone are not adequate for this distribution of metastases. It is common for vision to worsen during or for a period after completing radiation to the eyes; but subsequently, vision improves, and the final results are generally good.

WHAT’S NEW**WHEN TO START ADJUVANT CHEMOTHERAPY**

The use of adjuvant chemotherapy in early breast cancer has greatly contributed to improved survival. To date, there is no clear agreement on when chemotherapy should be started following breast surgery. Does it matter if it is started shortly after surgery, or is it just as effective if it is begun several months later? Generally, when clinical trials of various chemotherapies are designed, a number of days are specified during which chemotherapy should be started for a patient to be eligible for the study. These variable time periods have been selected in a relatively arbitrary manner for each trial for the purpose of maintaining uniformity among the participants. As an example, in the U.S., within 80 days from time of surgery has been a typical period used by the large “cooperative groups” studies. These specified time periods have been generally accepted by practicing oncologist even for patients that are not enrolled into a study.

In the past, several authors have published data on this question,

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WHAT'S NEW continued

but these data sets have been either retrospective or small randomized trials. There has not been a robust set of data with which to answer this important question. It is unlikely that there will be a well conducted study in the future. It is doubtful that either patients or their physicians would accept randomization to an early versus a later start date.

Are there biological reasons to believe that time does matter; that there is an advantage to starting chemotherapy shortly after surgery? Animal data suggest that micrometastases demonstrate an increase in growth and in formation of new blood vessels (angiogenesis) when the primary tumor is removed. This implies that the primary tumor exerts some control over distant metastases while it is in the patient. Mathematical models suggest that an increase in drug resistance develops during this time as well. It seems likely that starting therapy early should make a difference.

A recent report from Dr. Debora de Melo Gagliato and colleagues from The University of Texas MD Anderson Cancer Center in Houston, Texas, published in the March 10 issue of the Journal of Clinical Oncology adds further data to this topic which I believe is useful.

They performed a retrospective review of patients with stage I to III breast cancer treated with adjuvant chemotherapy at their institution from 1997 through 2011. They identified 6,827 women of whom 85% had stage I or II disease and the remainder had stage III breast cancer. In reviewing their records, they found that 40% had started chemotherapy within 30 days from their surgery, 44% had started their chemotherapy from 31 to 60 days from their surgery and 16% had started more than 60 days from surgery. The entire cohort of patients was followed for a median of 59.3 months. Recurrence of breast cancer and

survival were recorded. Their data demonstrate that when the entire group was considered, there was no difference either in the rate of recurrence or overall survival irrespective of when chemotherapy had been initiated.

They then subdivided the patients based on the stage of disease, the hormonal status and HER2 status of the tumor, and looked at recurrence and survival outcomes based on start of chemotherapy for each of these subcategories. In doing this, they found that for patients that had disease that was either of higher stage (II or III) or was more aggressive (triple negative or HER2 positive and treated with Herceptin containing therapy) than those whose chemotherapy had been started beyond 60 days, had an inferior outcome.

What can we conclude from this study? Does it provide an answer to the question of when we should start adjuvant chemotherapy? By the very nature of this large yet retrospective observational study, we have to conclude that it cannot give us a definitive answer. However, I believe that it does provide reasonable guidance. It reinforces the concept that not all breast cancers are the same; and that timing of chemotherapy is likely to be more critical for tumors that have more aggressive features versus those that do not. The author's suggestion that we should subdivide tumors based on risk categories is probably biologically valid. For most tumors that are small, node negative, hormone receptor positive and HER2 negative, we probably do not need to rush to start chemotherapy. For tumors that we recognize as more aggressive, starting therapy within the first month should probably be our goal.

Reference: Clinical Impact of Delaying Initiation of Adjuvant Chemotherapy in Patients With Breast Cancer, Deborah de Melo Gagliato, Ana M. Gonzales-Angulo, Xiudong Lei, Journal of Clinical Oncology, volume 32(8); March 10, 2014, pg735-744

PREVIOUS ISSUES

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QUESTIONS & ANSWERS

(Q) Dr. Martino, I had DCIS more than 10 years ago. I was treated with only a lumpectomy then. I did not have radiation nor was I placed on tamoxifen. I now have an invasive breast cancer close to the same area in my breast as I did then. My oncologist has told me that he believes that this is a different tumor than what I had before, but I think it is the same one that has come back. How can I be sure of which it is?

(A) The truth is that you cannot be absolutely certain that this tumor is new or a recurrence from the DCIS that you had in the past. Both types of events can occur. To some degree one can try to make this distinction based on a few features of the tumor. If the second tumor is identified shortly after the first one is treated, say a few years, it is more likely to be a recurrence versus if the second tumor is found many years later when a second primary is more likely. If the original lesion was a DCIS and the second lesion is an invasive lobular cancer, it is more likely to be a second primary. If the location of each lesion is clearly different, it is more likely to be a second primary. If the first lesion was hormone receptor negative and the second is hormone receptor positive, it is more likely to be a second primary. The reverse pattern is less helpful, since tumors that are hormone positive may become negative with time and treatment. If the original tumor was HER2 positive and the second tumor is HER2 negative, it is more likely to be a second primary. The reverse HER2 pattern is less helpful as HER2 negative tumors can become positive with progression. These are general rules, but none of them can truly answer your question.

From a practical perspective, the question may be less critical than you might anticipate. Whether the second lesion is a recurrence of the first or a truly second event does not alter the decisions that you and your doctors need to make relative

to your present therapy or your prognosis. Those are based on the qualities of the second lesion. So, the type of surgery, radiation or drug therapy that you need now are based on the size, location, nodal involvement, hormonal and HER2 status, presence of distant metastases or not of the present tumor.

ON THE IMPORTANCE OF EXERCISE

As a physician, I have always had some appreciation for the value of exercise. For most of my life, this appreciation has been more of a theoretical nature and less of a practical nature. I have from time to time purchased a membership to a gym or paid for classes. But during most of my life I have been too busy. Plus, my purpose in life has been primarily to take care of others and secondarily to take care of myself. Added to that, is the fact that as a physician, I have assumed that I knew enough about how to exercise and did not need much instruction. Certainly I have read enough books on the topic.

Recently one of my colleagues asked if I “worked out?” I responded that my husband and I walk our dogs several miles most days of the week. He was not satisfied with my answer and advised that I needed a personal trainer and nearly insisted that I meet his personal trainer. Unable to say no, I agreed to meet his trainer but expected to find many reasons to then turn her away. Having a personal trainer just sounded so self-indulgent to me. Something to be done by others but not a serious person such as me. In any case, I kept my word and met with her. I had low expectations. To my surprise, she turned out to be an intelligent adult woman who particularly favors working with “seniors.” At our first meeting, she performed a detailed interview and testing of my physical (limited) abilities. I realized that I was dealing with

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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.

EXERCISE continued

an experienced professional. I clearly was not the authority; she was. Though I hated spending the money, I decided that I would take some instructions from her. As I have done so, it is clear to me that not all exercise is the same. There are correct ways to do it. On our own, most of us only approximate what should be done and often we cause injury to ourselves. Having someone guide, instruct and correct you is actually important. I have gained respect for this field.

What follows is an interview with my recently acquired personal trainer. I no longer feel indulgent in using her services. I am now grateful.

Ms. Nadja Lewis – CPT/SFS

(Certified Personal Trainer/Senior Fitness Specialist)

www.fitnessbynadjalewis.com

Dr. Martino: Who should exercise and why?

Ms. Lewis: Everyone should exercise. People tend not to exercise, citing many excuses/reasons. Exercise is crucial to everyone's well-being. One is never too young, too old, too sick, too healthy, too fat, or too skinny to exercise.

There are many reasons why exercise is important. Exercise is good for both the body AND the mind. It can help lower blood pressure and cholesterol level. In diabetics, it lowers sugar levels and reduces the need for insulin. Other known benefits include:

- **Stimulation of the brain and heart**
- **Decreased risk of developing certain diseases including cancer**
- **Reduction in feelings of depression**
- **Stress reduction**

- **Improvement in self-esteem and self-image**
- **Increase in energy levels**
- **Improved sleep patterns**

Dr. Martino: Are there different types of exercise?

Ms. Lewis: There are four different forms of exercise. Most people tend to focus on one activity or type of exercise and think they're doing enough, but that is not the case. **Endurance/aerobic** activities keep your heart, lungs, and circulatory system healthy and improve your overall fitness. They delay or prevent many diseases that are common in older adults such as diabetes and heart disease. The more you build up your endurance, the easier it will be to carry out everyday activities. Examples of endurance activities include: Brisk walking, jogging, swimming, and even yard work such as mowing the lawn. **Strength exercises** help to make your muscles stronger. Small increases in strength should not be discounted as they can make a big difference in your ability to stay independent and carry out everyday activities, such as carrying groceries. These exercises are also called "strength training" or "resistance training." Using weights/dumbbells and/or resistance bands are needed for this type of training. **Balance exercises** are especially important to seniors, as they help to prevent falls, a common problem in older adults. Many lower-body strength exercises also will help improve balance if done on a consistent level. Examples of balance exercises include standing on one foot, heel to toe walk, and Tai-Chi. The fourth type of exercise is **Flexibility exercise**. These exercises stretch your muscles and can help your body stay limber. Being flexible gives you more freedom of movement for other exercises as well as for your everyday activities. There are different stretches for most parts of the body such as shoulders, back, and hamstrings. Everybody should try to stretch every day. It's not a long or

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EXERCISE continued

difficult process and it truly makes a difference.

Dr. Martino: Are there people for whom you would not advise exercise?

Ms. Lewis: Not really. Almost anyone can participate in some sort of physical activity/exercise. Even if you have a health condition like heart disease or diabetes; in fact, physical activity may help. It is best to talk with your doctor about how your health condition might affect your ability to be active.

Dr. Martino: Should patients with cancer exercise? Why?

Ms. Lewis: Everybody should exercise - including cancer patients. I advise that they get approval from their physician. Exercise is crucial for health promotion and to reduce both risk and recurrence of chronic diseases such as cancer. The underlying message is to avoid inactivity. For patients with cancer, a personal trainer may have to modify certain exercises to ensure safety and effectiveness.

Dr. Martino: What is the easiest way to get started in a regular exercise program?

Ms. Lewis: It is wise to consult your physician first before starting an exercise program, particularly if you do not have a habit of exercising. Having a personal trainer can help, especially to get a person started. I have chosen to function as an in-home Personal Trainer for many of my clients. I travel to people's homes, as this is of great convenience to them. They do not have to leave their familiar surroundings to get physical activity done in a safe and effective way. Some people do not feel comfortable at a gym, some do not like others to see them working out, or they may not feel up to driving themselves.

Dr. Martino: You have chosen to concentrate your work on seniors? Why did you choose that population? Are there

particular issues with seniors versus a younger population? Are the goals different?

Ms. Lewis: To live an active, healthy lifestyle, as a young child or a person in your 90's, you need to get proper exercise. While many seniors stop exercising due to various physical constraints, it is actually more important for older people to get regular workouts. As people get older, many tend to be less active. I realized that becoming a Certified Personal Trainer wasn't enough for me. I had to do more, to reach more people. So I decided to study further and become a Senior Fitness Specialist. Seniors need attention and need to be reminded time and time again, about the importance of exercise. It used to bother me when I would hear people say, 'She's old, let her rest', or, 'I am old now, no need to do much'. I decided it was my calling to help seniors see the light. I now teach several classes a week at Retirement Homes, Assisted Living facilities and Recreation Centers for seniors. Seniors are living longer and need to be less dependent on others.

Different people at different stages of their lives need to do different exercises, or at least at different intensity levels. While the younger population should be exercising on a consistent basis to prevent certain things from happening, such as a lack of strength and the onset of certain diseases; many of the older population need to exercise to try and reduce what they are already experiencing, such as loss of muscle mass. I love training everyone, the young and the 'older'...but seniors are extra special to me. They need that extra attention and are more aware of their bodies than the younger generation; hence they tend to be a bit more disciplined in certain areas.

Dr. Martino: Thank you, Ms. Lewis for helping to educate our readers on what is clearly an important and often neglected issue.

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