

Breast Cancer Advisor

BY DR. SILVANA MARTINO

November 2013



Dear Readers,

I want to thank all those who participated and contributed to the success of our educational and fundraising events during the month of October. The Angeles Clinic Foundation does not stand alone. We are inspired by patients and their families. We

are supported by friends and donors. We are committed to the cure of all cancers.

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

METASTASES TO BONE

The bones are probably the most common part of the body where metastatic disease from breast cancer is found. In the past, we thought of bone involvement as primarily a pattern seen with hormone positive disease, but many studies have demonstrated that it is also a common location for hormone negative disease as well.

In a simple way, you can picture a bone as having two parts; the outside part of bone which gives structure and movement, and the central or inner part called the bone marrow which is where many blood products are formed. Evidence suggests that in many patients, the bone marrow is involved early and that this location serves as a protective or hiding place for breast cancer cells; a place where breast cancer cells can lie undetected for perhaps many years while waiting for some signal to grow and spread

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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

to other parts of the body. We do not know what the triggering signals are that begin this process. Some studies, but not all, have shown a correlation between breast cancer cells in the bone marrow and the probability of tumor spread to other locations. These cells can only be identified by doing a bone marrow biopsy. Since not all studies have shown a correlation between a positive bone marrow biopsy in an otherwise asymptomatic patient and the subsequent development of obvious metastatic disease, it has not become common practice to look for these cells. At present, we would not know what to do if we found them.

All bones in the body can become damaged by breast cancer cells. The most common locations are the spine, the ribs, the pelvic bones, the skull and the upper part of the legs. It is uncommon to see metastases to the bones of the face, hands, feet and lower bones of the arms and the legs. The problems caused by bone metastases are pain, fractures, spinal cord compressions, elevated calcium levels, and if there is a lot of involvement of the bone marrow, one can see low blood counts. There are occasions when bone metastases are first noted on a scan, but most often, the patient presents with symptoms.

It is rare to have only one bone involved. More often, several bones are affected. For this reason, if one suspects bone metastases, all of the bones need to be scanned. Often, especially in patients with hormone positive breast cancer, the bones may be the only organ involved with tumor. At other times, bone involvement will be part of a more general process where other organs will also be involved. If at all technically possible, when bone metastases are suspected, a biopsy should be done to verify that one is dealing with breast cancer. This step may not be necessary if the metastatic process has been previously documented. If other

organs are simultaneously involved, other sites may be technically easier to biopsy. Hormonal receptor and HER2 analysis should be performed, though these measurements may be less reliable when performed on bone.

The treatment of bone metastases follows the same basic principles as are used to treat metastatic disease in other parts of the body. (Please refer to the August 2012 to January 2013 issues of this journal for review of the principles of the management of metastatic breast cancer.) One must promptly determine whether there are existing or impending complications that require immediate attention and simultaneously plan for systemic treatment. For example, spinal cord compression or certain bone fractures may require immediate surgery. Radiation therapy may be needed to reduce pain or prevent fractures. Hypercalcemia (elevated calcium level) may require hospitalization and specific management. The systemic treatment options that are considered include the usual categories of drug therapy; specifically, hormonal therapy, HER2 directed therapy and chemotherapy.

There is one additional treatment that is also considered as an adjunct to all the other therapies when bone metastases are present. These are agents that assist the bones to heal and also reduce further damage to the bones from the progressive breast cancer process. There are two classes of drugs available for this purpose. They are the bisphosphonates (Aredia and Zometa) and the RANKL inhibitor denosumab (Xgeva). We will discuss these agents in greater details in a future issue.

QUESTIONS & ANSWERS

(Q) Dr. Martino, I was treated for breast cancer 2 years ago. I now take Arimidex. I have moved and I now have a new doctor. My original oncologist who treated me did scans and tumor

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QUESTIONS AND ANSWERS continued

markers to check if the tumor was coming back. My problem is that the new doctor refused to do them. She told me that there are guidelines that say not to do them. I don't understand this. If I still have a chance that I will recur, is it not better to keep a close watch on me with scans and tumor markers as my original oncologist was doing?

(A) Since you are on Arimidex, I am making the assumption that your breast cancer was hormone positive (estrogen and/or progesterone positive). I am also making the assumption that you have not had a tumor recurrence since your original diagnosis two years ago. If so, then you are being watched to see if you will have a recurrence at some point in the future. It is logical to assume that doing scans and tumor markers on a regular basis will identify a recurrence earlier than if you did not do them. However, it has not been demonstrated by research studies that doing this allows one to find a recurrence early enough that it translates into a longer survival. It is, for this reason, that certain Medical Associations like the American Society of Clinical Oncology (ASCO) have recommended that these tests not be done on a routine basis but rather that they be done only if you experience a symptom that suggests a recurrence. Additionally, it has been found that doing these tests routinely results in extra tests and procedures that, at times, cause harm. There is also a cost involved with all of this.

Though it is true that occasionally doing tumor markers and routine scans will find a recurrence that was not suspected, most recurrences are not found by routine procedures. Rather, they are found by symptom that you, as the patient, note and bring to the attention of your doctor. Examinations of the breasts with mammography or MRI, however, should be done on a scheduled basis. Bone density measurements should also be done at regular intervals.

(Q) Dr. Martino, I have had breast cancer and I was tested and found to have a positive gene for breast cancer. I know that

this places all of my sisters and my two daughters at risk. The problem is that when I try to talk to them about this, several of my sisters and my youngest daughter don't want to know about it. I have tried several times but I get the same treatment. I am trying to help them, but I don't know what else to do.

(A) You mention that you have several sisters and two daughters. You do not state whether you also have brothers or sons. If you do, please recognize that they and their children may also carry the same gene and also need to be informed. I often find that many presume that these genes only affect the women in a family and not the men. That is not correct.

I understand your dilemma that not all of your sisters and that one of your daughters do not want to know about the genetic testing results. I have seen this many times with my own patients. You do have the responsibility to make each of them aware of your positive results and the fact that they may also have inherited the same pattern. You may also choose to offer them a copy of your results which may be helpful when they do choose to be tested. You may want to hide your name from the report. All you can do is make the information available to them. They each have the right to accept your offer or not. In my experience, some people never want to know this type of information. Others may not be ready the first or second time that you try to offer it to them but will change their mind and act on the information at a later time. Don't give up, but also don't push them. Be available to them as they are likely to change their mind as time passes.

FUNDRAISERS AND FRIENDRAISERS

BY NICK BELARDO

ADMINISTRATIVE DIRECTOR

THE ANGELES CLINIC FOUNDATION

Last month was a great month to raise awareness. October is

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PREVIOUS ISSUES

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FUNDRAISERS continued

nationally known as Breast Cancer Awareness Month, and The Angeles Clinic Foundation and friends worked hard to raise money towards research and to raise awareness in those not well informed on how staying ahead of one's health can save lives. Through FUNDRAISERS and FRIENDRAISER, many people had the opportunity to give back to The Angeles Clinic Foundation, and to learn how vital it is to be preventative about one's breast health.

On October 10th, 2013, Rebound Furniture hosted the PERFECT 10 FUNDRAISER, which was an absolute success; raising thousands of dollars for Breast Cancer. The owner of the store, Jeannie, a breast cancer survivor, opened her doors and turned Rebound Furniture into a great party. Not short of boutique shopping, food trucks, poker tournaments and more, The Perfect 10 Fundraiser raised thousands of dollars to benefit The Angeles Clinic Foundation's efforts in breast cancer research and education. Dr. Cathie Chung from The Angeles Clinic (Jeannie's oncologist) was on site to witness the amazing effort and to interact with guests, answering questions regarding the topic of breast cancer.

On October 25th, 2013, The Angeles Clinic Foundation's male models took to the streets of The Original Farmers Market to charm their way into the ears and hearts of many people at the MANOGRAMS for MAMMOGRAMS event. What most thought was merely a chance to take a picture with a handsome model, actually turned out to be one of the most important health conversations one could have. Our models looked the part, but more so, they knew the importance of mammography and early detection. President & CEO of The Angeles Clinic, Dr. Lawrence Piro was also on site to further educate and inspire guests. Through his experience as an oncologist and television personality, Dr. Piro has an amazing way to not only offer information, but to motivate one to take it with them further down the road and take action. With many guests photographed and spoken to, The Angeles Clinic Foundation feels proud to have

spread the word that mammography saves lives.

Breast cancer is just one cancer that needs to be exploited so that fewer lives are lost. The Angeles Clinic Foundation continues to honor those who have cancer, are in survivorship and those who have lost their life to cancer by continuing to educate the public, research the cure and support the community in learning about all aspects of health. With amazing establishments like Rebound Furniture hosting parties, and the support of events like the Manograms for Mammograms, The Angeles Clinic Foundation will continue to trail blaze in making early detection and cancer prevention a banner topic heard all over. We appreciate the support of everyone, and support you in finding ways to give back. If you have an event idea, or are interested in getting involved, please contact me, Nick Belardo, at 310.582.7909 or at nbelardo@TheAngelesClinic.org.



More pictures from the Manograms for Mammograms event located on our website, www.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.

GUEST WRITER

For many of us, one of the greatest joys of life is watching students and younger colleagues grow and mature into successful and prominent members of our profession. I have been blessed during my careers to have had this opportunity many times. It has been said that we all stand on the shoulders of others. This is certainly true. We are all part of a chain. We look to those that follow to be more advanced than we are and to move the field of medicine to a higher level.

I recently met a young student who came to speak with me about his desire to become a physician and the choices that are available to him. He is presently involved in research on circulating tumor cells. I asked him to provide some insight into this field. I hope you enjoy his article on this topic as much as I did.

Circulating Tumor Cells and Cancer

BY JAKE LICHTERMAN

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Introduction

Solid tumors are responsible for most new cancers in industrialized countries. A typical solid tumor is composed of millions of cancerous cells that contain individual mutation profiles that are driving them to proliferate and invade the tissue in which they reside. However, not all of these cells stay localized. Some of these cells, termed circulating tumor cells (CTCs), break off from the tumor site and enter the circulation. It is believed that these cells represent the seeds of metastasis, able to form new tumors at distant sites throughout the body. This makes CTCs a rare source of insight into the biology of a patient's cancer, which can potentially guide clinical decision-making and detect the spread of a cancer far earlier than any of the available high resolution

imaging technologies in current use. The biological information (DNA, RNA, and protein) contained within CTCs, can also provide valuable information into the biology of cancer needed to develop new biomarkers and therapies.

CTCs: A Difficult History

Circulating tumor cells were first noted in the peripheral blood of patients in 1869, but due to their extremely low abundance in the bloodstream (1-100 CTCs per billions of cells in a teaspoon of blood) scientists have been unable to isolate and study them until about ten years ago. The recent resurgence in CTC studies is due in large part to the emergence of amazing new technologies that have allowed for the isolation of CTCs from human blood samples. Many different approaches have been taken to isolate these cells; but as of yet, only one method has been FDA-approved to monitor disease status in cancer patients. This platform, CellSearch, relies upon antibodies against epithelial cell adhesion molecule (EpCAM), a protein that sticks out of the membranes of some CTCs, but not healthy blood cells. This platform uses 7.5ml of blood, which runs through a machine with magnetic beads coated with EpCAM antibodies, thereby selectively isolating these cells using a magnetic field. Then the CTCs are differentiated from immune cells using a standard immunostaining technique for a CTC marker (CK) and a white blood cell marker (CD45). The FDA approval of this technology opened the door for physicians to try and utilize CTC number as a biomarker. Physicians use biomarkers for diagnostic, prognostic, and disease monitoring purposes. CTCs represent the unmet need for a biomarker that can more accurately predict response to systemic therapy in real time.

Clinical utility of CTCs

At the present, physicians rely upon advanced imaging technologies and unreliable biomarkers (i.e. prostate specific antigen (PSA) in prostate cancer or CA 27-29 marker in breast

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GUEST WRITER continued

cancer) to estimate whether a therapy is effective and to monitor the progression of the disease. However, in the past decade, CTC number has emerged as a more reliable biomarker. CTC enumeration (using the CellSearch system) as a biomarker has been extensively evaluated in the context of controlled clinical trials. In 2004, a phase III trial concluded that in metastatic breast cancer patients, the number of CTCs present before and during therapy was an independent and significant predictor of both progression free survival and overall survival. This means that those patients with fewer CTCs lived longer than those with more CTCs. CTC number has also been qualified in a number of clinical trials in metastatic breast, colorectal, melanoma, lung, and prostate cancer patients. CTC number, while a promising biomarker, is limited by the fact that not all CTCs are detectable via the current technologies and that not all CTCs have been shown to have metastatic potential. Therefore, scientists have started looking inside CTCs to discover biomarkers that can better reflect the status of disease.

Beyond CTC Number - The future of CTCs and Cancer

Instead, it is necessary to obtain valuable genomic (DNA), transcriptomic (RNA), and proteomic (protein) signatures from the CTCs to design novel biomarkers that are able to accurately predict the aggressiveness of a patient's cancer and their response to systemic therapy. The characterization of these CTCs to discover these new biomarkers can be obtained via a "liquid biopsy." A "liquid biopsy" is a substitute for the conventional tissue biopsy, which is a procedure to procure a tissue sample from a patient's primary or metastatic tumor. On the other hand, a "liquid biopsy" involves nothing more than a simple blood test and is able to more accurately monitor the disease in real-time without the need for an invasive surgical procedure. This is incredibly important in that a successful "liquid biopsy" could provide physicians with updated information on the status of a patient's disease and

would guide them in personalizing treatments for each patient. CTCs, if shown to contain relevant biological information, can be captured from the blood and can be the source of information for a successful "liquid biopsy." Recently, advanced technologies, including the NanoVelcro CTC Chip developed at UCLA/Cedars Sinai in Los Angeles, have shown that they are able to capture and perform whole genome, whole exome, and RNA sequencing on CTCs. This technological innovation will pave the way for the realization of personalized medicine if true liquid biopsies are able to accurately monitor disease progression in an individual and help guide treatment selection based on a patient's unique biological information.

Conclusion

The potential of CTCs in the clinic is clear. CTC number has already been shown to be prognostically significant in a variety of different cancers. Yet, simple enumeration of CTCs without utilization of the precious biological information they contain will mean that the promise of CTCs will never be fully realized. Utilizing advanced technologies, such as the NanoVelcro CTC Chip, to fully characterize these cells will ultimately determine the clinical and biological significance of CTCs as both biomarkers and therapeutic targets.

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