

Breast Cancer Advisor

BY DR. SILVANA MARTINO

October 2013



Dear Readers,

October is Breast Cancer Awareness Month. For those of you who have had breast cancer, this month may not appear to be different. Yet, it is different. It is the month where each of us must turn to our families, our friends, our neighbors and co-workers

and educate them on the value of personal vigilance and early diagnosis. It is also, the month to be sure that we let other women know of the progress that is being made in the treatment and cure of breast cancer. Please take the opportunity to influence others.

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

CONTENTS

BIOLOGY BASICS

METASTASES TO THE HEART 1

WHAT'S NEW

MEETING UPDATE 2

PERJETA APPROVED AS NEOADJUVANT

THERAPY 4

GUEST WRITER

THE SOUND OF PINK

BY DAWN YOUNANI 6

BIOLOGY BASICS

METASTASES TO THE HEART

Involvement of the heart by breast cancer metastases is infrequent. It is rarely seen as a first site of metastasis or as the sole site. It is more likely to be part of a generalized process seen with advanced disease. The heart muscle, or the interior of the heart chambers, is a possible location of tumor metastasis from breast cancer, but by far the most frequent manifestation of heart related metastasis is the development of a pericardial effusion (fluid around the outside of the heart).

To picture the location of this fluid, consider the heart as a non-spherical ball that is surrounded by a sack. The fluid is positioned between the heart and its surrounding sack-like enclosure. As fluid accumulates, the sack will expand to accommodate the fluid. At some point, enough fluid is formed that the sack cannot

continued next page

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

expand adequately and the fluid will start to apply pressure on the heart itself. As this process continues, the heart will reach a point where it cannot function properly. Circulation of blood through the body and lungs will be restricted. If the accumulation of pericardial fluid is gradual, the heart has a better opportunity to adapt and try to compensate. If the accumulation of fluid is rapid, deterioration will occur more quickly and become an emergency (cardiac tamponade).

At times, the recognition of a pericardial effusion occurs by doing a chest x-ray or a CT scan. The patient may be completely asymptomatic. Most often it is symptoms that lead to the diagnosis of a pericardial effusion.

Typical symptoms of pericardial effusion include shortness of breath, especially on exertion, cough, chest pain or a feeling of chest discomfort, fever and swelling of the legs. Some patients will experience vague discomforts that may be hard to describe. At times, a feeling of weakness and tiredness may be noted without more specific complaints. Since many of these symptoms can be caused by progressive tumor in other parts of the body, it may not be apparent that pericardial effusion is the underlying problem. Often, pericardial effusion is seen in conjunction with pleural effusion (fluid around the lungs). If the pleural effusion is corrected, but shortness of breath persists, an undiagnosed pericardial effusion should be considered.

When a pericardial effusion is suspected, an echocardiogram is performed to confirm the diagnosis, describe its size and give information about heart function. A small amount of effusion that does not cause symptoms and may have been diagnosed incidentally can, at times, simply be observed closely and not immediately removed. If the effusion is more than minimal in

quantity or is causing symptoms, treatment is required. The goals of treatment are to relieve symptoms, to identify the cause of the effusion and to prevent the re-accumulation of the fluid. A sample of fluid is analyzed to look for cancer cells and to rule out other causes of pericardial effusion such as infection. Cancer cells are identified only 50 to 60 % of the time. Analysis of a portion of the pericardium (the sac that encloses the heart) will increase this number, but, even so, one does not always find tumor cells.

Treatment of pericardial effusion can be considered in two stages. The first is the removal of fluid using a needle. This will quickly improve symptoms. The second is considering a procedure that will reduce the likelihood that the fluid will re-accumulate. This can be done by removing a portion of the pericardial sac, a process often termed a “pericardial window.” One can also introduce an irritating agent into the pericardial space between the heart and the remaining pericardium to try and close off that space. In addition, and importantly, one must use anticancer therapy to obtain control of the underlying cancer process.

WHAT'S NEW**MEETING UPDATE**

I recently attended the Tenth Main Meeting of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) in Oxford, England. This group was first organized in 1983 and led by Sir Richard Peto who continues to guide the process. The purpose of this collaboration has been to obtain data on all randomized clinical trials performed worldwide in early breast cancer and to analyze the data in a collective manner. It requires much coordination, cooperation and sharing of data.

The information provided to the process is actual data at multiple

continued page 4

THANK YOU

We wish to extend our sincere gratitude to the staff of REBOUND for their successful fundraising event on behalf of The Angeles Clinic Foundation!

TheAngelesClinic
FOUNDATION



In honor of National Breast Cancer Awareness Month
The Angeles Clinic Foundation presents...

The Breast Cancer Photo Booth

Friday, October 25th 2013

11am - 4pm

at The Original Farmers Market at the Grove
6333 W. 3rd Street Los Angeles CA 90036

spreading awareness of the value of mammography
in the fight against breast cancer

Join the fight.



www.theangelesclinicfoundation.org



WHAT'S NEW continued

time points from patients in each study. This does not mean a summary report, but actual detailed and updated information about each participant. New studies are added to the process. Old studies are continued and updated. They are not eliminated and replaced. Therefore, each year the number of patients followed and the amount of data obtained continues to increase. This is a considerable task. The complexity of the process continues to evolve and multiply. A total of 205 research groups now contribute data on 444 research trials. In my estimation, the value of the published results that are the final product of this effort continues to increase with time.

The original management and analysis of the data was originally in the hands of Sir Richard Peto and a group of statisticians from Oxford University. The process was changed about ten years ago when many clinicians assumed a larger part of the responsibility. Various committees were established to oversee portions of the data and prepare various publications. Much of the work takes place between the meetings of the full group.

The recent three day meeting was dedicated primarily to decision making and discussion on how to proceed on various problems. One critical issue discussed is the fact that most trials, especially in the U.S., do not follow patients long term. Follow up is often ended at 10 or 15 years. Research studies are rarely funded to continue beyond that point. Consequently, long term comparisons between treatments as well as long term toxicities are not available. We need to convince funding agencies that such follow up is critical and must be considered in designing trials.

Another issue that received considerable attention was that of cardiac dysfunction from radiation, chemotherapy and HER2-directed therapy. Cardiologists have now been added to the group to assist with this issue. The use of bisphosphonate drugs in the adjuvant setting is a new topic that will be analyzed as will

the results of neoadjuvant (giving drugs pre-surgery) therapy that is now an increasing treatment approach for early breast cancer. Also, we will be evaluating data on obesity and its relationship to breast cancer outcome. And lastly, high dose therapies versus standard dose therapies will be analyzed.

We have recognized for decades that few studies include women that are age 70 and above. Though this age group is at highest risk for breast cancer, there are minimal data that inform us on outcome and toxicities experienced by this population. Consequently, the manner in which this age group is treated is extrapolated from younger cohorts. A sub group has now been formed to address this major shortcoming of the research process.

Up until this point, the EBCTCG has limited its interest to treatment trials in early breast cancer. A decision was made at the last meeting to now begin to look at screening trials and their outcomes. This will be an entirely new area for the EBCTCG to consider.

Some physicians and researchers remain critical of the meta-analysis process used by the EBCTCG. They favor conclusions reached by single, well conducted, randomized trials. Though I sympathize with their thinking, and have conducted many such trials myself, I believe that in many ways the process of the EBCTCG and its conclusions are more applicable to the general population. The narrowness of a specific trial limits its findings to a specific and highly selected population. It does not fit most patients and the results cannot be as easily generalized. The meta-analysis encompasses many more patients and therapies, and I believe it to be a much more generalizable and realistic set of conclusions that can be applied to the treatment of women everywhere.

PERJETA APPROVED AS NEOADJUVANT THERAPY

An important step was recently taken by the Food and Drug Administration (FDA). It gave accelerated approval to the use of pertuzumab (Perjeta), trastuzumab (Herceptin) and chemotherapy

continued next page

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.

WHAT'S NEW continued

in the neoadjuvant setting. This was not a simple or quick decision. Much preparation has gone into this novel approach.

The concept of pre-surgical or neoadjuvant drug therapy had its origins in the management of locally advanced and inflammatory breast cancer. These are cancers where trying to do surgery first resulted in positive margins and a high rate of local recurrence. Even the addition of post-operative radiation did not result in adequate control. Giving chemotherapy first resulted in some degree of tumor shrinkage allowing a more effective surgery for most patients. As we moved from performing mastectomies to the concept of breast preservation via a lumpectomy and radiation, it became apparent that there were still women whose tumors were large enough that a lumpectomy was not feasible. The concept of neoadjuvant chemotherapy was extended to this situation. Could we make more women candidates for lumpectomy if we reduced the size of their tumor by giving chemotherapy before surgery? The answer to this question was affirmative. Neoadjuvant therapy increased the number of women who could have breast sparing surgery. This was a step forward.

During this period, an additional important observation was made. In some women, the tumor shrank to such a degree that when surgery was done, essentially no tumor remained. This was termed a pathological complete response (pCR). It was further observed, that patients who achieved a pCR had a particularly good long term prognosis. This observation was confirmed many times. This is particularly true in tumors that appear more aggressive such as triple negative and HER2 positive cancers. Achieving a pCR has now become the major goal of neoadjuvant therapy.

The next step was deciding whether achieving a pCR was a good enough predictor of long term outcome, such as time-to-first-recurrence and survival. This question is not completely resolved but most clinicians and researchers believe that the

final answer will be, "yes." The ensuing step was whether there existed enough data in support of this relationship that we could actually change how we do research studies when evaluating different drug therapies. Why was this important? Primarily so that we could shorten the time for drug approval. Traditional adjuvant trials, where drug therapy is given after surgery, and where the endpoints are the number and time to first recurrence and survival take thousands of patients that must be followed for years before a therapy is declared to be a success or not. In the neoadjuvant setting, where pCR rate is the objective, the number of women needed to declare a therapy to be a winner is only a few hundred and they only have to be observed for a few months.

In May 2012, the FDA, in recognition of the preceding information, issued a statement supporting the use of pathologic complete response data as an endpoint to achieving accelerated approval for new therapies. The first such approval was given on September 30, 2013 to the use of Perjeta, Herceptin and chemotherapy.

Approval was based on a randomized, multicenter, open-label neoadjuvant study that included 417 participants who were randomly assigned to one of four treatment groups: (1) trastuzumab plus docetaxel (Taxotere), (2) Perjeta plus trastuzumab and docetaxel, (3) Perjeta plus trastuzumab or (4) Perjeta plus docetaxel. Seventy percent of the patients had node positive disease. Thirty two percent had locally advanced disease. Only seven percent had inflammatory breast cancer. Forty seven percent had hormone positive tumors. The number of women who achieved a pCR was highest (39%) in the group that received all three drugs and was 21% in the group that received only Herceptin and Taxotere without Perjeta. The lowest value was seen in those who received the Herceptin and Perjeta without chemotherapy suggesting that the chemotherapy is a key ingredient.

The most common side effects were hair loss, diarrhea, nausea and low white cell count. Cardiac dysfunction was also noted.

continued next page

HOW TO RECEIVE FUTURE ISSUES

You may request future issues of this newsletter by e-mailing your request to:

smartino@theangelesclinicfoundation.org

WHAT'S NEW continued

The combination of Perjeta, Herceptin and chemotherapy was previously approved in the treatment of metastatic breast cancer and is in common use. That this combination is good therapy when given in the pre-operative setting is not surprising. The point not to be missed in this recent FDA approval is that the approval was based on a limited number of patients who achieved a pCR when treated in the neoadjuvant setting. This is a clear change in how we have done things during the past three decades and will alter the design of most, if not all, future studies in early breast cancer.

GUEST WRITER

Several months ago, after returning from a trip, I walked into my office and found a large package. With it was a note lovingly written by two of my patients informing me that the package was a gift created by the daughter of one of them. I unwrapped it, stood back, looked at it and understood. It represented not only artistic skill, but it was the product of personal experience. It combined beauty, elegance, sadness and strength all into one. I recognize this combination. I have seen it many times in my patients.

As the artist was the daughter of one of my patients, I was again reminded that a diagnosis of cancer has an effect on each member of a family. I asked my two patients if I could include the picture in the Breast Cancer Advisor and if they would contribute their thoughts on the effect that their breast cancer diagnosis has had on their children. The entry that follows is their experience.

THE SOUND OF PINK

BY DAWN YOUNANI

As a grown-up, hearing the words, “you have breast cancer,” are amongst the hardest words one will ever hear. I remember

watching the lips of my own doctor as she spoke those words, later realizing that I heard nothing after the word “cancer,” lost in a state of limbo, paralyzed with fear and wondering if I would see my own two children grow up. During the ensuing months my boys would see their mommy lose her hair, sleep a little more often, and eat a little bit less. I often wondered what they thought of this new reality or how much they really understood. “Do they see the changes taking place?” They would come home from school, immerse themselves in homework, and bring down their usually rambunctious behavior to a mere decibel of what had been. When I tried to talk to them, my own words were met with those that would be quite expected out of the mouths of young children. They just didn’t want to talk about it.

I was lucky. I had a wonderful husband, a sister who had been through breast cancer herself just four years prior, and a lifelong, dear friend, Katy, who had been diagnosed with breast cancer long ago, and then again several years later. I sought solace in the knowledge that both were able to give – in my sister I found a rock and an advocate and in Katy, a mom who had the same questions and concerns as I did. What did our children think and how much did they really understand?

It would not be until years later that our questions would be answered, following a recurrence of Katy’s cancer. Her daughter, Jhanna Veadov, now a 21-year-old university art major, created this beautiful pencil drawing, “The Sound of Pink.” From the memories of a young girl, the unanswered questions, the feelings of loss, and the sound of her mother’s silent tears as she cried softly into her pillow each night, would come this special piece of artwork, born out of pure and raw emotion. While the pink ribbon itself has become a world-recognized symbol in the fight for a cure, The Sound of Pink brought forth the words of a young child that for

*continued next page***YOUR SUPPORT**

The **Breast Cancer Advisor** newsletter is funded by donors like you.

Help us keep the content pure, with no outside influence, by donating to The Angeles Clinic Foundation.

Make a donation directly online by clicking

[Donate Now](#)

or mail to: The Angeles Clinic Foundation, 2001 Santa Monica Blvd., #560W, Santa Monica CA, 90404

Your gift to The Angeles Clinic Foundation is fully tax deductible.

MEETING REVIEW continued

years had remained unspoken.

The passion of this picture led both Katy and I to the answers that we often asked when our children were young. We learned that at just five-years-old, our children's thoughts were real. For Jhanna, she was all too aware of the changes taking place in her own life and found solace in her art, while mine found solace in the written word. What had once been a blank page for Jhanna filled with stick figures, trees, and clouds, soon became pictures of hope filled with rainbows, sunny skies and colors that would move on to express families that grew together and stronger. Out of the hands and minds of a young girl, Jhanna would sit by her mother's side and draw, finding that just being close was where she found her strength and where a young girl's dream would become a reality and a child would become an artist. Now, as an art major, Jhanna continues to tell her life's stories through the arts – whether it be oils, clay, or any of the fine art mediums.

It is often said that our children find their own way through the challenges their parents face. As the years passed and Katy has continued to be in and out of treatment, Jhanna's stick figures and finger painting have grown into the work of a talented young artist, a woman whose artful dreams were born out of hope.

The Sound of Pink continues to receive recognition from many different organizations across the United States and the spirit of Jhanna's work represents the encompassing emotions that one feels with a breast cancer diagnosis. Unable to speak upon hearing the words, the tears that follow, and the hold that grasps us so tightly that we can't breathe, finally becomes one of floating ribbons as we move forward from the life as a patient into that of becoming a survivor.

Whether young or old, male or female, a parent, a sister, a brother, a friend, a husband or a wife, while the words themselves are the hardest we will ever hear, Jhanna has shown through her art that there is a future of hope, one which tells a story all its own. The beauty of The Sound of Pink, although created just one year ago, really began in the life and the heart of a little girl, just five-years-old as she sat beside her mother with her pencils, her paper, and a little girl's wish.



VISIT OUR WEBSITE AT

www.theangelesclinicfoundation.org

or call us at (310) 582-7909