

Dear Readers,

This month we, in the U.S., celebrate the feast of Thanksgiving. Like many of our holidays, it has become commercialized. Nevertheless, its basic intent is to recognize the many wonderful things that are part of our lives and reminding us to be grateful. You, my readers, are a wonderful part of my life, and I am grateful for each of you. I wish all of you a joyous holiday.

Best Regards,
Dr. Silvana Martino



Breast Cancer Advisor

BY DR. SILVANA MARTINO • November 2012

BIOLOGY BASICS

In this issue, I will continue to discuss the management of metastatic breast cancer. I will focus on the use of chemotherapy drugs. There are several classes of chemotherapy drugs. They are generally classified based on how they interfere with a cell's ability to replicate. Most chemotherapy drugs are formulated to be given directly into the blood. A few are available as tablets to be taken by mouth. There is a general desire to make more drugs available as tablets in the future. Chemotherapy drugs work by different mechanisms, have different schedules of how they are to be given, and vary in the side effects that they cause.

Not all chemotherapy drugs work against all types of cancers. You can think of this like the use of antibiotics. You have to match the correct antibiotic to the specific bacteria causing the infection. Likewise, when dealing with breast cancer, there are chemotherapies that have been shown to work and others that have not and are not used.

In metastatic breast cancer, chemotherapy is used for tumors that are hormone receptor negative (estrogen and progesterone receptor negative). However, even tumors that are hormone positive

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The Angeles Clinic FOUNDATION

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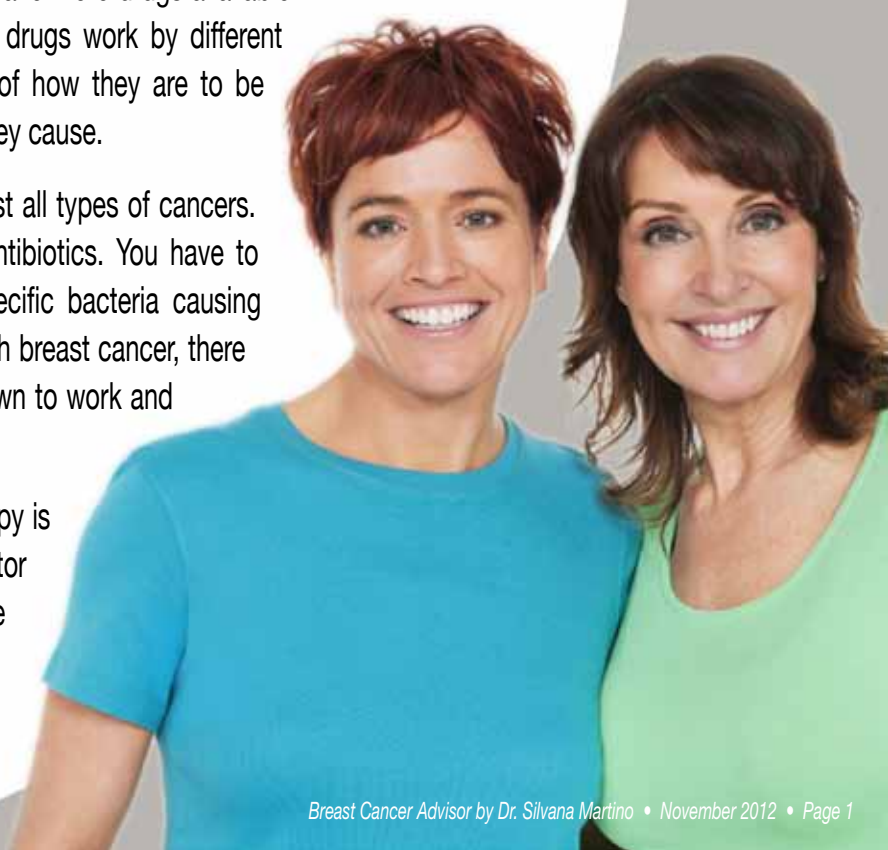
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Biology Basics continued

do not always respond to hormones. In those situations, chemotherapy is used. Even in tumors that are receptor positive and initially respond to hormonal therapy, a point is always reached when the tumor stops responding to hormones and chemotherapy is needed. All tumors that appear very aggressive are treated with chemotherapy irrespective of other features.

Breast cancers that are HER2-positive are also treated most often with a combination of chemotherapy and HER2 directed therapy. I will discuss this further in the next issue.

In choosing which chemotherapy to use, one must know whether a person previously received chemotherapy at the time of their original diagnosis (adjuvant chemotherapy). This information is particularly important for the drug Adriamycin since it has the ability to damage the heart. This specific risk is related to the total amount of Adriamycin that a person has received over their life time irrespective of when they received the drug. In addition, one prefers not to reuse the same drugs that had been used before especially if only a short time has elapsed since those drugs were



given. The assumption is that if a tumor recurred within 6 months from when the drugs were used as adjuvant therapy, the tumor is unlikely to respond to them later. If it has been a minimum of six months and preferably one year, then one can consider reusing the same chemotherapy.

The order in which chemotherapy is chosen is primarily based on the level of antitumor activity demonstrated in research studies for the various chemotherapy drugs. Those with the highest activity are used first. The expected side effects of a drug are also considered in making decisions. One must assess which side effects an individual may tolerate best.

Below is a list of chemotherapy drugs that are commonly used to treat metastatic breast cancer. At times they are used as single drugs and other times they are used in combination. This decision is based on the extent and pace of disease. Combination therapies are used for disease that appears more aggressive.

Anthacyclines (Adriamycin, Doxil, Epirubicin)

Taxanes (Taxol, Taxotere, Abraxane)

Cyclophosphamide (Cytoxan)

Antimetabolites (5 FU, Xeloda, Methotrexate, Gemzar)

Platinums (Cisplatin and Carboplatin)

Mitosis inhibitors (Navelbine, Ixempra, Halaven)

Participating in research studies is always an important part of treatment. If you have the opportunity to participate in studies that are looking at new drugs, I would encourage you to participate. Not only will this provide you with additional opportunities, but realize that research is the only way that we can ensure that future treatments will be better than our present therapies and results.

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

WHAT'S NEW

1. Aspirin, Other Anti-Inflammatories, and Acetaminophen for Breast Cancer Prevention

Until breast cancer is easily cured, the best treatment is its prevention. Initial reports suggested that the use of aspirin and other anti-inflammatory drugs (NSAIDs) appeared to decrease the incidence of breast cancer. This resulted in additional attempts to look at this issue in various populations. The results have been mixed and have resulted in confusion. Dr. Xuehong Zhang and colleagues from Brigham and Women's Hospital and Harvard Medical School have recently updated results from the Nurses' Health Study (NHS). This study includes 121,700 registered female nurses in the U.S. who were ages 30 to 55 in 1976. Since then, these women have been mailed questionnaires every 2 years in order to

collect lifestyle information and history of their medical events.

Included in this population were 84,602 postmenopausal women who were free of cancer in 1980 and who have been followed for 28 years. During this period they have been questioned via questionnaire about their use of aspirin, NSAIDs, and acetaminophen. The most common reasons for using these products were headache, prevention of heart disease, arthritis, and other musculoskeletal pain. Women who reported no use of these products either at base line or at any subsequent time point were classified as "non-users." All others were classified either as current or past users based on the information they provided on periodic questionnaires. If breast cancer developed, records were obtained and reviewed.

During this period, they documented 4,734 cases of invasive breast cancer in this group of postmenopausal women. No difference in breast cancer incidence was found between non users and either current or past users with aspirin, NSAIDs, or acetaminophen.

I consider these to be important data. The Nurses' Health Study is a large and well conducted study with long term follow-up. Many insights about women's health have

No difference in breast cancer incidence was found between non users and either current or past users with aspirin, NSAIDs, or acetaminophen.

come from this population. It is unlikely that aspirin, NSAIDs, or acetaminophen have the ability to exert much influence on the initial development of breast cancer. Though they may be beneficial relative to prevention of cardiovascular disease and colon cancer, I am not persuaded that they prevent breast cancer.

Reference: Zhang X, Smith-Warner S, Collins L, Rosner B, Willett W, Hankinson S., *Journal of Clinical Oncology*, Vol.30 (28), October 1, 2012, pp3468-3477



QUESTIONS & ANSWERS

(Q) Dr. Martino, I am on tamoxifen but I have strictures of the esophagus so I have a hard time swallowing the pills. Can I crush them?

(A) If you are unable to swallow the tamoxifen tablets you may want to consider taking the liquid form of tamoxifen which is available under the name of Soltamox. You should use the same dose as your tablets.

(Q) Dr. Martino, I have heard that the drug Arimidex is not as good in women who are overweight. Is this true? Should I be on a different drug or a different dose?

(A) Since you are on Arimidex, I am assuming that you are postmenopausal. In general, there is a relationship between your weight and your estrogen levels. This is

often measured by the body-mass index, which is a mathematical calculation of your overall size. Women who are lean have a lower estrogen level than women who are overweight. In treating hormone receptor positive breast cancers with hormonal therapy, the goal is to reduce estrogen level. The level is never actually reduced to zero. From small studies, it appears that drugs such as Arimidex and Femara do not reduce the measured estrogen levels to the same degree in women who are obese as in lean women. This raises the question of whether this will result in a lesser degree of effectiveness in women who are overweight. At this point, we do not know that these differences are biologically important. There is not enough information to prompt me to either change the dose or change to another drug. One additional bit of data is worth noting. In general, the drug Femara reduces estrogen levels to a greater degree than does Arimidex. Whether overweight women might do better with Femara is also unclear at this point.

E-mail your questions to:

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BOOK REVIEW

It has been clear to me for a long time that cancer is not exclusively a personal event; rather, it affects all those around you who are aware of the diagnosis. In my personal experience, the people around the patient often have a very difficult time. They don't know what to say or what to do. Should they pretend as if nothing is wrong or should they now treat you as a complete invalid? Often, their solution is to stay away and avoid you, simply because they are afraid of doing or saying the wrong thing. I generally explain this dilemma to my patients and advise them that they need to take on the role of helping others be comfortable around them.

A book has recently been published that speaks specifically to this issue. It is entitled THE BEST FRIEND'S GUIDE TO BREAST CANCER by Sonja L. Faulkner, Ph.D. Dr. Faulkner is a breast cancer survivor and writes from personal experience which is very obvious in every



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Book Review continued

chapter of this excellent book. The book is divided into various phases of the breast cancer experience. It provides some information about the disease itself and the various decisions that are made as one plans therapy. It provides very practical insights into the patient's experience. It then guides the "best friends" about do's and don'ts. I found these sections particularly valuable as knowing what not to do and what not to say is as important as what to do and what to say. Comments from other survivors add to the wisdom found in this book. The book is well written, easy to read, and above all it is practical. No doubt, many of you will see your own experience resonate in its pages. Encourage your family and friends to read it. Both you and they will benefit from the experience.

An interview of the author follows.

Dr. Sonja L. Faulkner, shown pictured with her son.



AUTHOR INTERVIEW

SONJA L. FAULKNER, PhD

AUTHOR OF THE BEST FRIEND'S GUIDE TO BREAST CANCER

Dr. Martino: The material in your book makes it clear that you have personal experience with breast cancer. Can you summarize the types of therapies you received and how far from your diagnosis you were when you started to write the book?

Sonja Faulkner: I had a lumpectomy, then a double mastectomy and reconstruction, followed by six rounds of chemotherapy. I'm currently taking tamoxifen for five years, and when done, will switch to an aromatase inhibitor for five years. I wrote the book almost a year after completing treatment.

Dr. Martino: Many have chosen to write about their own personal emotions and experiences with breast cancer, but you chose to write to those who surround the patient. What motivated you to do this?

Sonja: I was intrigued by the wide range of responses I encountered during my illness. For the most part, people took my breath away with their support and kindness, including those I hadn't been in touch with for years and even some I didn't know well. At the other end of the spectrum were some friends I had known for years and years who never reached out to me once—not one phone call, card, email, or letter saying, "I'm thinking of you" or "Hang in there." It was confusing, so I decided to write a one-stop resource to coach friends and loved ones through all phases of a breast cancer illness.

Dr. Martino: Do you think people have a hard time when they have a family member, friend or colleagues with breast cancer? What are their issues?

Sonja: I think it depends on the person. Some people aren't wired to step up in a crisis, whereas others shine. Perhaps the biggest stumbling block is not knowing what to say or do. If you're close to a woman who's been diagnosed, there are other, more serious issues to contend with, such as watching someone you love get sick and dealing with those moments when she's feeling discouraged or depressed. Of course, the biggest source of stress for close friends and family members is the fear of losing their loved one.

Dr. Martino: How important are other people when you have a diagnosis of breast cancer?

Sonja: The message of the book is that the healing power of social support is truly extraordinary, so in my opinion,

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Author Interview continued

it's a critical piece of the puzzle in getting well. It makes the journey lighter and more manageable if you allow those around you to help and support you.

Dr. Martino: What do other people do that is useful?

Sonja: Reaching out and expressing support uplifts and sustains us during this scary, difficult time. The “I’m here for you” and “You won’t have to face your illness alone” messages give us much-needed strength to forge ahead on our cancer journey. It may seem like a simple, insignificant thing to do, but it’s actually profound.

Also, help with “logistics”—the mundane, nitty gritty of life, such as housework, yard work, cooking, grocery shopping, taking care of children or pets, and running errands is wonderful. Activities that make us feel normal are real treats, too. These include going to dinner, a movie, comedy club, or concert, or getting a massage, pedicure, or manicure. A simple drive is a great escape, too.

Dr. Martino: What do people do that is not useful?

Sonja: It’s difficult to hear things like, “It could be worse,” “Be grateful that it’s not x,” “None of us knows how long we have,” and “Just be positive.” Although well-intentioned, each of these comes across as extremely flippant and dismissive. Once we move into the recovery phase, it’s annoying to hear, “Now that that’s all over with, you can get on with your life.” People should know that it’s never really over for us because of endless doctors’ appointments, fear of recurrence, and the pesky, long-term side effects

that we must deal with daily.

Dr. Martino: Do your relationships change when you have a diagnosis of breast cancer?

Sonja: I think they get stronger or weaker, but they don’t stay the same. The people who touch your heart with their kindness and support either surprise you in a very pleasant way, or reinforce why they’re special to you. But then there are those who don’t reach out to you when you need them the most, and it’s likely to weaken the relationship. The important point to make, though, is that it’s never too late to let someone know that you’re thinking of her and wishing her well.

Dr. Martino: Thank you.

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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