Dear Readers,

Though it is not my habit to make New Year resolutions, each January I am inspired. I feel that a new page has been turned. There is a sense of a new beginning. Something in me is fresh and ready to start anew. I hope you share that feeling.

With best personal regards,
Dr. Silvana Martino

BIOLOGY BASICS

I want to continue the theme of the management of metastatic breast cancer. In the last several issues, I reviewed the three main classes of drugs that are used: specifically, hormones, chemotherapy and HER2 directed therapies. I want to now review how one decides whether a therapy is effective or not.

Once a new therapy is started, the first decision that must be made is whether the individual patient can tolerate the therapy. Side effects must be evaluated by both the patient and the doctor. Some dose adjustments (reduction) may be needed. When adjusting dose, the goal is to minimize toxicity but not reduce the dose to such a degree that it renders the therapy ineffective. This is similar to taking too low a dose of an antibiotic or pain medicine. They will not be effective and it may be best to find an alternative.

If the patient can tolerate the therapy, then the next important question is to decide if the therapy is working. This simply means that the tumor or tumors are getting smaller or at minimum are remaining the same and neither growing nor appearing in new areas of the body. How does one make this decision? It is done by measuring the size of the tumor either by...
scans or by physical exam or both. The concept is to measure the tumor when you start a therapy and then to repeat the same measurements after one has been on a certain therapy a minimum of 6-8 weeks. Ideally, the same scans that were done at the start of therapy should be re-done later. Bone scans may be a bit confusing, especially when used alone, as both the process of healing and progression of tumor may look alike.

There are blood tests that can be helpful in deciding if a therapy is working against metastatic breast cancer. They are not good enough to be used alone in place of scans or clinical measurements. Some breast cancers express a protein that can be measured in blood (the tumor markers CA 27-29, CA 15-3, or CEA). If these are elevated and decrease with treatment, they can offer the first clue that a tumor is responding. Not all tumors express these proteins, however. A second blood test that can be useful and which can also offer an early clue that a tumor is responding is the measurement of circulating tumor cells in blood (CTC’s). Again, one should measure these levels when a therapy is started so that one can properly interpret the subsequent measurements. A decrease in number of CTC’s, especially to less than 5, suggests a favorable outcome. I have found this assay particularly useful in circumstances where a patient’s disease is limited to their bones and x-rays or scans are difficult to interpret.

The other key feature in determining whether a therapy is working or not is assessing how a patient is functioning and feeling. Are their symptoms less than before? There is not always a correlation between symptom level and response to therapy. Sometimes it is only the scan that appears to be getting better but the patient is not improving. The decision to stay on therapy in such a case is difficult and requires serious consideration by both the patient and the doctor. Having a close relationship with your medical oncologist so that they are very familiar with both you and your disease is crucial to ensure that the correct decision is made.

**QUESTIONS & ANSWERS**

(Q) Dr. Martino, my mother and grandmother have had breast cancer. My mother was tested for the BRCA genes and was found to be positive for BRCA 1. Both my sister and I have also been tested. My sister is positive but I am negative. Does this mean that I do not have a risk of getting breast cancer?

(A) No, it does not mean that you do not have a risk of getting breast cancer. There are many risk factors to developing breast cancer, not just whether you carry the known breast cancer genes (BRCA 1 and 2). The simple fact that you are a female gives you a certain risk. This is why all women are at risk as long as they have any breast tissue. Getting older is the other risk that we all share. Other known risk factors are more personal and include hormonal factors, radiation exposure, breast density, body size, diet, alcohol intake, and others. We anticipate that there are other risk factors that we have yet to recognize. That you do not carry the BRCA 1 gene found in your mother does lower your risk of both breast and ovarian cancer relative to the level of being positive, but it does not guarantee that you will not develop these cancers.

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versus longer use. The larger study was from the U.S., and the smaller study was from Europe. Those results demonstrated that women treated for longer than 5 years had more side effects, especially endometrial cancers, and that they did not have less breast cancer recurrences. In fact, there was a suggestion that there might be more recurrences with longer use. The decision was not unanimous; in part, because some of us felt that there were too few node positive patients included in the two studies.

Two additional studies have continued to look at this question. They are the ATLAS and the ATOM trials. The ATLAS trial is a large international study with long term follow-up. The results from ATLAS demonstrate that there is better survival for women treated with tamoxifen for 10 years rather than 5 years. The difference is most apparent in years 10-15 from the time of starting therapy. These results will change how we practice. This information is not applicable to women who are taking aromatase inhibitor hormones. It is applicable to women with invasive breast cancer who are usually treated with tamoxifen. Therefore, it applies primarily to premenopausal women and to postmenopausal women who cannot tolerate aromatase inhibitors and are treated with tamoxifen. It does not apply to women treated for DCIS or women who have not had breast cancer but are at high risk when tamoxifen is being used as a preventive drug.

We still await mature results from the ATOM trial.

2. Faslodex: New Dose

Faslodex is an injectable (intramuscular) hormone used for metastatic, hormone positive breast cancer. For many years, its dose has been a single 250 mg injection every 28 days. Many of us were not favorably impressed with this drug as its activity seemed low. It was then concluded that its lack of activity was because it took too long at this dose for the body to build up a stable level sufficient for the cancer to be affected. To resolve this, a loading dose was introduced. That is, we would start with 500 mg on the first day, repeat that in 2 weeks and again in 2 more weeks before starting the usual dose of 250 mg every 28 days. This did appear to improve the overall activity of Faslodex.

The entire dose level then came into question. Was the dose just too low? This led to a comparison of the standard 250 mg dose versus a 500 mg dose continuously. This study was reported in San Antonio, and demonstrated that the higher dose of 500 mg every 28 days results in better survival. This is now the new standard.
3. Herceptin Adjuvant Therapy

Several Herceptin trials were updated: the U.S. Intergroup trials and the HERA and PHARE trials from Europe. A summary of the results is that there is now long term and clear evidence that the addition of Herceptin therapy in the adjuvant treatment of patients with HER2 positive breast cancer improves both the time to recurrence and overall survival rate. We also have good evidence that two years of therapy are not better than one year. There was hope that 6 months might be as good as one year of therapy, but it is not certain at this point that this shorter time period is equally as effective. Based on how the data look to me, it may ultimately turn out that 6 months may not be much worse, however. So, even though one year appears optimal, in patients who are having a difficult time tolerating Herceptin, six months may provide most of the benefit.

4. Avastin Studies Negative

Two Avastin studies were presented. Avastin is an antiangiogenesis drug that interferes with blood vessel formation as a way of trying to starve a tumor from receiving nourishment. One study was in metastatic patients who were receiving the hormone Femara. One half of them also received Avastin and the other half did not. There was no difference in outcome between the two groups. The second trial was in women with triple negative early breast cancer (BEATRICE trial). They all received chemotherapy. One half were also given Avastin. There was no difference in outcome with or without Avastin.

Though there was much excitement with this drug when it was first available and initial preliminary results were positive, these two studies further confirm that, in breast cancer, Avastin adds little benefit yet adds toxicity. This is further proof that we cannot let optimism cloud our judgment. It is not the first time that we have done that.

5. Treatment of Local-Regional Recurrence

Some patients with breast cancer will experience a recurrence limited to the breast or surrounding chest wall area. This is referred to as local-regional recurrence. Their treatment generally includes a surgical resection of the area and often a course of radiation to the area. The question has been whether they should be given chemotherapy as well. During the past 20 years there have been several attempts to study this question but without much success. We have never been able to convince enough doctors and patients to allow a randomization (like the flip of a coin) between giving chemotherapy or not in this setting. The CALOR trial was designed to answer this important question. Three research groups combined their efforts. Even so, it was a difficult trial to complete and they were unable to enroll all the patients they had planned on. In spite of this, they found a statistically significant survival advantage for the group that was randomized to receiving chemotherapy. This was particularly true for patients with hormone negative breast cancer.

Since this trial did not complete its accrual, the results are not as solid as one might wish. In my judgment, it is unlikely that any other trial will prove more successful. This is probably the best we will do with this question. However, I do consider these results important and I have a bias to treating such patients with chemotherapy, especially if their disease is estrogen and progesterone receptor negative.

6. Radiation Therapy

Radiation to the whole breast is generally given over 5-6 weeks following breast conserving surgery. At times there is also a period of 1 to 2 additional weeks during which a boost to the specific area of tumor is given. Several studies have been done designed to look at shorter time periods. Different doses have to be given to accommodate this time period. Data from the U.K. were presented that demonstrate that a three week program gives equal results and with good cosmetic outcome as well. The data presented were mature with 10 year follow-up. In Canada and England, this approach has become standard radiation therapy. It has not become a routine therapy in the U.S., however. I was impressed with these data. I think a shorter treatment period with equal results has many advantages. It is easier for patients, especially those who are older and more fragile for whom the daily routine of going for treatment is more physically demanding. Chemotherapy can be started and ended sooner. The cost will be less.
Meryl Wecksler
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In the October 2012 issue of the Breast Cancer Advisor, I introduced our Foundation’s BREAST PALS program. It is a program designed to provide breast cancer patients with a pal or companion who has gone through the experience before and who can provide one-to-one guidance and assistance during a frightening and difficult time. This concept was first pioneered many years ago by the American Cancer Society. Its value has stood the test of time. Many similar programs exist around the country. Mrs. Meryl Wecksler has organized the program for The Angeles Clinic Foundation. She has experience, having organized a similar program in the Los Angeles area in the past. I wanted to interview her and find out why she finds this work so important.

Dr. Martino: What motivated you to serve as a new “friend or pal” to others with breast cancer?

Mrs. Wecksler: For my 50th birthday, I received a diagnosis of stage 2 breast cancer. Having never had a history of cancer in my family and being in perfect health, this news came as the ultimate shock. Though my husband was compassionate and understanding, I spent that first night calling my girlfriends for the comfort and support I needed. I realized it was easier to discuss my diagnosis with my women friends as they could readily identify with my fears.

Dr. Martino: When, in your own experience with breast cancer, did the idea of turning this type of help into a program first occur to you?

Mrs. Wecksler: That very first week, two amazing ladies, friends of friends, breast cancer survivors, and virtual strangers, called me to talk. One of the ladies even had to explain what chemotherapy was, that’s how much I didn’t know about cancer. From those conversations, my idea was born. I wanted to start a breast cancer support group but it would be on a “one-to-one” basis. I never wanted to participate in a support group but I did feel that if you were diagnosed with breast cancer, it would be nice to have a new friend in the process.

Dr. Martino: What kind of help do you think people need from a friend or pal?

Mrs. Wecksler: No one really knows what it’s like to be diagnosed with breast cancer until you’ve been there. Talking with someone who gets it is so vitally important to the healing process. It’s hard to realize what it’s like to go from a fully functioning woman to a cancer patient in an instant. I wanted to show other women what “the other side of the cancer journey looks like” and let them know they will eventually get back to where they were before this life-changing diagnosis.

Dr. Martino: Can one’s own friends and family provide the same type of help?

Mrs. Wecksler: Unfortunately, they can’t provide the same type of support and level of understanding that breast cancer survivors can. There are so many symptoms, reactions, simple home remedies and health and beauty information that only survivors know about and share with each other. Additionally, women don’t necessarily want to burden their family and friends with their negative feelings. It is much easier to complain to another survivor who has had similar emotions.

Dr. Martino: Is there an ideal time in the course of breast cancer care when you feel this type of program is most beneficial to patients? When should it start and when should it end?

Mrs. Wecksler: Every woman is different and handles her breast cancer diagnosis in a different way. For me, I found it incredibly helpful to talk with a survivor right away so I knew exactly what was ahead of me, rather than reading books or getting information on the internet. It is important to have a positive, reassuring woman to explain things to you that your doctors or nurses might not have time to discuss during your appointments. I believe this type of program is beneficial at any point; before treatment, after treatment, and even up to a year after treatment. Dealing with your breast cancer...
becomes the major part of your life for quite a while and it is always good to have someone to talk to.

**Dr. Martino:** Are there patients for whom this type of assistance is not useful?

**Mrs. Wecksler:** Yes, there are some women who are very private and might find it intimidating to discuss their problems with women they do not know. However, having dealt with women with breast cancer for over ten years, I’ve found that the majority of women want a comforting and knowledgeable person to share their feelings with.

**Dr. Martino:** What qualities do you look for when you consider a survivor to serve as a breast pal?

**Mrs. Wecksler:** A woman who possesses compassion, understanding, empathy and has a positive outlook on life. She must be able to be a healthy role model, a cheerleader, an advisor and a really good listener.

**Dr. Martino:** In what ways have you found participating as a breast pal to be most rewarding to you?

**Mrs. Wecksler:** I had formed this type of breast pal support group many years ago with a few other survivors. Not only did we have our own pals but we also had different events where we brought all our pals together. Watching these women bond and suddenly become good friends, laughing, hugging and sharing their similar experiences was extremely rewarding. To be able to give the gift of my cancer knowledge and friendship to help another person is a very fulfilling experience.

**Dr. Martino:** What are the difficulties in setting up such a program? What advice can you give to others who may wish to create such a program?

**Mrs. Wecksler:** The difficulty is for health care professionals to appreciate the value of having survivors help with the emotional needs of their patients during this critical time. Once the doctors realize that this type of program is an important adjunct to their medical treatment of breast cancer, this program becomes easy to implement. There will always be women who are willing to volunteer their time to help other women through their cancer journey.

**Dr. Martino:** Thank you.