Dear Readers,

In early June, the American Society of Clinical Oncology (ASCO) will have its annual meeting in Chicago. It is a large and prominent cancer meeting and it attracts scientists from all over the world. Many of the presentations will be reported by the public media. During the subsequent few months, I will review selected material from this meeting in the Breast Cancer Advisor as well.

Best personal regards,
Dr. Silvana Martino

BIOLOGY BASICS

In this issue, I want to review a version of breast cancer called “inflammatory” breast cancer. The name is derived from the appearance of the breast when this tumor is present. It looks red, inflamed, swollen, and can be warm to the touch. Often, a series of events precede this diagnosis. A woman relates that her breast became pink and warm. A physician was contacted who suspected the breast to be possibly infected and prescribed antibiotics. This treatment may have improved but not resolved the problem. Often, a second antibiotic is prescribed, but again the problem does not resolve. It is at this point that malignancy is considered and a mammogram and surgical evaluation is advised. At this point the diagnosis is suspected. It is an inflammatory breast cancer. A biopsy including of the affected skin is done to confirm the diagnosis. In addition to finding cancer cells in the breast biopsy, one may find tumor cells within the lymphatic system of the skin. This finding confirms the diagnosis of inflammatory breast cancer, but its absence does not mean that it is not an inflammatory breast cancer. The clues that are most important in making the diagnosis are the clinical appearance of the breast.
In this scenario, there may not be a specific mass noted. Rather, the entire breast may appear to be involved in the process. Mammography may or may not find a mass. It may demonstrate calcifications and thickening of the skin of the breast. Additional imaging using ultrasound and MRI are likely to be done. In addition, scans to look for evidence of metastatic disease such as a CT scan, a bone scan, and a PET scan are needed.

In general, inflammatory breast cancers are more aggressive, and require coordinated care. Surgery is not the first treatment. Rather, drug therapy is given first to begin the process of reducing the tumor size and volume. Once this has been achieved, then surgery is performed. The surgery is almost always a mastectomy to encompass all of the affected area. Radiation is also planned. The drug therapy that is chosen is based on the estrogen receptor, progesterone receptor, and HER2 status of the tumor.

Though it is true that typically inflammatory breast cancer presents in a more advanced state, and is more aggressive in its behavior, it is also true that many patients do well even with this diagnosis.

**Biology Basics continued**

**What’s New**

1. **AROMATASE INHIBITORS IN PREMENOPAUSAL WOMEN**

The use of aromatase inhibitor hormonal therapy (Arimidex, Femara, Aromasin) is now well established for women with hormonal positive breast cancer who are postmenopausal. Overall, they have been found to be superior to tamoxifen once you are postmenopausal. An unanswered important question is whether they are better than tamoxifen in women who are premenopausal as well as in men with breast cancer.

Norikazu Masuda and colleagues from Japan have recently published results from the STAGE study comparing these two therapies in 197 premenopausal women with breast cancers measuring 2-5 centimeters, node negative, hormone positive and HER2 negative. The women had not yet had surgery so their tumors could be measured during therapy. The group was randomized (like the flip of a coin) to either 6 months of tamoxifen plus goserelin (a hormone designed to turn off their ovarian function) or to Arimidex and goserelin. The tumors were then measured periodically during treatment. The primary goal of the study was to measure whether either therapy resulted in more tumor shrinkage than the other.

The results demonstrated that the group treated with the aromatase inhibitor, Arimidex plus goserelin, experienced more tumor shrinkage than the group treated with tamoxifen plus goserelin when assessed by calipers. Measurements by ultrasound, MRI, and CT also favored the Arimidex and goserelin group. More women in the Arimidex and goserelin group were able to have breast sparing surgery versus a mastectomy.

We are continually faced with great opportunities which are brilliantly disguised as unsolvable problems.

— Margaret Mead
What’s New continued

The results of this study suggest that even in premenopausal women, the use of aromatase inhibitors combined with ovarian suppression may be as good or possibly better than the use of tamoxifen and ovarian suppression. The authors advise that this should now be considered an appropriate therapy for premenopausal women.

This article is accompanied in the same journal by an editorial by Dr. Catherine M. Kelly from University Hospital, Dublin, Ireland, and Dr. Aman U. Buzdar from M.D. Anderson Cancer Center, Houston, Texas. Their view is that this study is “underpowered to provide meaningful long-term outcome data.” I agree with them. Defining whether the administration of aromatase inhibitors is better therapy for premenopausal women is a very important question. The real issue is whether it matters long term. Is there a difference in recurrence and in survival? The group of patients in this study is too small to answer these questions now or with longer follow-up. There are ongoing larger studies that are designed for the long term questions. Nevertheless, the present study reminds us of the importance of resolving the question of which of these two approaches is best in premenopausal women.

2. TAMOXIFEN THERAPY FOR DCIS

Ductal carcinoma in situ (DCIS) is considered an early form of breast cancer and believed to often precede invasive breast cancer. It is not clear whether all invasive breast cancers begin with an in situ phase. DCIS was an uncommon finding in the past, but once screening mammography was introduced, an increasing number of women have been diagnosed at this early stage. Today it accounts for 20% to 30% of all breast cancers.

The surgical treatment of DCIS is either a mastectomy, or lumpectomy, with or without radiation. Radiation does reduce the rate of local recurrence in patients who choose a lumpectomy. Even so, there is still a risk of local (in breast) recurrence. Approximately half of such recurrences are again DCIS, but half are invasive disease. To deal with this risk, tamoxifen is often advised.

Dr. D. Craig Allred and colleagues report the ten year follow-up results from a group of 1,804 DCIS patients treated with lumpectomy and radiation who were randomized to either 5 years of tamoxifen or placebo (NSABP Protocol B-24). When this study was begun, estrogen and progesterone receptors were not done routinely for DCIS, so this information was available on only 41% of the patients or 732 participants. They are the basis of this updated study. The researchers found that 76% of this subgroup had estrogen receptor positive disease. Two thirds of the women were over age 50, and the DCIS had been detected by mammography in over 75%.

The primary goal of the analyses was the occurrence of any breast cancer subsequent to the original diagnosis of DCIS. This included any recurrence within the treated breast, a cancer in the opposite breast, or any sign of distant recurrence. Their results demonstrate that patients with estrogen receptor positive DCIS had a significant reduction in recurrence. They did not find this reduction in those given tamoxifen whose DCIS was estrogen receptor negative. They did, however, find some reduction of breast cancer in the opposite breast even in those with hormone negative disease.

Though these are important results, and further solidify the recommendation for tamoxifen in hormone positive DCIS, it must be kept in mind that this is a selected group of patients within a larger study, so the number of participants is modest. It is also a retrospective study.


QUESTIONS & ANSWERS

(Q) Dr. Martino, I am very confused about what to eat now that I have a diagnosis of breast cancer. I want to do what is best for my health but my oncologist has told me that there is no special diet that he can recommend. I have tried to look on the internet, but it is all very confusing. What should I do?

(A) I wish I had a simple answer for you, but I don’t. The fact is that there is no clear data that there is in fact an optimal diet to keep you healthy after a diagnosis of breast cancer. It is very hard to do diet studies. Ideally, you would have to have large groups of people who were the same in every other way except that they ate different diets for a long period of time. Even if you could find such groups, it is difficult in a free society like ours to keep them on a particular diet for years. Some attempts to do this have been made. The WINS trial was a randomized study in postmenopausal women with breast cancer who were randomized to staying on their own died versus a very low fat diet. This required considerable education of the low fat group and a lot of record keeping of what both groups ate. I participated in this study and I can tell you first hand that it was not easy for my patient to maintain such a low fat diet. The study did show that women on the low fat diet, especially if they had hormone negative breast cancer, had less recurrences. Other studies have not found the same results.

Most of us discourage a diet high in estrogen containing foods such as soy. Even this is controversial. Some authorities advise a more oriental type of diet since women from Asia have less breast cancer. A “Mediterranean” type diet is now popular. Whether either approach is valuable after a diagnosis of breast cancer is unclear. The bottom line is that diet, which we all suspect is important in overall health, is one of the aspects of health that we know least about. There is more theory than fact.

My personal advice, given the lack of factual information that exists on this topic, is to keep in mind some basic concepts of general good health: do not smoke, do not drink more than three small glasses of alcohol per week (not all glasses are the same size), watch your weight, eat foods that are as close to nature as possible. The less processed the better. Food does not grow in boxes or cans. Reduce sugar intake. Eat fresh fruits and vegetables. Try to eat animal products from animals raised on an open range and without hormones. Exercise portion control. Extreme diets or very limited diets should probably not be your goal.

E-mail your questions to:
smartino@theangelesclinicfoundation.org
Nipple Sparing Mastectomy

For most of the 20th century, a radical, or modified radical, mastectomy was the standard treatment for breast cancer. With removal of the breast gland and overlying skin, surgeons were able to give patients the lowest chance that cancer would come back (recur) on the involved side. Unfortunately, this approach also produced a horribly mutilating cosmetic outcome. For the last 40 years, the oncologic community has attempted to improve the cosmetic outcome of breast cancer treatment.

Lumpectomy was offered to patients in an effort to “conserve” their breast tissue. When the treated breast was also radiated after the lumpectomy, the chance of cancer recurrence was significantly reduced. Large, prospective studies showed that lumpectomy was as safe as mastectomy as long as patients got mastectomies when breast cancers recurred.

Photograph 1:
A patient with a small, non-invasive breast cancer wished to have both of her breasts removed so as to minimize the risk of recurrence or the appearance of new cancer in her breasts.

Photograph 2:
Because the cancer was found not to involve the tissue beneath the nipple directly, nipple sparing mastectomy and reconstruction with a breast implant was possible. This patient did not require radiation therapy.
Surgeons in England initially proposed that the cosmetic outcome of the mastectomy operation could be improved in cancer patients by leaving or “sparing” the nipple and surrounding skin. The chance of cancer recurring in these patients was the same as when the nipple was removed during the mastectomy procedure. Thus, the cosmetic outcome of the mastectomy operation can be improved if the nipple can be spared.

Two lines of evidence converge in support of the safety of nipple sparing mastectomy: first, the randomized, prospective studies done to show the safety of breast conservation compared to mastectomy failed to demonstrate any survival advantage for initial removal of the nipple; and, second, retrospective studies are now accumulating that support the safety of nipple sparing mastectomy in selected patients.

By reducing the cosmetic deformity of mastectomy, this technique allows more patients to opt for mastectomy when indicated.

Guest Writer continued