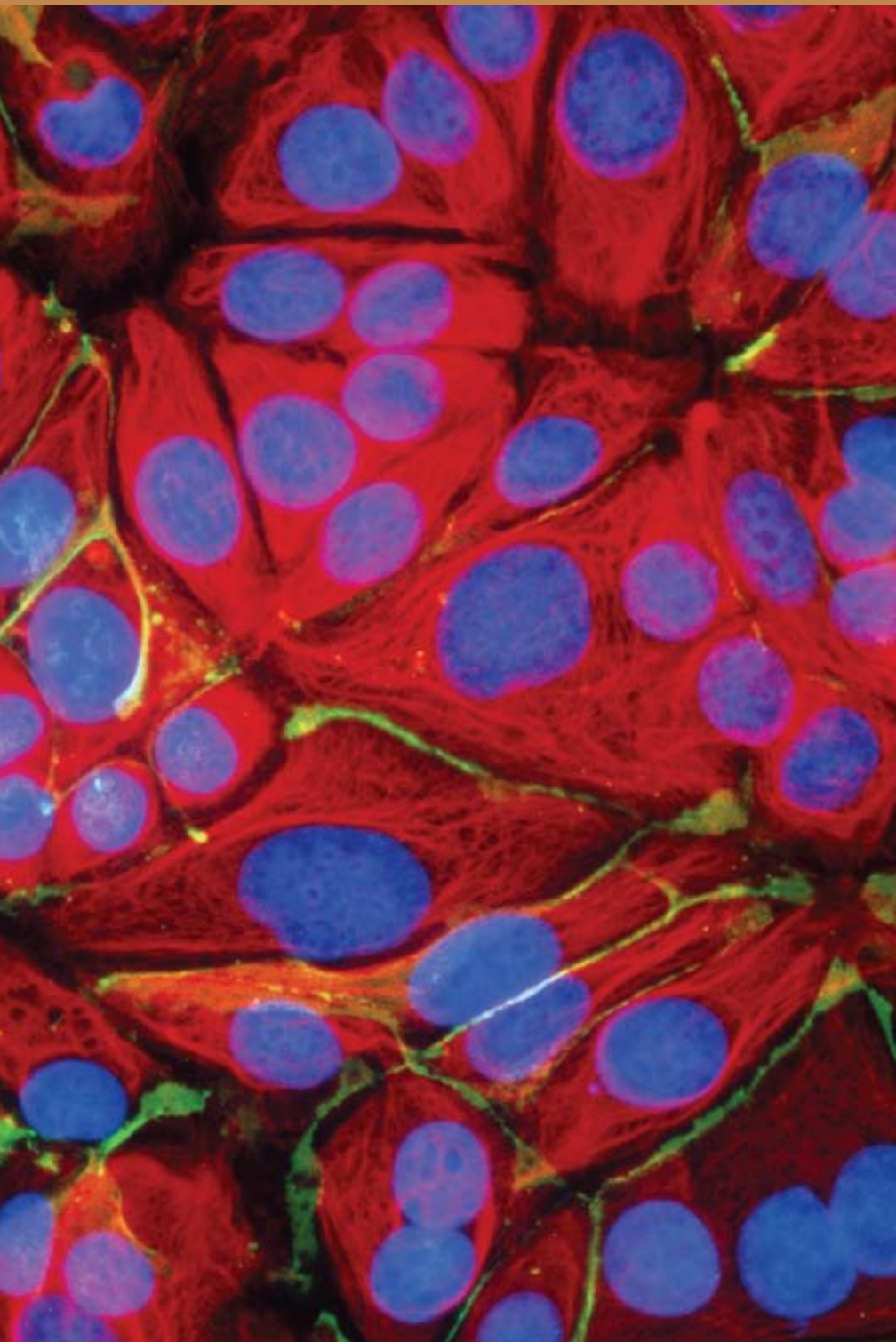


## BREAST CANCER





# Breast Cancer

*Highlights from the 2009 Annual Meeting of the American Society of Clinical Oncology*

Edited by

**William J. Gradishar, MD**

Robert H. Lurie Comprehensive Cancer Center  
of Northwestern University  
Chicago, Illinois

## **27 Early-Stage Breast Cancer**

### **Reducing Recurrence of Early-Stage Breast Cancer (p 27)**

*Women with small tumors that involve few lymph nodes may benefit from radiation treatment after surgery.*

*Surgically removing lymph nodes in the armpit may help reduce the return of cancer to this area in some women.*

## **29 Locally Advanced or Metastatic Breast Cancer**

### **PARP Inhibitors for Locally Advanced or Metastatic Breast Cancer (p 29)**

*This new class of targeted treatments is very promising for women with aggressive breast cancers.*

### **Bevacizumab Combinations for Locally Advanced or Metastatic Breast Cancer (p 31)**

*Adding the targeted drug bevacizumab (Avastin) to chemotherapy may delay the growth of tumors.*

*Combining bevacizumab with a newer form of paclitaxel (Abraxane) appears to help women go longer before their tumors grow.*

*Ixabepilone (Ixempra) plus bevacizumab seems to be an encouraging combination for shrinking tumors.*

*contents continued on the following page*

## Combination Treatment With Trastuzumab for Metastatic Breast Cancer (p 33)

*Combining trastuzumab (Herceptin) with a new medication called DM1 appears to shrink HER2-positive tumors.*

*The combination of trastuzumab and the new oral drug neratinib may be a more effective treatment for women with HER2-positive breast cancer.*

---

**E**very year in the United States, approximately 192,000 women are diagnosed with breast cancer. Doctors diagnose breast cancer by stages according to the size of the tumor and the extent of its spread. In this chapter we talk about three main stages of breast cancer:

- **Early-stage** refers to smaller tumors that have not spread to other parts of the body and that may or may not have spread to the lymph nodes in the armpit. (Lymph nodes are a linked system of small bean-shaped structures throughout the body that filter out and destroy bacteria and other harmful substances.) When cancer spreads to the lymph nodes, it can travel to other parts of the body.
- **Locally advanced** is a term that refers to one of two situations: either the tumor is confined to the breast but is too large to be effectively removed or it has spread to nearby areas outside the breast, such as the lymph nodes in the armpit, neck, or chest wall.
- **Metastatic** is the most advanced stage of breast cancer. At this stage, cancer cells have spread past the breast and nearby lymph nodes to other areas of the body, where they continue to grow and multiply. The most common parts of the body to which breast cancer spreads are the bones, lungs, and liver.

Doctors also describe breast tumors by whether or not their

growth is fueled by the female hormones estrogen and progesterone or by overproduction of a substance called HER2. Such estrogen-, progesterone-, or HER2-receptor positive breast cancers are treated with medications that block the activity of these hormones and substances.

However, some breast cancer cells are estrogen-, progesterone-, and HER2-receptor negative. That is, they do not respond to treatments that block these



substances. These so-called triple-negative breast cancers are also discussed in this chapter.

## Early-Stage Breast Cancer

### **REDUCING RECURRENCE OF EARLY-STAGE BREAST CANCER**

*Women with small tumors that involve few lymph nodes may benefit from radiation treatment after surgery.*

Many women with early-stage breast cancer are treated with radiation after mastectomy—that is, surgery to remove the breast or as much breast tissue as possible. Previous research has shown that women who have larger tumors (more than five centimeters, or about two inches) that involve at least four lymph nodes benefit from radiation after surgery. New research shows that radiation treatment after surgery also seems to reduce the chances of recurrence in women with smaller tumors that involve fewer lymph nodes.

More than 3,700 women with early-stage breast cancer who had had a mastectomy were included in this clinical trial. All of these women had tumors that were smaller than five centimeters and involved one to three lymph nodes. Some of the women had a mastectomy without radiation; others had a mastectomy followed by radiation.

Compared with women who received radiation, the women who did not have radiation had a 38 percent higher risk of distant recurrence (return of cancer in a part of the body far away from the original tumor).



Researchers are optimistic that radiation treatment after mastectomy may also extend survival. However, this treatment needs to be studied further to confirm these results.

It should be noted that all women who have a lumpectomy—

that is, surgery to remove the tumor but conserve the breast—require radiation treatment to the breast.

---

***Surgically removing lymph nodes in the armpit may help reduce the return of cancer to this area in some women.***

According to the recent results of a large clinical trial, researchers have found that completely removing the lymph nodes in the armpit in certain women with early-stage breast cancer may reduce the chances of cancer returning to this area. This surgical procedure, called complete axillary lymph node dissection, removes all the lymph nodes found in and around the armpit.

More than 2,500 women who had early-stage breast cancer took part in this clinical trial. In these women, collections of tumor cells measuring between 0.2 and 2.0 millimeters (tiny fractions of an inch) were found on the sentinel lymph node, which is the first lymph node to which cancer cells are likely to spread from the original tumor.

Some of these women were treated with complete axillary lymph node dissection. Others were treated with sentinel lymph node biopsy, which is the removal and examination under a microscope of the sentinel lymph node.

Five years after their diagnosis of breast cancer, the women who did not have the surgery to completely remove all the underarm lymph nodes were almost five times more likely to have a recurrence of cancer to this region than women who had received the surgery. Although researchers are encouraged by these early results, further studies should help them learn which women with early-stage breast cancer would benefit most from this treatment.

## Locally Advanced or Metastatic Breast Cancer

### **PARP INHIBITORS FOR LOCALLY ADVANCED OR METASTATIC BREAST CANCER**

*This new class of targeted treatments is very promising for women with aggressive breast cancers.*

One of the most exciting developments in breast cancer research is a new type of targeted treatment called PARP inhibitors. (Unlike chemotherapy, targeted treatments block specific cell mechanisms that are thought to be important for cancer cell growth. Targeted treatments are meant to spare healthy tissues and cause less severe side effects.)

According to two recent clinical trials, two different drugs



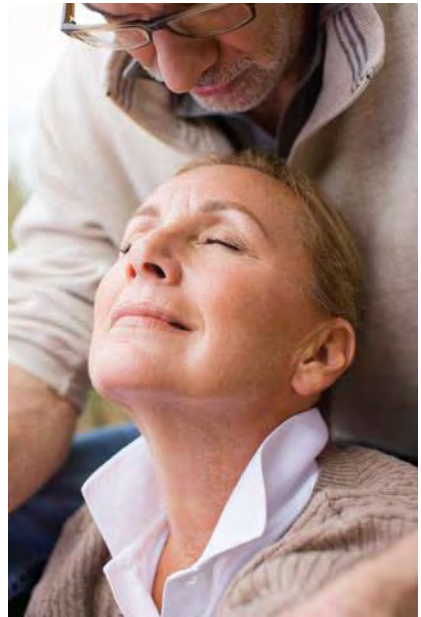
from this new class of targeted treatments—BSI-201 and olaparib—may slow the growth of breast cancer and help women with this diagnosis live longer.

PARP is short for “poly(ADP-ribose) polymerase.” These new drugs block a cancer cell’s ability to repair itself when damaged by radiation or chemotherapy, for example. PARP inhibitors may increase the effectiveness of other treatments.

In the first clinical trial, BSI-201 was combined with two other chemotherapy drugs—gemcitabine (Gemzar) and carboplatin (Paraplatin and others). About 100 women with metastatic triple-negative breast cancer took part in the study. Half of the women were treated with the new three-drug combination, and the others were given just gemcitabine and carboplatin.

Of the women treated with BSI-201, the tumor stopped growing or shrank in about 60 percent. Of the women who received only chemotherapy, the tumor stopped growing or shrank in 21 percent. In addition, the women who received BSI-201 lived about four months longer than the women who did not receive the drug.

In the second clinical trial, olaparib was given to about 50 women with advanced breast cancer. These women had mutated (changed) BRCA genes. Mutations in the BRCA genes are associated with an increased risk of breast cancer as well as other cancers.



The patients' tumors had not responded to several rounds of standard chemotherapy. But when the women were treated with olaparib, 40 percent of their tumors shrank.

Researchers are excited about these early results with PARP inhibitors. However, these drugs are still in an early stage of development. Further studies are needed to find out how these new drugs can best be used to treat breast cancer.

### **BEVACIZUMAB COMBINATIONS FOR LOCALLY ADVANCED OR METASTATIC BREAST CANCER**

*Adding the targeted drug bevacizumab (Avastin) to chemotherapy may delay the growth of tumors.*

There are many chemotherapy drugs for women with advanced breast cancer. In the continued search to improve the treatment of these women, researchers have studied various combinations of these medications. One of the most promising combinations includes the use of the targeted treatment bevacizumab (Avastin) with traditional chemotherapy. Bevacizumab has been used to treat metastatic lung cancer and colorectal cancer.

More than 1,200 women took part in a clinical trial called RIBBON-1. These women had HER2-negative metastatic breast cancer. For the study, bevacizumab was added to a few different first-line (first-time) chemotherapy treatments to find out whether bevacizumab added a benefit compared with chemotherapy alone.

In the women treated with bevacizumab and a newer chemotherapy called capecitabine (Xeloda), it took nearly nine months for the cancer to continue growing. On the other hand, in the women who were treated with capecitabine alone, it took about six months for the cancer to continue growing. Similar results were seen when bevacizumab was added to other chemotherapies, compared with the chemotherapies alone.



Adding bevacizumab to chemotherapy was also more effective at shrinking tumors. For instance, the tumor stopped growing or shrank in about 50 percent of the women treated with the combination of bevacizumab plus chemotherapy. However, the combination treatments did not appear to extend survival. Nevertheless, delaying the time until the disease progresses is important to many patients and their quality of life.

---

***Combining bevacizumab with a newer form of paclitaxel (Abraxane) appears to help women go longer before their tumors grow.***

More than 150 women with HER2-negative metastatic breast cancer took part in a clinical trial in which bevacizumab was added to a newer form of the standard cancer drug paclitaxel (Abraxane). This newer version of paclitaxel is used to treat cancer that has spread or come back after chemotherapy. Some women in this clinical trial received the combination weekly, and others received it every three weeks.

Tumors completely disappeared or shrank in more than 40 percent of both groups of women, regardless of whether they received the treatment weekly or every three weeks. However, the weekly treatment did a better job of stopping tumor growth (for nine months versus about seven-and-a-half months).

Researchers were encouraged by the early results with this combination treatment. They plan to study it further in future clinical trials and suggest giving it for three straight weeks followed by a one-week break. Doctors often use this kind of schedule to make it easier for people to continue with their treatment plan while limiting possible side effects.

---

***Ixabepilone (Ixempra) plus bevacizumab seems to be an encouraging combination for shrinking tumors.***

Another clinical trial is also using bevacizumab in combination treatment in the hope of finding a more effective way to treat metastatic breast cancer. In this clinical trial, bevacizumab was combined with a drug called ixabepilone (Ixempra).

Ixabepilone has been used to treat locally advanced or metastatic breast cancer that has not improved after treatment with other anti-cancer drugs. However, in this clinical trial, the bevacizumab-ixabepilone combination was studied as a first-line treatment in more than 100 women with metastatic breast cancer.

Early results of this ongoing study show that the combination of these two drugs may be an effective way to shrink tumors in these women and perhaps stop the tumors' growth. The combination appeared to be effective whether it was given weekly or every three weeks.

Tumors disappeared or shrank in approximately half of the women taking part in the trial.



### **COMBINATION TREATMENT WITH TRASTUZUMAB FOR METASTATIC BREAST CANCER**

*Combining trastuzumab (Herceptin) with a new medication called DM1 appears to shrink HER2-positive tumors.*

A new treatment option has shown impressive early results for women with metastatic HER2-positive breast cancer. Doctors are now combining trastuzumab (Herceptin), a targeted treatment for HER2-positive breast cancer, with DM1 to create a new treatment approach called T-DM1.

In a recent clinical trial, more than 100 women whose HER2-positive breast cancer did not respond or no longer responded to treatments that included trastuzumab or lapatinib (Tykerb) were treated with T-DM1. Nine and a half months after treatment, the tumor had shrunk or completely disappeared in 25 percent of the women.

Researchers are so pleased with these early results, they plan to study T-DM1 as a second-line treatment in another clinical trial of women with advanced HER2-positive breast cancer. Second-line treatment is given when the first treatment either does not work or stops working.



---

***The combination of trastuzumab and the new oral drug neratinib may be an effective treatment for women with HER2-positive breast cancer.***

Forty-five women who had HER2-positive metastatic breast cancer that did not respond or no longer responded to treatment with trastuzumab took part in a recent clinical trial. In the trial, they were

treated with the combination of trastuzumab and a new oral targeted treatment called neratinib.

Only 33 women have been evaluated so far, but the tumor has shrunk in more than 25 percent of them. In addition, at 16 weeks after treatment, the tumor had neither grown nor shrunk in half the patients.

Researchers plan to learn more about this combination treatment. Breast cancer often metastasizes to the brain,

and researchers are hopeful that neratinib may be able to prevent this spread.

---

**Please note:** *Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.*