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Latest News in Breast Cancer Research

Highlights from the 2011
San Antonio Breast Cancer
Symposium

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This special edition of the CancerCare Connect® booklet series highlights cutting-edge research presented at the 2011 San Antonio Breast Cancer Symposium, which took place December 6–10 in San Antonio, Texas.

Some of the treatments discussed in this booklet are still in the very early stages of research and may not be available to the general public outside of a clinical trial.

The information contained in this booklet is intended for discussion with your doctor. He or she can let you know whether these advances in the treatment of breast cancer affect your treatment plan and whether a clinical trial is right for you.

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Personalizing Treatment

Because there are so many different types of breast cancer, treatment is no longer a “one size fits all” approach. Researchers and doctors now focus on personalized treatments that target each patient and her specific type of breast cancer. (Although it’s rare, men do get breast cancer. But for purposes of this booklet, we refer to patients as women.) This was the theme of the 2011 San Antonio Breast Cancer Symposium: The most effective treatments are those that target the individual and her kind of tumor.

New Test Predicts Risk of Breast Cancer Recurrence

A new test has been developed that can help predict whether a certain type of breast cancer is likely to return. This information would help doctors decide whether a woman can be effectively treated with surgery alone or whether she would need radiation after surgery.

In a clinical trial, researchers tested tumors from more than 300 women with ductal carcinoma in situ (DCIS), a common type of breast cancer that is confined to the milk ducts and has not spread into other parts of the breast tissue. (DCIS may increase a woman’s risk of developing an invasive breast cancer that may spread later on.) Researchers used a modified version of the *Oncotype DX* Recurrence Score, which has been available since 2004, to study the genetic makeup of each woman’s tumor.

With this new version of the test, they were able to predict the chance that cancer would return in each patient.



What Patients Need to Know

Researchers consider this new test a major advance for women with DCIS. It is the first time that a test has been used to identify lower-risk and more aggressive forms of this type of breast cancer. The test will help doctors better understand the biology of DCIS and accurately select the best treatment for a given patient.

DCIS is usually treated with surgery and then radiation or hormone therapy. Now, women who have a low risk of their cancer returning can be treated effectively and spared having to receive radiation after surgery. Those who have a high risk of their cancer returning can be treated with radiation after surgery.

Radiation Treatment

Radiation is an important tool in breast cancer treatment. This section describes the first national comparison of forms of the treatment.

Radiation to the breast is often given after lumpectomy—breast-conserving surgery in which only the tumor is removed and not the entire breast (mastectomy). This treatment helps reduce the risk that the cancer will come back in the breast or nearby lymph nodes. Radiation may also be recommended after mastectomy in patients with either a cancer larger than 5 centimeters or when cancer is found in the lymph nodes.

If the breast cancer spreads to other areas such as the bones or brain, radiation is also used as treatment.

Standard breast radiation is called whole-breast radiation. In this technique, external beams are directed to the entire affected breast after lumpectomy. A newer approach now being studied is accelerated partial-breast irradiation (APBI). This technique generally delivers radiation only to a portion of the breast, focused on the area where the lumpectomy took place. APBI can be delivered by internally implanted devices (called APBI-brachytherapy) or with external radiation. Generally, APBI is delivered to a more focused area than whole-breast radiation and over a much shorter time.

Partial Radiation Treatment for Older Women With Breast Cancer

APBI-brachytherapy has been considered an alternative to standard radiation treatment after breast-conserving surgery. However, the treatment may not be as effective as whole-

breast radiation. APBI-brachytherapy may also cause more side effects than whole-breast radiation in older women with early-stage breast cancer.

A recent study showed that more women treated with APBI-brachytherapy had to have a mastectomy (removal of the breast) later on than did women who were treated with standard whole-breast radiation.

Using Medicare claims from 2000 to 2007, researchers looked at the medical records of more than 130,000 women (older than age 66) who were treated for breast cancer. The use of APBI-brachytherapy increased during that period from less than 1 percent to 13 percent. Five years after treatment, the risk of needing a mastectomy was twice as great in women who received APBI-brachytherapy than in those who received standard whole-breast radiation.

Women treated with APBI-brachytherapy also had more side effects and hospital visits than did those who received standard whole-breast radiation. Side effects included breast pain and rib fractures (breaks).

What Patients Need to Know

This is the first national comparison of APBI-brachytherapy versus standard whole-breast radiation in older Medicare patients. APBI-brachytherapy has become an increasingly popular treatment for older patients diagnosed with early-stage breast cancer. However, these results show that whole-breast radiation remains the standard treatment for these older women. APBI-brachytherapy may still benefit certain women, offering advantages such as shorter treatment times and less exposure to radiation. A large clinical trial of APBI-brachytherapy compared with other radiation approaches is planned for the future.

Bone-Strengthening Drugs for Breast Cancer

Bisphosphonates, also known as bone-strengthening drugs, are often used to treat osteoporosis (bone thinning that causes the bones to become fragile) and other related bone diseases. Researchers are studying these drugs in postmenopausal women with early-stage breast cancer to see whether they may be an effective treatment for breast cancer. The reports that follow here highlight the mixed results in clinical trials with three of these bone-strengthening drugs—zoledronic acid (Zometa), clodronate, and ibandronate (Boniva)—in women with early-stage breast cancer.

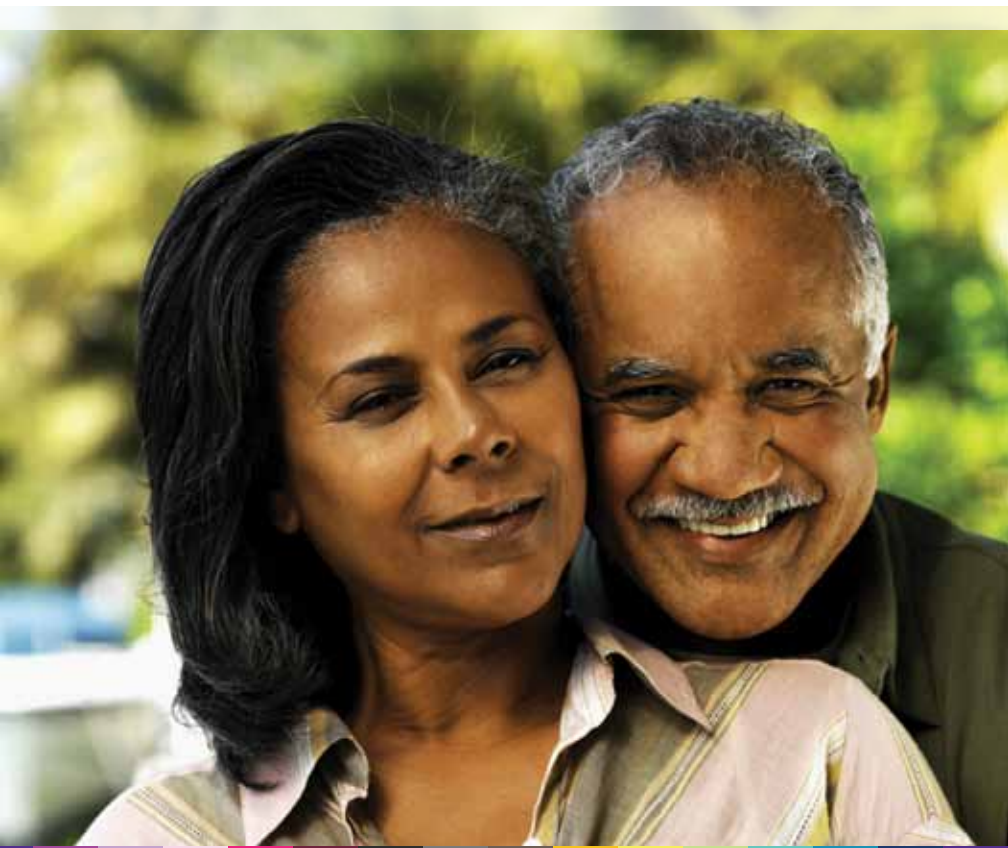
Zoledronic Acid

Adding zoledronic acid to ongoing hormone treatment may help women with early-stage estrogen receptor (ER)-positive breast cancer to live longer without a return of cancer symptoms. Researchers reached this conclusion in two different clinical trials.

The first study is called the ABCSG-12 trial. More than 1,800 premenopausal women with early-stage, ER-positive breast cancer took part in this clinical trial. They all received hormone therapy to block estrogen as well as tamoxifen (Nolvadex and others) or anastrozole (Arimidex and others). In addition, some women in the study received zoledronic acid every six months for three years, whereas others did not. More than five years after treatment, the chance of the cancer coming back was reduced by 28 percent in the women treated with zoledronic acid. The women who received

zoledronic acid had a 36 percent chance of living longer than those who did not receive the drug.

In the second study, known as the ZO-FAST trial, more than 1,000 postmenopausal women with early-stage, ER-positive breast cancer received letrozole (Femara and others). Again, some of the patients received zoledronic acid every six months, and others did not. (Letrozole belongs to a class of anti-cancer drugs called aromatase inhibitors. They block the action of a substance called aromatase, which is needed for the production of estrogen. That's important because ER-positive breast tumors depend on the female hormone estrogen for their growth.) Patients who received zoledronic



acid had a 34 percent decrease in the chance of their cancer returning.

What Patients Need to Know

Zoledronic acid has been successfully used to treat osteoporosis-related bone loss in postmenopausal women. It is also used to treat cancer patients whose cancer has spread to the bone. According to the results of the ABCSG-12 and ZO-FAST trials, zoledronic acid may help reduce the chance of cancer returning and extend the lives of women with early-stage, ER-positive breast cancer. This exciting news may enable doctors to expand the options they have to treat breast cancer. However, additional studies are needed to help doctors learn which women with breast cancer would be best treated with zoledronic acid.

Clodronate

According to the results of a large clinical trial, clodronate does not reduce the spread of breast cancer to other parts of the body. More than 3,000 women with early-stage breast cancer received daily doses of clodronate or a placebo (a look-alike medication that has no active ingredient). Approximately 78 percent of the women had ER-positive breast cancer, and 64 percent were older than age 50.

More than eight years after treatment, the cancer returned or spread to other parts of the body in similar numbers of patients in both groups. Researchers had expected to see better results with clodronate, but there did not seem to be much difference between clodronate and placebo in these patients. However, the study results suggest that clodronate might be more effective when used to treat breast cancer patients who are older than age 50.

What Patients Need to Know

Although the results of this clinical trial did not live up to researchers' hopes, this remains the largest study of an oral bone-strengthening drug in women with early-stage breast cancer. Future studies may show whether clodronate might benefit older women with breast cancer.

Ibandronate

When given in combination with chemotherapy, ibandronate did not appear to help women with early-stage breast cancer to stay free of cancer after treatment. More than 3,000 patients took part in a clinical trial called the GAIN study. They were divided into two groups, both of which received chemotherapy. One group also received ibandronate, and the other did not. At 39 months after treatment, there was no difference in improvement between those who received ibandronate and those who did not.

Researchers reviewed the results of this trial and compared them with other similar studies of bone-strengthening drugs in treating women with early-stage breast cancer. They think it may be possible that these less-than-positive results with ibandronate in the GAIN study may have been affected by the high doses of chemotherapy given to the patients.

What Patients Need to Know

Even though the results of the GAIN study did not show a benefit to adding ibandronate to treatment of early-stage breast cancer, the drug may still prove to be of use in the future. Researchers emphasized that other studies with ibandronate have shown promise in a select group of patients. Continued clinical trials with these bone-

strengthening drugs for the treatment of early-stage breast cancer are needed.

Researchers note a few important points:

- Across all the studies reported at the San Antonio meeting, women with ER-positive breast cancer seem to benefit from the use of bisphosphonates.
- Where benefit was seen, there was limited chemotherapy given.
- For the most part, the patients were postmenopausal or had hormone therapy to block their ovaries from making estrogen.

A number of studies are under way to identify which women would benefit most from these medications.



Locally Advanced or Metastatic Breast Cancer

There are many different treatments available for women with locally advanced or metastatic breast cancer. However, cancer cells can become resistant to these drugs. And sometimes, their long-term use can lead to side effects. That is why researchers are always looking for drugs that are effective while causing fewer side effects. A number of studies show that combining treatments can benefit women with locally advanced or metastatic breast cancer.

Combining Treatments for ER-Positive Metastatic Breast Cancer

Anastrozole and fulvestrant A combination of two hormonal drugs—anastrozole and fulvestrant (Faslodex)—helped women live longer without their cancer growing than did anastrozole alone (15 months versus 13.5 months). About 700 postmenopausal women with ER-positive metastatic breast cancer took part in this study, with anastrozole given orally and fulvestrant given as an injection.

Overall, the women who received the combination treatment as their first treatment for the return and spread of their cancer lived longer than those who did not. Women who had not received any anti-estrogen treatment for early-stage breast cancer before their cancer returned had the best results with the combination treatment. They lived 17 months without their cancer returning, compared with 12.6 months for those treated with anastrozole alone.

What Patients Need to Know

The researchers found that two drugs used in combination were effective in women who had not had treatment already. These results, which are from a large clinical trial conducted by the National Institutes of Health, suggest that anastrozole and fulvestrant may prove to be a new first-time option for postmenopausal women with ER-positive metastatic breast cancer.

Pertuzumab, trastuzumab, and docetaxel Adding pertuzumab (Perjeta) to the combination treatment of trastuzumab (Herceptin) and docetaxel (Taxotere and others) helped women with HER2-positive metastatic breast cancer live six months longer without their cancer growing than women who received trastuzumab plus docetaxel without pertuzumab (18 months versus 12 months). In addition, the tumor shrank in more than 80 percent of patients who were treated with pertuzumab, compared with 69 percent of those who did not receive this drug.

These results come from a large clinical study called the CLEOPATRA trial. About 800 women with HER2-positive metastatic breast cancer took part.

What Patients Need to Know

HER2-positive breast cancer tends to grow more rapidly than other types of breast cancers. Pertuzumab is a new type of targeted treatment designed to block HER2, which is present in about 20 percent of breast cancer patients. Researchers are continuing to discover that drugs used in combination may be more effective in treating metastatic breast cancer than drugs used alone. Thus, adding HER2-targeted drugs such as trastuzumab, lapatinib (Tykerb), and pertuzumab to a

standard chemotherapy treatment like docetaxel may provide added benefits for these patients.

Bevacizumab, trastuzumab, and docetaxel Adding bevacizumab (Avastin) to trastuzumab and docetaxel enabled patients with HER2-positive breast cancer to live longer without their cancer growing than those treated with trastuzumab and docetaxel alone (16.5 months versus 13.7 months). The tumor shrank or did not grow in 74 percent of those who received all three drugs compared with 70 percent of those who received only trastuzumab and docetaxel.

More than 400 women took part in this clinical study known as the AVEREL trial.

What Patients Need to Know

Bevacizumab is a type of targeted treatment that blocks a tumor's ability to grow new blood vessels. Without its blood vessels, tumors are "starved" of the nutrients they need to grow and divide. The AVEREL trial is the first large-scale trial to study the addition of bevacizumab in women with HER2-positive metastatic breast cancer. These early results seem to suggest that the combination of bevacizumab, trastuzumab, and docetaxel may prove to be an effective treatment for women with this type of breast cancer. Further studies should help doctors learn which women with HER2-positive metastatic breast cancer would benefit most from first-time treatment that includes bevacizumab.

Neratinib A new oral drug called neratinib, when given alone, is less effective than the standard treatment combination of lapatinib plus capecitabine (Xeloda) in women with HER2-positive locally advanced or metastatic breast cancer. When patients received lapatinib plus



capecitabine, it took 6.8 months before their cancer started to grow again. In the women who took neratinib, it was 4.5 months before their cancer began to grow again.

This recently completed clinical trial included 240 women with HER2-positive metastatic breast cancer. All of the women had received one or two prior treatments for their breast cancer, which had returned. Neratinib did show anti-cancer activity. The tumor shrank or did not grow in 44 percent of the women who were treated with neratinib. This finding suggests that the drug may prove to be a beneficial treatment in the future for women with locally advanced or metastatic breast cancer.

What Patients Need to Know

Although studies like these may seem to be disappointing, researchers have learned two things. First, the combination of lapatinib and capecitabine remains the standard treatment

for women with HER2-positive locally advanced or metastatic breast cancer who have had treatment before. Second, though it may be too early to tell whether neratinib will be an effective drug for these women, it is a promising option that should be studied further, perhaps in combination with chemotherapy.

Everolimus and exemestane The combination of everolimus (Afinitor) and exemestane (Aromasin and others) helped postmenopausal women with ER-positive advanced breast cancer to live 7.4 months without their cancer growing. (Exemestane is an aromatase inhibitor, a drug that blocks estrogen production.) Women treated with exemestane alone lived 3.2 months before their cancer began to grow again. Also, the tumor shrank in 12 percent of patients who received the combination, compared with about 1 percent of those who did not.

These results are from a clinical trial called BOLERO-2. More than 700 women took part in this study. In all of the patients, previous treatment with other aromatase inhibitors—*anastrozole* or *letrozole*—no longer worked. However, women in the group treated with exemestane plus everolimus did experience more side effects, such as mouth inflammation and fatigue.

What Patients Need to Know

Researchers are very encouraged by these promising results with everolimus and exemestane. Their hope is that this combination treatment may prove to be effective for women whose ER-positive advanced breast cancer no longer responds to other medications.

Estrogen-targeted therapy is an important treatment for the 80 percent of breast cancers that are fueled by this female

hormone. Most breast tumors respond to anti-estrogen therapy at first but eventually become resistant to this treatment and begin to grow and spread. Clinical trials have studied ways to overcome tumor resistance to anti-estrogen therapy, including adding the use of drugs that target other cell mechanisms. Everolimus is one such drug.

Treating Breast Cancer That Has Spread to the Skin

When breast cancer spreads to other parts of the body, it can appear on the skin. These lesions are not skin cancer; rather, they indicate that the breast cancer is more advanced. Standard treatments are available, but early studies suggest that there may be a new effective drug combination for breast cancer that has spread to the skin.

Imiquimod and albumin-bound paclitaxel In an early and very small clinical trial, breast cancer that spread to the skin had completely or partly disappeared in all five patients treated for three months with imiquimod (Aldara, Zyclara, and others) plus a newer, albumin-bound form of the drug paclitaxel (Abraxane). For all of these women, standard treatment had stopped working. (Binding paclitaxel to the protein albumin makes it easier to concentrate the drug in the tumor.)

Imiquimod is a cream applied directly to the skin. Called a biological therapy, this medication helps the body's immune system attack cancer cells. Albumin-bound paclitaxel is a chemotherapy drug given as an injection.

Researchers believe that the two drugs given together may enhance their ability to stop cancer cells from multiplying. Larger studies with imiquimod and albumin-bound paclitaxel

should shed more light on whether the combination will prove to be an effective treatment of metastatic breast cancer to the skin.

What Patients Need to Know

Skin lesions often develop shortly after breast cancer is diagnosed. But they also can occur during or after treatment for breast cancer. That is why it is important for women being treated for breast cancer to check areas of their bodies for any skin changes, such as rashes, bumps, or other unusual growths, and then inform their health care team.

New Treatment Options for Triple-Negative Breast Cancer

Triple-negative breast tumors are made up of cancer cells that do not depend on estrogen, progesterone, or HER2 for their growth. Approximately 15 percent of all breast cancers are triple-negative tumors. These tumors tend to grow more quickly and are usually larger than other types of breast tumors.

Because there are fewer effective treatment options for women with triple-negative breast cancer, researchers are looking for new ways to combine chemotherapy and targeted drugs. Testing new combinations may show doctors which ones would offer the most benefit to women with triple-negative breast cancer.

Panitumumab in combination with chemotherapy The combination of standard chemotherapy plus the targeted treatment panitumumab (Vectibix) appears to be an effective way to treat women with triple-negative breast cancer before surgery, according to the results of an early clinical trial. In the

60 women who received the new combination treatment, the tumor shrank and disappeared in nearly 30 percent of these women. It shrank somewhat or did not continue to grow in about another 30 percent.

The standard chemotherapy consisted of three drugs: 5-fluorouracil, epirubicin (Ellence and others), and cyclophosphamide (Cytoxan and others). After the women were given panitumumab and chemotherapy, they received docetaxel. All 60 patients in the study were candidates for surgery.

What Patients Need to Know

Studies have shown that giving chemotherapy before surgery, called neoadjuvant treatment, may shrink tumors, which improves the chances of successful surgical removal of these tumors. It also allows researchers to study how the tumor responds to chemotherapy. For women with triple-negative breast cancer, combination treatment with panitumumab, a monoclonal antibody, holds promise as a treatment that may shrink tumors before surgery. (This type of monoclonal antibody tracks down tumor cells and binds to their surface to disrupt the cells' function.)

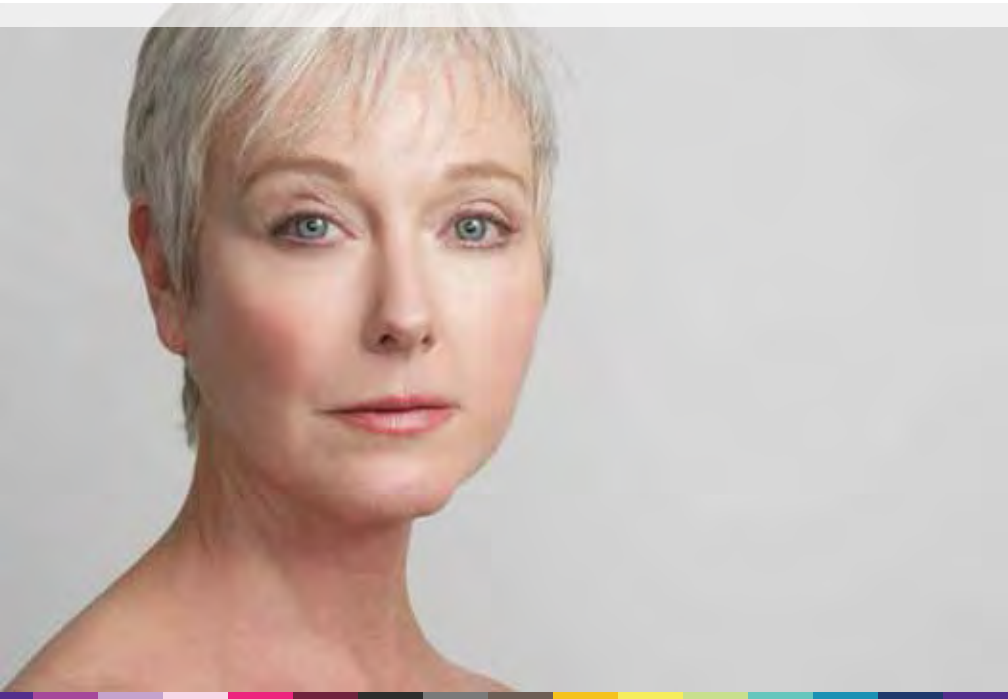
Ixabepilone plus carboplatin Another promising option for women with triple-negative breast cancer is the combination of the newer chemotherapy drug ixabepilone (Ixempra) and the older drug carboplatin (Paraplatin and others). According to early results from the ECLIPSE study, the tumor shrank by half or did not grow in 26 percent of the 50 or so women with triple-negative breast cancer who received ixabepilone and carboplatin. All of these patients had already received treatment for their metastatic breast cancer.

The combination of ixabepilone and capecitabine is currently approved for patients with metastatic breast cancer whose cancer no longer responds to other treatment. The ECLIPSE study is looking at whether this new treatment may lead to longer lives with fewer side effects for these women.

What Patients Need to Know

Researchers continue to evaluate different combinations of anti-cancer drugs to learn which group of patients may benefit the most. The early findings from the ECLIPSE study suggest that the combination of ixabepilone and carboplatin may prove to be an effective option for women with metastatic triple-negative breast cancer.

Veliparib plus cisplatin and vinorelbine Adding a new targeted drug called veliparib to two standard chemotherapy medications—cisplatin (Platinol and others) and vinorelbine



(Navelbine and others)—has shown some benefit in women with locally advanced triple-negative breast cancer. Of the 11 women who received this new combination treatment, the tumor shrank by at least 50 percent in six of them, and the tumor did not grow in five of them. These are very early results from an ongoing study.

Veliparib belongs to a new and exciting class of drugs known as PARP inhibitors. PARP is an abbreviation for poly ADP ribose polymerase. These drugs block a cancer cell's ability to repair itself when damaged by radiation or chemotherapy. PARP inhibitors may make these other treatments more effective.

What Patients Need to Know

PARP inhibitors are a new type of anti-cancer drug that has shown promise in patients with locally advanced triple-negative breast cancer, as well as tumors that test positive for *BRCA1* and *BRCA2* mutations (gene changes). This very small clinical trial is testing different doses of veliparib to see which one is the most effective and has the fewest side effects. As more women take part in this ongoing study, more will be learned about how best to use veliparib in combination with cisplatin and vinorelbine in this group of patients.

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