

Additional medicines can reduce recurrence risk, but come with their own issues

October 7 2012, by Julie Deardorff

After surgeons removed the tumor from her breast last November, Karen Hajiaskari, of Hamburg, N.Y., was deemed cancer-free. But for the next five years she will take a drug called tamoxifen, a medication that's commonly used to prevent a breast cancer recurrence.

Given the persistent nature of cancer, drug treatment often extends for years, even if [cancerous cells](#) can't be visibly detected. More than 50 drugs and five [drug combinations](#) have been approved for [breast cancer treatment](#), according to the National Cancer Institute. Newer therapies on the horizon include vaccines and drug combinations.

Any treatment given after the primary therapy, which is usually surgery, is considered "adjuvant." The additional treatment can reduce the risk that cancer will return. But experts caution that not everyone has a success story; the potential benefits must be balanced with the side effects, which can be debilitating.

[Treatment decisions](#) are based on many factors, including the type of [breast cancer](#) a woman has, the size of the tumor, whether it has spread and if she is post-menopausal. New ways to characterize tumors and their characteristics can also inform treatment decisions, said Dr. Mark Pegram, head of the breast oncology and medical therapeutics programs at Stanford University Medical Center.

"Breast cancer is not just one disease; it's a collection of different diseases," said Pegram. "Two patients in the same waiting room might

get very different treatments."

In a study on the genomics of breast cancer, researchers have identified four genetically distinct types of the disease. These findings, published online Sept. 23 in the [journal Nature](#), suggest that some drugs already approved for cancers in other parts of the body could lead to new treatments for breast cancer.

Most adjuvant drug therapies use substances that travel through the bloodstream, reaching [cancer cells](#) all over the body. The therapies that are used to stave off a recurrence include chemotherapy, hormonal therapy, the targeted drug Herceptin and a combination of treatments. Though radiation is not a drug, it is also commonly used as an adjuvant therapy. Vaccines, which researchers hope will help inspire immune cells to more aggressively destroy tumors, have shown promising effects, but they are still at least five years away. Here's how the [drug therapies](#) work to attack cancer.

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CHEMOTHERAPY

Used when: The cancer has spread to the lymph nodes. Also used with "triple-negative" breast cancer, which means the tumor lacks three specific types of receptors.

How it works: Chemotherapy drugs can stop the growth of cancer cells, either by killing the cells or stopping them from dividing. Usually more than one drug is given; they can be taken by mouth or injected into a vein or muscle, depending on the type and stage of cancer, according to the National Cancer Institute. "Patients get a substantial benefit in risk of relapse and even improvement in survival," said Pegram. But not everyone needs chemotherapy, he added, particularly in cases where it

hasn't spread to the lymph nodes.

Side effects: Chemotherapy can affect healthy cells in the bone marrow, the digestive tract and hair follicles. Patients may have an increased risk of infection, bruises and fatigue. They may also lose their hair and appetite, or experience nausea, vomiting, diarrhea or mouth sores. Some chemotherapy drugs, called anthracyclines, can increase the risk of heart problems.

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HORMONAL THERAPY

Used when: The cancer is fueled by hormones, also known as estrogen-positive.

How it works: Hormonal therapy robs breast cancer cells of the hormone estrogen, which many breast cancer cells need to grow, according to the cancer institute. For example, the drug tamoxifen, the most commonly used hormone therapy, binds to the estrogen receptor inside the tumor cell and blocks estrogen, which slows or stops the growth of cancer cells already in the body, said Pegram.

Post-menopausal women using hormonal therapy are often given a newer type of drug, called an aromatase inhibitor (AI). Instead of blocking the estrogen receptor, these drugs prevent the body from making estrogen in the first place. They do this by preventing the aromatase enzyme from turning androgen into estrogen, according to the institute.

For pre-menopausal women, adding a bone-building drug (bisphosphonates) may prevent a [breast cancer recurrence](#), research suggests.

Side effects: In general, the side effects of tamoxifen are similar to the symptoms of menopause and include hot flashes, vaginal discharge and nausea. Tamoxifen can also increase the risk of cataracts and the chances of blood clots in the legs and lungs. Tamoxifen leaves women feeling extremely fatigued. It also may be less effective if a woman is also taking certain medicines for hot flashes or depression.

Aromatase inhibitor drugs can also trigger menopausal symptoms, women can experience joint or muscle pain and have a higher risk of heart problems than those taking tamoxifen, according to the [National Cancer institute](#). These medications, known as AI drugs, also reduce bone density and increase the risk of bone fractures.

Hajiaskari, 45, has had only one side effect: leg cramps. Her doctor recommended drinking tonic water; she receives massage therapy twice a week.

After surgery, Haralee Weintraub was supposed to take Arimidex (anastrozole) for five years. She quit after eight months because of bone pain. After that she tried another AI called Femara (letrozole) but three months later, she stopped after "the same aches and pains impacted my quality of life," she said.

Pegram suggested switching AI drugs to cope with bone pain. "For reasons we don't know, it sometimes helps," he said. "If that doesn't work, use tamoxifen instead."

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TARGETED THERAPY

Used when: The cancer is HER2-positive.

How it works: About 20 percent of women have a type of breast cancer cell that makes too much - or over-expresses - protein called Human Epidermal growth factor Receptor 2 (HER2), which helps tumor cells grow. HER2-positive breast cancers tend to be more aggressive than other types of cancer, according to the American Cancer Society and are less responsive to hormone treatment. The drug Herceptin (trastuzumab) reduces the risk of recurrence by targeting the receptors on the HER2-cell surface. It binds to the HER2 receptor and blocks the signals the cancer needs to grow. It can also stimulate immunity against the tumor, said Pegram, who helped develop the treatment that combines standard chemotherapies with Herceptin. "Antibodies can recruit infection infighting cells," he said. "They can release hostile substances that attack and kill the target," he said.

Given by infusion every one to three weeks for a year, Herceptin is used in combination with chemotherapy for about a quarter of breast cancer patients. This combo has been shown to prolong survival in Stage 4 cancer that has spread throughout the body. It also reduces the risk of mortality by about a third when used in early stage breast cancer, said Pegram.

Side effects: Heart failure, nausea, vomiting, hot flashes and joint pain.

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VACCINES

Used when: Researchers are working to develop vaccines that prevent breast cancer or are used after a diagnosis.

How they work: Several studies are looking at vaccines designed to teach the body how to respond to the HER2-based protein fragment so that it would recognize cancer when it recurs and attack it, said Elizabeth

Mittendorf, a surgical oncologist at the University of Texas MD Anderson Cancer Center in Houston who specializes in breast cancer immunotherapy.

Data from two trials has shown that one type of a HER2-based vaccine triggered the desired immune response in women with an HER2-positive tumor. The vaccine is still at least five years away from being made widely available, said Mittendorf.

In addition to HER2 vaccines, some researchers are looking at genetically engineered vaccines that prompt the release of a substance to enhance the immune system response.

Others researchers are studying vaccines in combination with drugs. In one small preliminary study of 10 patients, researchers at Penn's Abramson Cancer Center showed a one-time infusion of the drug Zenapax (daclizumab) improved the survival of breast cancer patients given several doses of cancer vaccines by 30 percent, compared to those patients not taking daclizumab.

The combination of a vaccine and Femara increased survival when tested in mice. Mittendorf's research group is looking at vaccines in combination with Herceptin.

Despite an enormous amount of research, with rare exceptions, vaccines haven't yet been proven effective, said Pegram. Because cancer cells originate within the body, the immune system generally doesn't recognize them as foreign and won't mount an attack.

"In many cases, tumors have ways of outsmarting the human defense system and avoiding surveillance. The problem is just starting to be addressed," he said.

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