

## Adjuvant Therapy for Breast Cancer: Questions and Answers

Researchers have been studying breast cancer for many years to learn how best to treat this disease. They have given special attention to ways to prevent breast cancer from recurring (returning) after primary treatment.

Scientists once thought that breast cancer metastasizes (spreads) first to nearby tissue and underarm lymph nodes before spreading to other parts of the body. They now believe that cancer cells may break away from the primary tumor in the breast and begin to metastasize even when the disease is in an early stage.

Adjuvant therapy is treatment given in addition to the primary therapy to kill any cancer cells that may have spread, even if the spread cannot be detected by radiologic or laboratory tests. Studies have shown that adjuvant therapy for breast cancer may increase the chance of long-term survival by preventing a recurrence.

### 1. What types of primary therapy are used for breast cancer?

Primary therapy for breast cancer generally involves lumpectomy and radiation therapy or modified radical mastectomy. A lumpectomy is the removal of the primary breast tumor and a small amount of surrounding tissue. Usually, most of the underarm lymph nodes are also removed. A lumpectomy is followed by radiation treatment to the breast. A modified radical mastectomy is the removal of the whole breast, most of the lymph nodes under the arm, and often the lining over the chest muscles. The smaller of the two chest muscles is sometimes taken out to help in removing the lymph nodes.

Doctors are evaluating a new procedure, called sentinel lymph node biopsy or sentinel node biopsy, in which only a single lymph node is removed and tested to determine if the breast cancer has spread to lymph nodes under the arm. Clinical trials (research studies with humans) are in progress to determine the role of this procedure in the treatment of breast cancer.



## 2. What types of adjuvant therapy are used for breast cancer?

Because the principal purpose of adjuvant therapy is to kill any cancer cells that may have spread, treatment is usually systemic (uses substances that travel through the bloodstream, reaching and affecting cancer cells all over the body). Adjuvant therapy for breast cancer involves chemotherapy or hormone therapy, either alone or in combination:

- **Adjuvant chemotherapy** is the use of drugs to kill cancer cells. Research has shown that using chemotherapy as adjuvant therapy for early stage breast cancer helps to prevent the original cancer from returning. Adjuvant chemotherapy is usually a combination of anticancer drugs, which has been shown to be more effective than a single anticancer drug.
- **Adjuvant hormone therapy** deprives cancer cells of the female hormone estrogen, which some breast cancer cells need to grow. Most often, adjuvant hormone therapy is treatment with the drug tamoxifen. Research has shown that when tamoxifen is used as adjuvant therapy for early stage breast cancer, it helps to prevent the original cancer from returning and also helps to prevent the development of new cancers in the other breast.

The ovaries are the main source of estrogen prior to menopause. For premenopausal women with breast cancer, adjuvant hormone therapy may involve tamoxifen to deprive the cancer cells of estrogen. Drugs to suppress the production of estrogen by the ovaries are under investigation. Alternatively, surgery may be performed to remove the ovaries.

(Although this fact sheet focuses on *systemic* adjuvant therapy, radiation therapy is sometimes used as a *local* adjuvant treatment. Radiation therapy is considered adjuvant treatment when it is given before or after a mastectomy. Such treatment is intended to destroy breast cancer cells that have spread to nearby parts of the body, such as the chest wall or lymph nodes. Radiation therapy is part of primary therapy, not adjuvant therapy, when it follows breast-sparing surgery.)

## 3. What are prognostic factors, and what do they have to do with adjuvant therapy?

Prognostic factors are characteristics of breast tumors that help predict whether the disease is likely to recur. Doctors consider these factors when they are deciding which patients might benefit from adjuvant therapy.

Several prognostic factors are commonly used to plan breast cancer treatment:

- **Tumor size.** Prognosis (probable outcome of the disease) is closely linked to tumor size. In general, patients with small tumors (2 centimeters (a little more than three-quarters of an inch) or less in diameter) have a better prognosis than do patients with larger tumors (especially those that are more than 5 centimeters (2 inches) in diameter).

- **Lymph node involvement.** Lymph nodes in the underarm are a common site of breast cancer spread. Doctors usually remove some of the underarm lymph nodes to determine whether they contain cancer cells. If cancer is found, the nodes are said to be “positive.” If the lymph nodes are free of cancer, the nodes are said to be “negative.” Breast cancer that is node-positive is more likely to recur than cancer that is node-negative because, if cancer cells have spread to the lymph nodes, it is more likely that they have also spread elsewhere in the body.
- **Hormone receptor status.** Cells in the breast contain receptors for the female hormones estrogen and progesterone. These receptors allow the breast tissue to grow or change in response to changing hormone levels.

Research has shown that about two-thirds of all breast cancers contain significant levels of estrogen receptors. These tumors are said to be estrogen receptor positive (ER+). About 40 percent to 50 percent of all breast cancers have progesterone receptors. These tumors are said to be progesterone receptor positive (PR+).

ER+ tumors tend to grow less aggressively than ER- tumors. The result is a better prognosis for patients with ER+ tumors.

- **Histologic grade.** This term refers to how much the tumor cells resemble normal cells when viewed under the microscope. Tumors composed of cells that closely resemble normal breast cells and structures are called well-differentiated. Tumors with cells that bear little or no resemblance to normal breast cells are called poorly differentiated. Tumors that have “in between” cells are called moderately differentiated. For most types of invasive breast cancer, patients who have tumors with cells that are well-differentiated tend to have a better prognosis.
- **Proliferative capacity of a tumor.** This factor refers to the rate at which the cancer cells divide to form more cells. Cells that have a high proliferative capacity divide more often and are more aggressive (fast growing) than those with a low proliferative capacity. Patients who have tumors with cells that have a low proliferative capacity (i.e., divide less often and grow more slowly) tend to have a better prognosis.

Scientists estimate the proliferative capacity of the tumor using such tests as flow cytometry, which includes the S-phase fraction measurement. The S-phase fraction is the percentage of tumor cells that are dividing. Tumors with a high S-phase fraction tend to have an increased risk of recurrence.

- **Oncogene activation.** The activation of an oncogene (a gene that causes or promotes unrestrained cell growth) can make normal cells become abnormal or convert a normal cell into a tumor cell. Patients whose tumor cells contain an oncogene called HER-2/neu, also called *erb* B-2, may be more likely to have a recurrence. Some research studies suggest that HER-2/neu may be associated with resistance to certain anticancer drugs; however, more research is needed.

**4. Who is given adjuvant therapy?**

Although prognostic factors provide important information about the risk of recurrence, they do not enable doctors to predict exactly who will be cured by primary therapy and who may benefit from adjuvant therapy. Decisions about adjuvant therapy for breast cancer must be made on an individual basis, taking into account the prognostic factors described above, the woman's menopausal status (whether she has gone through menopause), her general health, and her personal preference. This complicated decision-making process is best carried out by consulting an oncologist, a doctor who specializes in cancer treatment.

Clinical trials are in progress to learn how to identify women most likely to benefit from adjuvant therapy and those who do not require this treatment (see question 8).

**5. When is adjuvant therapy started?**

Adjuvant therapy usually begins within 6 weeks after surgery, based on the results of clinical trials in which the therapy was started within that time period. Doctors do not know how effective adjuvant therapy is in reducing the chance of recurrence when treatment is started at a later time.

**6. How is adjuvant therapy given, and how long does it last?**

Chemotherapy is given by mouth or by injection into a blood vessel. Either way, the drugs enter the bloodstream and travel throughout the body. Chemotherapy is given in cycles: a treatment period followed by a recovery period, then another treatment period, and so on. Most patients receive treatment in an outpatient part of the hospital or at the doctor's office. Adjuvant chemotherapy usually lasts for 3 to 6 months.

In adjuvant hormone therapy, tamoxifen is taken orally. Tamoxifen enters the bloodstream and travels throughout the body. Most women take tamoxifen every day for 5 years. Studies have indicated that taking tamoxifen for longer than 5 years is not any more effective than taking it for 5 years. Premenopausal women may receive hormones by injection to suppress ovarian function. Alternatively, surgery can be performed to remove the ovaries.

**7. What are some of the side effects of adjuvant therapy, and what can be done to help manage them?**

The side effects of chemotherapy depend mainly on the drugs the patient receives. As with other types of treatment, side effects vary from person to person. In general, anticancer drugs affect rapidly dividing cells. These include blood cells, which fight infection, cause the blood to clot, and carry oxygen to all parts of the body. When blood cells are affected by anticancer drugs, patients are more likely to get infections, bruise or bleed easily, and may have less energy during treatment and for some time afterward. Cells in hair follicles and cells that line the digestive tract also divide rapidly. As a result

of chemotherapy, patients may lose their hair and may have other side effects, such as loss of appetite, nausea, vomiting, diarrhea, or mouth sores.

Doctors can prescribe medications to help control nausea and vomiting caused by chemotherapy. They also monitor patients for any signs of other problems and may adjust the dose or schedule of treatment if problems arise. In addition, doctors advise women who have a lowered resistance to infection because of low blood cell counts to avoid crowds and people who are sick or have colds. The side effects of chemotherapy are generally short-term problems. They gradually go away during the recovery part of the chemotherapy cycle or after the treatment is over.

In general, the side effects of tamoxifen are similar to some of the symptoms of menopause. The most common side effects are hot flashes, vaginal discharge, and nausea. As is the case with menopause, not all women who take tamoxifen have these symptoms. Most of these side effects do not require medical attention.

Doctors carefully monitor women taking tamoxifen for any signs of more serious side effects. Women taking tamoxifen, particularly those who are receiving chemotherapy along with tamoxifen, have a greater risk of developing a blood clot. The risk of having a blood clot due to tamoxifen is similar to the risk of a blood clot when taking estrogen replacement therapy. Women taking tamoxifen also have an increased risk of stroke.

Among women who have not had a hysterectomy (surgery to remove the uterus), the risk of developing endometrial cancer (cancer of the lining of the uterus) and uterine sarcoma (cancer of the muscular wall of the uterus) is increased in those taking tamoxifen. Women who take tamoxifen should talk with their doctor about having regular pelvic exams, and should be examined promptly if they have pelvic pain or any abnormal vaginal bleeding.

Careful studies have shown that the risks of adjuvant therapy for breast cancer are outweighed by the benefit of the treatment—increasing the chance of survival. Still, it is important for women to share any concerns they may have about their treatment or side effects with their doctor or other health care provider.

More information and printed materials about the side effects of chemotherapy and tamoxifen can be obtained from the Cancer Information Service or the other resources listed below.

## **8. How are doctors and scientists trying to answer questions about adjuvant therapy for breast cancer?**

Doctors and scientists are conducting research studies called clinical trials to learn how to treat breast cancer more effectively. In these studies, researchers compare two or more groups of patients who receive different treatments. Such studies can show whether new treatments are more or less effective than standard ones and how the side effects

compare. People who participate in clinical trials have the first opportunity to benefit from new treatments while helping to increase medical knowledge.

Women with breast cancer who are interested in taking part in a clinical trial can ask their doctor whether this would be appropriate for them. Information about current clinical trials can be obtained from the National Cancer Institute (NCI)-supported Cancer Information Service (see below) or the clinical trials page of the NCI's Web site at [http://cancer.gov/clinical\\_trials/](http://cancer.gov/clinical_trials/) on the Internet.

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### **Sources of National Cancer Institute Information**

#### **Cancer Information Service**

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

#### **NCI Online**

##### ***Internet***

Use <http://cancer.gov> to reach the NCI's Web site.

##### ***LiveHelp***

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

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