

PACCT-1 Trial: TAILORx

*A Clinical Trial Assigning Individualized
Options for Treatment (Rx)*

Treatment Options

The TAILORx trial is designed to find out if a new test (Oncotype DX) will be able to help doctors and their patients with early breast cancer make better treatment decisions. Each patient who enrolls in the study will receive a numerical Recurrence Score (RS), which will be determined by the Oncotype DX assay (ODX) and that RS will determine to which study group a patient will be assigned. Patients with a RS of 10 or lower will have hormonal therapy; patients with a RS of 26 or higher will have hormonal and chemotherapy; and patients with a RS of 11 to 25 will be randomized to either hormonal therapy or hormonal and chemotherapy.

While a patient's RS will determine the study group she will be in, the exact treatment or regimen (choice of drugs, timing of treatments, etc.) will be made by the doctor and the patient. There are many different hormonal and chemotherapy treatments that are considered "standard of care." As long as the regimen is considered a standard treatment, it will be accepted

Oncotype DX Recurrence Score (RS)	TAILORx Study Group	Treatment
0 - 10	Low	Hormonal therapy (aromatase inhibitor or tamoxifen as determined by physician and patient)
11 – 25	Mid	Randomized to have hormonal OR hormonal AND standard chemotherapy
26 and higher	High	Hormonal AND standard chemotherapy (specific hormonal and chemotherapy treatment to be determined by physician and patient)

Chemotherapy

Normal cells in the body grow and divide in a controlled way. Cancer cells, however, grow and divide very rapidly and in an uncontrolled manner. Chemotherapy is a general term used to describe various drugs to treat cancer that work throughout the body. Many drugs used to treat breast cancer interfere with and kill cells that grow and divide very fast. Because tumors are made up of different kinds of cells, chemotherapy often consists of two or more drugs each having a different way of killing cancer cells. This is called combination chemotherapy.

Patients in the TAILORx trial will have early stage-breast cancer that measures 1.1 to 5.0 cm, is ER/PR positive, node negative and HER2 negative. The TAILORx trial allows those patients who are randomized to receive chemotherapy to use any standard chemotherapy. The National Comprehensive Cancer Network (NCCN) cancer treatment guidelines mention several drugs that are used in various combinations and are given on different schedules for the treatment of this stage of breast cancer. The list of the brand and generic names below can help you become familiar with the drugs doctors may mention. Only the patient and her physician can make the decision about which chemotherapy regimen is best (brand name/generic names shown).

- Adriamycin/doxorubicin
- Cytoxan/cyclophosphamide
- Ellence/epirubicin
- "5-FU"/fluorouracil
- Methotrexate (has many brand names)
- Taxol/paclitaxel
- Taxotere/docetaxel



These therapies will be given in the medical oncologist's office. Some regimens may be given over a period of time in a specific number of cycles.

Side Effects from Chemotherapy

As noted above, chemotherapy drugs are designed to interfere with or kill fast growing cancer cells and that may affect other fast growing cells in the body. Side effects are the result of chemotherapy drugs affecting non-cancer cells in the body. It is important to know that today many of the problems from side effects can be managed and that many disappear after treatment is completed. Having or not having a side effect is not related to whether the treatment is working or not. Because each person is different, some patients won't have a specific side effect while for others the side effect will range from mild to severe.

Specific side effects are related to the type of cell the chemotherapy drug is affecting. Hair loss, fatigue, risk of infection, nausea and vomiting are some side effects that are commonly associated with chemotherapy treatments. These side effects may vary by individual patient and the chemotherapy drug regimen. The table below lists some of the common side effects during chemotherapy treatment:

Side effect	Reason	Management of symptom	After chemotherapy ends
Hair Loss	Hair follicles contain fast growing cells and this is why many patients lose their hair during treatment		Hair usually grows back when treatment is completed.
Nausea, vomiting, diarrhea, constipation	Damage to the gastrointestinal cells that line the digestive tract	Effective treatment to manage or counteract	Symptoms usually stop when treatment is completed
Fatigue, dizziness, shortness of breath	Slow production of red blood cells due to chemotherapy affecting the bone marrow	Effective treatment to counteract	Symptoms usually stop when treatment is completed and red blood cell production increases
Risk of infection	Low white blood count	Effective treatment to counteract	Symptoms usually stop when treatment is completed and white blood cell production increases
Abnormal blood clotting	Low platelet count	Effective treatment to counteract	Symptoms usually stop when treatment is completed and platelet count returns to more normal levels.
Burning tingling, weakness or numbness in hand or feet	Nerve damage	Sometimes managed by reducing amount of chemotherapy drug	Symptoms usually stop when treatment is completed
Fertility issues, sexuality, early menopause for women	Chemotherapy drugs can cause genetic changes in sperm or egg cells that could lead to birth defects	Both men and women are encouraged to use birth control throughout their treatment. If infertility is a concern, patients should talk to their doctor before any treatment begins. There are sometimes options for people who wish to maintain their fertility.	For men and women there may be temporary or permanent infertility (inability to conceive a child)
Inability to concentrate, changes in thinking and memory (cognitive changes)		Activities that improve memory and problem-solving skills can sometimes help.	Usually improves after treatment is completed

Hormonal Therapy

Estrogen contributes to the growth of breast cancer in women whose tumors are estrogen/progesterone receptor positive (ER/PR+). Estrogen can sit on the receptor and signal the tumor to grow. Hormonal therapies either reduce the amount of estrogen produced in postmenopausal women or block estrogen from reaching the receptor in both pre- and postmenopausal women. Hormonal therapies that are considered “standard of care” are:

- Aromatase inhibitors (AIs)* which reduce the amount of estrogen produced in postmenopausal women. Currently available aromatase inhibitors include (brand/generic names shown):
 - Arimidex/anastrozole
 - Aromasin/exemestane
 - Femara/letrozole
- SERMs (Selective estrogen receptor modulators) block estrogen from reaching the cell by attaching to the receptor and preventing a signal to the cancer cell.
 - Tamoxifen (This drug is produced under different brand names.)

Side Effects from Hormonal Therapy

Because all hormonal therapies lower the effects of estrogen in many areas of the body, often the side effects are similar to menopause. Symptoms associated with SERMs and AIs are: hot flashes, weight gain or bloating, vaginal dryness, mood swings, and depression. Menopausal-like symptoms like these can be mild to severe.

Pre- and postmenopausal women may take tamoxifen. Some side effects reported with tamoxifen are fertility issues and hair and nail thinning. Potentially more serious side effects are: blood clots, endometrial cancer, abnormal growth of uterine tissue (endometriosis), and stroke. It is important to note that in women taking tamoxifen these serious side effects were reported in less than one percent of patients.

Possible side effect:	AIs	Tamoxifen
Bone loss	Yes	No
Joint pain, arthritis	Yes	No
Increase in cholesterol levels	Yes	No
Upset stomach or mild nausea	Yes	No
Mild to severe menopausal symptoms (hot flashes, weight gain or bloating, vaginal dryness, mood swings, and depression)	Yes	Yes
Fertility issues	No (AIs only for postmenopausal women)	Yes
Hair and nail thinning	No	Yes
Blood clots	No	Yes More serious side effect (reported in less than 1% of patients taking tamoxifen)
Endometrial cancer	No	Yes More serious side effect (reported in less than 1% of patients taking tamoxifen)
Abnormal growth of uterine tissue (endometriosis)	No	Yes More serious side effect (reported in less than 1% of patients taking tamoxifen)
Stroke	No	Yes More serious side effect (reported in less than 1% of patients taking tamoxifen)

* Note - By FDA indication, only anastrozole would be considered standard for treatment with aromatase inhibitors. In clinical practice, the three drugs (anastrozole, exemestane, and letrozole) are used somewhat interchangeably.

Only women who are postmenopausal can take aromatase inhibitors. Patients taking an AI may experience bone loss, joint pain, arthritis, increase in cholesterol levels and upset stomach or mild nausea. There are effective treatments for some of these side effects.

After reading a list of the possible side effects of chemotherapy and/or hormonal therapy, some patients may ask if the treatment is worse than the disease. It is important to remember that most side effect symptoms can be treated and many disappear when treatment is completed. We know that chemotherapy and hormonal therapy can be very effective in treating breast and some other types of cancer. Millions of people today are cancer survivors because of chemotherapy and hormonal therapy drugs. Patients should not be deterred from treatment because of possible side effects.

