Questions and answers on breast cancer

Guideline 7: Anticancer drug treatment for node-negative breast cancer

What is node-negative breast cancer?

Node-negative breast cancer means that no cancer cells from the breast have been found in the lymph nodes (sometimes called "glands") in the armpit area. If your cancer is node negative, there is a lower risk of the cancer returning and spreading than if it is node positive.

I will be having surgery and radiation treatment for breast cancer. Do I need anticancer drug treatment too?

Although node-negative cancer indicates a smaller risk of the cancer returning than node-positive cancer, there is still a risk. Even when it seems certain that the whole tumour has been removed, cancer still returns elsewhere in the body ("metastasizes") in up to 30% of all women with node-negative breast cancer.

However, this is simply an average. Some kinds of cancer are more likely to recur than others, and this will influence your treatment options. Your cancer will be examined and classified as having a *high*, *medium* or *low* risk of returning, depending on several factors outlined below.

- *Its size*. The larger the cancer, the higher the risk. Most cancers smaller than 1 cm in diameter are at a very low risk of recurring after surgery and radiation.
- *The type of cells it contains*. Some cell features are found more often in "aggressive" cancers, cancers that are more likely to recur and spread. Your pathologist will "grade" your cancer from I to III depending on its cell features. A grade I cancer is less likely to return than a grade III cancer.
- *Whether the cancerous cells have invaded nearby blood vessels and lymph channels*. When vessel invasion is found under the microscope, the cancer is more likely to return.
- *Whether your cancer was diagnosed as "ER positive" or "ER negative."* "ER" stands for estrogen receptor. This is a receptor or "docking site" to which estrogen can bind. Women with cancers that have these receptors (ER-positive cancers) are at a slightly lower risk of the cancer returning. Also, such cancers react differently to treatment than ER-negative cancers.

All these factors must be considered when judging your overall risk of the cancer returning. This, in turn, will determine whether you should have additional treatment and, if so, which treatment is best for you.

What is the risk that the cancer will return if I have only surgery and radiotherapy, but no additional drug treatment?

If your cancer is classified as *low risk*, there is less than a 10% chance it will return in the next 10 years. In other words, it will come back in fewer than 10 women out of every 100 who have this type of cancer.

If cancer is classified as *intermediate* risk, the chance of the cancer returning is somewhere between 10% and 20%. Additional treatment will reduce this risk.

Women with *high-risk* cancers have a greater than 20% risk of the cancer returning and spreading. This risk is sometimes as high as node-positive breast cancer. For this group also, additional treatment will reduce this risk.

My cancer has been classified as *low risk*. Do I need additional treatment?

No. In your case, additional drug treatment is not recommended, since only 1 or 2 out of every 100 women would benefit from it. Your doctor may discuss the use of hormonal therapy with tamoxifen.

My cancer is classified as *high risk*. What additional treatment is recommended for me?

Chemotherapy is recommended for all premenopausal women and for postmenopausal women with ER-negative tumours.

Tamoxifen plus chemotherapy is recommended for postmenopausal women with ER-positive tumours. The increased toxicity of chemotherapy must be considered.

These treatments are discussed in more detail below.

What is recommended for women with *intermediate-risk* cancer?

If the cancer is ER positive, hormonal therapy with tamoxifen is recommended. This treatment is discussed in more detail below. (ER-negative cancers are usually classified as high risk.) Chemotherapy provides additional benefit to tamoxifen. However, the magnitude of the benefit is small, and the increased toxicity of chemotherapy must be considered.

Chemotherapy

What is chemotherapy?

Chemotherapy is treatment with drugs that kill cancer cells.

My doctor recommends chemotherapy. What are the pros and cons?

Anticancer drugs also affect healthy cells. This means they can have undesirable side effects, some of which are severe. For this reason, chemotherapy is recommended only when there is a good chance that you will benefit from it and are healthy enough to take it.

For premenopausal women and for women with ER-negative cancers, chemotherapy is the most effective means available for guarding against a return of the cancer. Since it can prolong your life, it would be unwise to refuse it without good reason. As described below, there is some room for choice between drug combinations in terms of specific side effects and length of treatment.

How is chemotherapy given?

There are two recommended combinations of drugs for treating women with node-negative breast cancer: CMF and AC. Both have proved effective.

The combination you choose is given in “cycles” as shown below.

- CMF (cyclophosphamide, methotrexate and 5-fluorouracil)

  With this choice, you would take cyclophosphamide by mouth every day for 2 weeks. On the first day of each of these weeks you would also receive methotrexate and 5-fluorouracil by intravenous injection. Then there is a 2-week “rest period” when no drugs are given. This completes 1 full cycle. Six cycles are given altogether, for a total of 6 months of treatment.

- AC (Adriamycin [doxorubicin] and cyclophosphamide)

  With this combination you do not have to take daily medication. Instead, you would receive the drugs by intravenous injection and then have a rest period of 21 days (3 weeks) when no drugs are given. On the 22nd day you would begin the second cycle. Four cycles are given altogether. The whole treatment lasts a little over 2 months.

What are the most common side effects of chemotherapy?

Side effects can include the following:

- Nausea and vomiting. If you are being treated with the CMF combination, nausea and vomiting will be mild to moderate and will last throughout treatment. However, it can be effectively relieved with medication. If you choose the AC combination, nausea and vomiting are likely to be more severe, but will be much briefer.
- Fatigue is common.
- Some weight gain may occur in about 14% of patients.
- Temporary hair loss. Hair loss is complete with AC. With CMF, 30% of patients have no hair loss at all, and only 40% have severe hair loss.
- Mild irritation of the eyes, the lining of the mouth and throat, and inflammation of the bladder.
- Temporary stoppage of monthly periods during treatment. In older women this may become permanent.
- Temporary suppression of the body's immune system during treatment. This increases the risk of infection. In a few individuals (2%), it may cause fever, requiring hospitalization.
- Severe side effects are rare, occurring in less than 1% of women receiving the usual doses of chemotherapy. However, they do happen, and chemotherapy can very rarely even be fatal. There is a very small risk of heart damage with AC. There is also a very small risk of leukemia developing in later life (perhaps 1 in every 1000 to 10 000 patients).

When should chemotherapy begin?

Chemotherapy should begin as soon as possible after your operation, usually within 8 weeks.

If I take chemotherapy, do I need any other treatment?

If you have a lumpectomy, radiotherapy will also be recommended. If you are having chemotherapy, the radiotherapy is usually delayed until the chemotherapy is finished. For more information on radiotherapy, see guideline 6 in this series.

Hormonal therapy

My doctor has recommended hormonal therapy. What does this mean?

The ovaries produce hormones such as estrogens, which can encourage the growth of breast cancers, especially those that are ER positive. Hormonal therapy with the drug "tamoxifen" interferes with this process without stopping the body's hormone production.

Tamoxifen has been found to prolong life in women with breast cancer, and it also reduces the chances of getting cancer in the opposite breast.

For how long should tamoxifen be taken?

It is recommended that you take the standard dose of tamoxifen (20 mg) by mouth every day for 5 years.

What are the side effects of tamoxifen?

Tamoxifen can cause temporary hot flashes in up to 20% of patients. Blood clots in the veins will develop in about 1 in every 100 patients taking tamoxifen. Rarely, these may pass into the lung, endangering life. Very rarely (about 1 woman in every 500 treated), tamoxifen can cause cancer in the lining of the uterus (endometrial cancer). For this reason, women taking tamoxifen should promptly report any vaginal bleeding — even slight spotting. Very rarely tamoxifen can cause cataracts.

Tamoxifen lowers the chance of cancer in the opposite breast and reduces the risk of osteoporosis — a common cause of "brittle bones" and fractures in postmenopausal women.