

Appendix 2

Questions and answers on chemoprevention and breast cancer

A guide for women and their physicians

Is this guide for me?

This guide is for women who have never had breast cancer and are thinking about taking a drug called tamoxifen to prevent breast cancer. If you are concerned about your risk of getting breast cancer, you may want to read on. Note that this guide is about taking tamoxifen to prevent breast cancer — it does *not* cover other ways to prevent breast cancer.

What is chemoprevention?

Chemoprevention refers to the use of medications to reduce a person's chance of developing cancer. You and your doctor may want to discuss chemoprevention if your risk of breast cancer is higher than the risk of other women your age.

Estrogen plays an important role in the development of breast cancer. Drugs that can block the action of estrogen have been studied to see if they can prevent breast cancer. Two of these drugs are tamoxifen and raloxifene.

What is tamoxifen?

Tamoxifen can affect the growth of cancer cells by blocking estrogen. The use of tamoxifen to prevent breast cancer has developed from its use to treat women with breast cancer. Research has shown that women with early breast cancer who take tamoxifen as part of their cancer treatment have a reduced risk of recurrent breast cancer. Studies have also shown that women with breast cancer treated with tamoxifen have a reduced risk of cancer in the opposite breast.

What have researchers learned about tamoxifen?

Three studies have examined tamoxifen for breast cancer prevention: the National Surgical Adjuvant Breast and Bowel Project P-1 (NSABP P-1) Study, which took place in Canada and the United States, the Italian Tamoxifen Prevention Study and the Royal Marsden Hospital Trial, which took place in the United Kingdom. All of the studies compared women taking tamoxifen and women taking an inactive drug called a "placebo."

Women with a higher risk of breast cancer who took tamoxifen in the largest trial (the NSABP P-1 study) had a significant reduction in breast cancer events (about 50%). However, women in the 2 smaller trials (Italian and Royal Marsden) did not. At this time we do not know if taking tamoxifen will increase a woman's chance of living longer.

Women taking tamoxifen were more likely than those taking a placebo to experience problems with stroke and blood clots in the lung or leg veins. In the NSABP P-1 study, there was an increase in cases of uterine cancer among women taking tamoxifen.

What are the benefits and risks of using tamoxifen for chemoprevention?

Tamoxifen can reduce the chance of breast cancer developing

in women at higher risk of the disease. It can also cause harmful side effects. Side effects associated with the use of tamoxifen include stroke, blood clots in the lung or leg veins, cancer of the uterus, hot flashes and vaginal dryness. Obviously some of these effects are more serious than others.

In general, the likelihood of some of the side effects increases with a woman's age. The benefit of protection against breast cancer is more likely to outweigh the risks in women aged 35 to 50. As age increases, the risk of side effects (especially stroke and blood clots in the lung) will increase, and at some point outweigh, the potential benefits of taking tamoxifen.

How do I find out about my risk of breast cancer?

"Risk" is the likelihood that a particular disease will develop in a particular person during a particular time. Determining risk is not easy. Your doctor will assess your risk of breast cancer by looking at a number of factors, including the following:

- Your age
- When you had your first menstrual period
- When you had your first child
- Whether you have had a biopsy for breast cancer
- Whether you have a close relative (mother, sister or daughter) with breast cancer
- Your ethnic origin

What is the Gail risk assessment index?

The Gail risk assessment index is a model used to estimate an individual woman's risk of breast cancer. The index uses a series of risk factors (age, age at first period, age at first live birth, number of breast biopsies, family history and ethnic origin) to calculate a "baseline risk." This is a woman's chance of invasive breast cancer developing over the next 5 years and over her lifetime.

For example, if your baseline risk of breast cancer is estimated to be 2%, during a 5-year period you have a 2% chance of breast cancer developing (and a 98% chance of the disease *not* developing). Another way to think about this is that, in the next 5 years, breast cancer would develop in 2 out of 100 women like yourself, and it would not develop in 98. Your individual risk is then compared with the risk of women the same age considered to be at *average* risk of breast cancer. For example, although your risk of breast cancer might be 2%, the risk of women in your age group with average risk factors might be 1%.

If you and your doctor are concerned that you may be at increased risk of breast cancer, the risk assessment index can help you begin thinking and talking about chemoprevention (see the Breast Cancer Risk Assessment Tool at <http://bcra.nci.nih.gov/brc>).

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Should the Gail risk assessment index be used routinely to make treatment decisions?

No, a family physician should not use the Gail index on every woman. Although this index was used for enrolling women in the NSABP P-1 study (the one study that showed a potential benefit of tamoxifen use in preventing breast cancer), it has not yet been evaluated for routine use in your physician's office. In addition, you should know that the Gail index was developed using information from a large number of white women and a very small number of non-white women; it is unknown whether this model can be used with the same degree of accuracy in women of all ethnic origins. However, when a woman or her physician are concerned about her increased risk of breast cancer, the index can be useful in deciding whether to further discuss the benefits and harms of taking tamoxifen.

What information will I need to decide about using tamoxifen to prevent breast cancer?

First, you will need to know more about your risk of developing breast cancer during the next 5 years. You and your doctor or a specialist at a counselling centre might use the Gail index to estimate your risk. You will then need to consider evidence from the NSABP P-1 trial, in which women with a baseline risk of at least 1.66% at 5 years, according to the Gail index, participated. Results from the study suggest that taking tamoxifen will reduce your risk. Next you will have to learn more about the possible benefits of taking tamoxifen and the possible harms of side effects.

I am at low or normal risk of breast cancer (less than 1.66% at 5 years, according to the Gail index). Should I consider chemoprevention?

No. Researchers and physicians do not recommend chemoprevention for women at low or normal risk of breast cancer because the potential for harm outweighs the possible benefit of tamoxifen therapy.

I am at higher risk for breast cancer (1.66% or greater at 5 years, according to the Gail index). Should I consider chemoprevention with tamoxifen?

Yes, but you will need to discuss the possible effects of tamoxifen with your doctor and perhaps with a specialist at a counselling centre. You will want to consider how you might be affected by breast cancer versus how you might be affected by a stroke or blood clots in the lung. You will also want to consider quality-of-life issues such as tamoxifen-associated hot flashes and vaginal dryness. You will need to weigh the potential benefits of chemoprevention against the potential harms of side effects. The value you place on the different possible outcomes will influence your choice. For example, you might feel that a tamoxifen-induced stroke would be far worse than breast cancer and decide against taking tamoxifen. Another woman might feel that breast cancer would be far worse than a stroke and decide to take tamoxifen. You will have to determine the value you place on the possible consequences of taking or not taking tamoxifen after a full discussion with your doctor. If you decide to take tamoxifen, it is recommended that you take it for 5 years.

Should I consider chemoprevention with the drug raloxifene?

Raloxifene, like tamoxifen, can block estrogen and affect the growth of cancer cells. It was originally studied in women with osteoporosis — a common cause of brittle bones and fractures in postmenopausal women. One study has suggested that raloxifene reduces the risk of the development of breast cancer. Although raloxifene research is promising, a study designed specifically to evaluate its use for the prevention of breast cancer has not been completed yet. A trial that will compare raloxifene and tamoxifen for breast cancer prevention (NSABP STAR trial) is underway. Researchers hope it will answer some of the many questions about the effects of raloxifene. Current evidence does not support the use of raloxifene for chemoprevention of breast cancer outside of a clinical trial.
