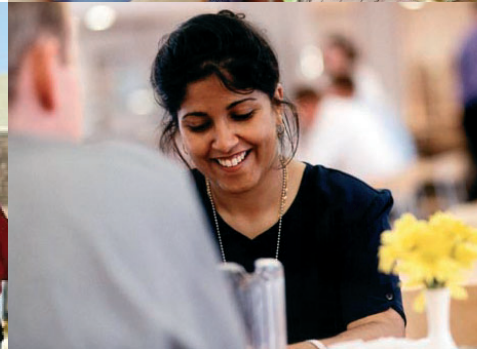


Young women and breast cancer:



The facts and your choices

Patient information booklet for premenopausal women with hormone receptor-positive breast cancer



This patient information booklet is intended to provide you with some information to help you choose a treatment after surgery for your hormone receptor-positive breast cancer. The exact treatment you receive should be decided in consultation with your doctor.

This patient leaflet has been developed by AstraZeneca in association with representation from several breast cancer advocacy groups and Mr Richard Sainsbury, Breast Cancer Surgeon, University College, London.

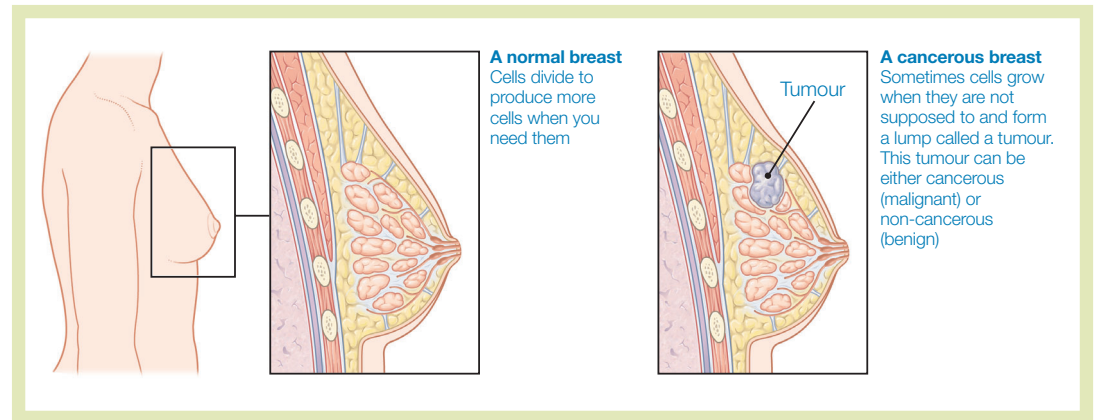
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Breast cancer: the facts

Your body is made up of individual units called cells. All cells divide to produce more cells when you need them. However, sometimes cells divide when they are not supposed to. If these cells grow out of control they can form a lump called a tumour, which can be either cancerous (malignant) or non-cancerous (benign). A cancerous tumour is very small when it starts, but may increase in size over time.

A normal breast and a cancerous breast



In some cases, breast cancer cells may not stay in the breast, but spread to other parts of the body ('metastasis'). This spread can damage normal tissues, such as the bones, lungs or liver, leading to problems at these sites.

Breast cancer: the figures

- Each year, more than 700,000 new cases of breast cancer are diagnosed worldwide.
- Breast cancer is the most common form of cancer among women in Western countries, accounting for 18% of all female cancers.
- One in nine women will develop breast cancer during their lifetime; one in four of these women will be under 50 years old.
- Each year, almost 8000 women under 50 years old are diagnosed with breast cancer.

The risk of breast cancer increases with age, but the incidence of breast cancer is increasing, particularly among young women that are premenopausal (women under 50 years of age who are still having their periods).

Metastasis:

Spread of cancer from one part of your body to another part. When there is one site of spread, it is called metastasis. When the cancer has spread to more than one part of your body, it is called metastases.

Premenopausal:

The time of life from when your periods start (puberty) to when they begin to stop (menopause).

What stage is my breast cancer?

Before treating your breast cancer, your doctor must determine the stage of your disease. This is done by measuring the size of the tumour and assessing whether your cancer has spread to other parts of your body.

Localised breast cancer:

Your tumour is confined entirely to where it began. There is no sign that your tumour has spread to other areas.

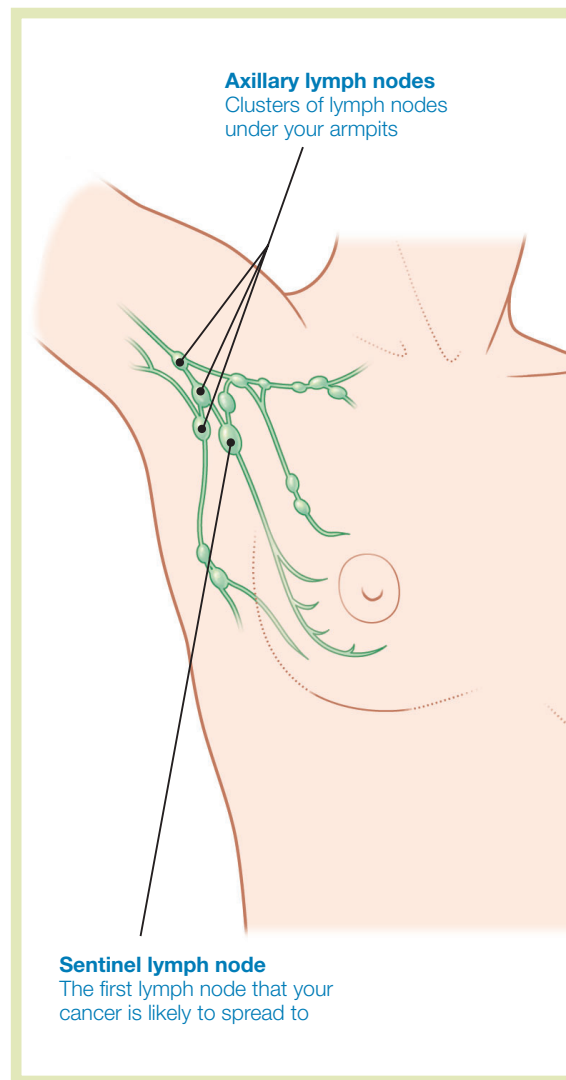
Lymph nodes:

Glands located throughout your body that store special cells that filter out and trap bacteria, viruses, and other unwanted substances, to make sure they are safely eliminated from your body. Clusters of lymph nodes can be found in your armpits ([axillary lymph nodes](#)), groin, neck, chest and abdomen. The first lymph node that your cancer is likely to spread to is referred to as the [sentinel lymph node](#).

Stages of breast cancer

Stage 0	Your cancer has not spread (<i>in situ</i>), for example, ductal carcinoma <i>in situ</i> .
Stage I	Your tumour is localised, is less than 2 cm wide and has not obviously spread.
Stage II	Your tumour is small (2–5 cm), has spread to armpit (axillary) lymph nodes, or both.
Stage III	Your tumour size is larger than 5 cm and has probably spread to axillary lymph nodes; may have spread to your chest or overlying skin.
Stage IV	Your tumour is of any size, usually affecting lymph nodes; has spread to other parts of your body such as bones, lungs or liver ('secondary tumours').

The location of your axillary and sentinel nodes



What is my tumour type?

In addition to the stage of breast cancer, the type of tumour you have differs between women. One of the main factors determining what type of treatment you will receive is based on what is making the tumour grow.

Hormones are chemicals produced naturally in the body and that circulate in the blood. Some cancer cells need the natural female sex hormone oestrogen to stay alive. Blocking the production or action of this hormone using 'hormonal therapies' can prevent or help slow growth of tumours by starving them of the oestrogen they need to grow. As a result, the cancer cells shrink or die.¹

Hormones: the facts

- In premenopausal women, hormones stimulate approximately 60% of breast cancers to grow.² These types of tumours are called 'hormone receptor-positive' – also known as 'oestrogen receptor-positive', 'hormone-sensitive' or 'oestrogen-sensitive' tumours.
- Hormone receptor-positive tumours are stimulated to grow by the natural female hormone oestrogen.
- The main source of oestrogen and the levels in your body differ depending on whether you are premenopausal or postmenopausal.
 - In premenopausal women, the ovaries produce most of your oestrogen.
 - In postmenopausal women, fat, muscle, liver, adrenal glands and the breast itself produce most of your oestrogen. Only a small amount of oestrogen is produced by your ovaries.

Oestrogen:

A female sex hormone that is made mainly in the ovaries of premenopausal women and in muscles and fat tissue in postmenopausal women.

Ovaries:

Oval structures in which your eggs are developed. The ovaries are located in the pelvis, one at each side of your womb.

Premenopausal:

The time of life from when your periods start (puberty) to when they begin to stop (menopause).

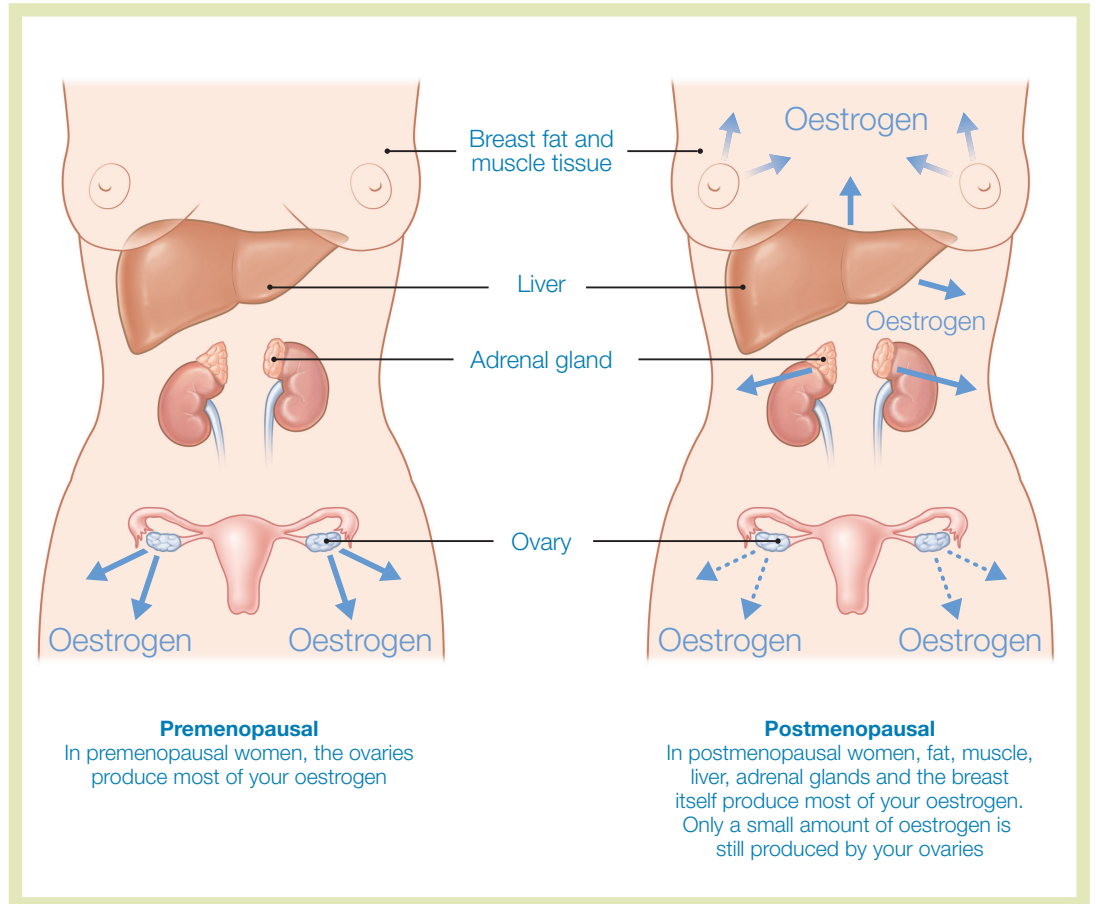
Menopause:

The time of life when your body changes from having monthly periods to them stopping permanently. Also called 'the change of life'.

Postmenopausal:

The time of life from when you experience no more periods.

Major sources of oestrogen in pre- and postmenopausal women



The main sources of oestrogen in premenopausal and postmenopausal women therefore differ and thus the choices for treatment are somewhat different. This booklet focuses on providing you, a premenopausal woman with hormone receptor-positive breast cancer, with some information to help you choose a treatment to reduce the risk of your cancer coming back after surgery.

Adjuvant therapy (also known as additional therapy):

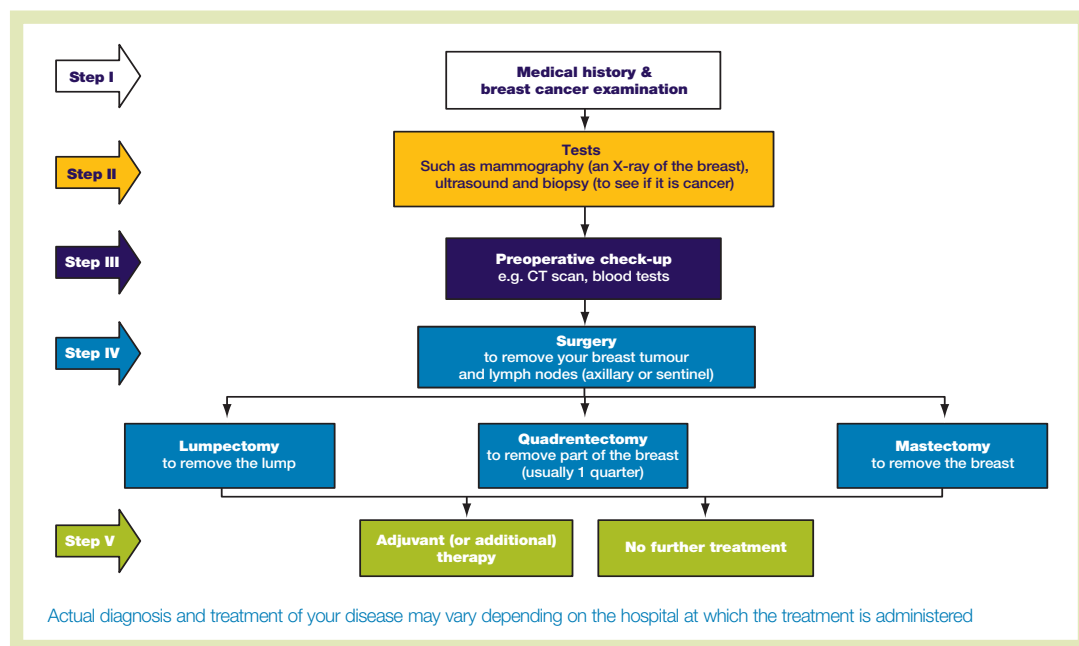
Treatment usually given after surgery to destroy any cancer cells still remaining in your body. It is given to help reduce the possibility of the cancer coming back or spreading somewhere else. Adjuvant therapy may include radiotherapy, chemotherapy, hormonal therapy or further surgery.

How will my doctor treat my breast cancer?

The type of treatment you receive for breast cancer will depend on the stage at which it is diagnosed, the type of breast cancer that you have, whether you have reached the menopause, and your own personal circumstances.

The aim of breast cancer treatment is to remove all the cancer from your breast and prevent it from coming back.

Possible treatment and diagnosis of your breast cancer



When discussing possible surgery options with your doctor, ask about sentinel lymph node removal (dissection of the first lymph node that your cancer is likely to spread to) as an alternative to the standard axillary lymph node removal (dissection of the cluster of lymph nodes under your armpits). Sentinel lymph node removal involves your surgeon only removing and analysing the sentinel node (and those closest to it) as this is the most likely lymph node to contain cancer cells that are breaking away from your tumour and travelling to other parts of your body. Axillary lymph node removal involves removing ten or more lymph nodes under your arm and analysing all of them for cancer.

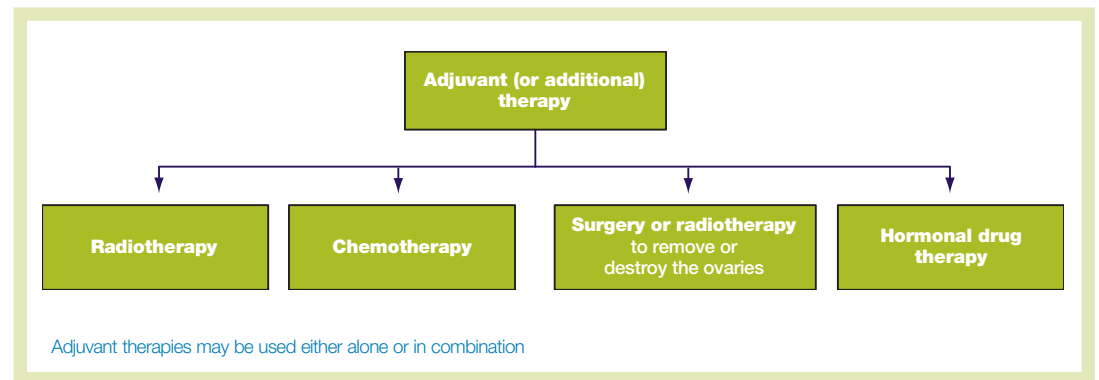
What is adjuvant therapy?

After surgery, microscopic deposits of the disease, undetectable by current methods, may sometimes remain behind. These deposits may, after several years or even decades, develop into a clinically detectable tumour. To reduce the risk of the disease coming back you may be given the option of additional therapy, also known as adjuvant therapy. The longer you remain free from cancer, the less likely it is that your disease will return in the future.¹

What are my treatment choices?

There are several different types of adjuvant therapy:³

Adjuvant treatment options



What are my treatment choices with non-hormonal therapies?

Radiotherapy

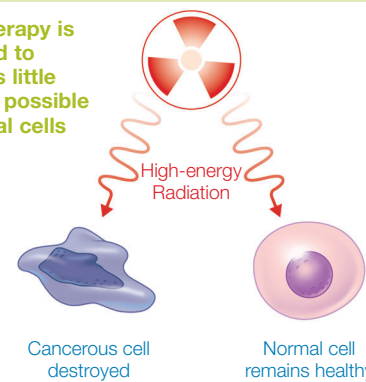
Radiotherapy uses carefully measured doses of X-rays to treat where the breast tumour was situated as well as the surrounding area. The doses given are more intense than a mammogram or other common types of X-ray, as they are precisely calculated to destroy any cancer cells that may remain in your body after surgery.

There are a few side effects of radiotherapy such as:

- reddening of the skin (erythema or burn), feeling sick and tiredness.⁴

Most women find they can continue with their routine life during radiotherapy.

Erythema:
A redness of the skin.



Radiotherapy is designed to cause as little harm as possible to normal cells

Radiotherapy is given every working weekday for several weeks and can be given

- after surgery (adjuvant therapy)
- before surgery to shrink the tumour (neoadjuvant therapy)

Side effects of radiotherapy may include

- sensitive skin
- swelling
- tiredness
- redness of skin (erythema) or burn

Side effects stop after treatment ends

Chemotherapy

Chemotherapy is a widely used and effective treatment for breast cancer.³ It can be used before surgery to shrink a tumour in order to make surgery easier. It is used after surgery for tumours that are both hormone receptor-positive (where oestrogen is responsible for making the tumour grow) and negative (where other factors are making the tumour grow).

Chemotherapy: the facts

- Chemotherapy works by destroying all rapidly growing and dividing cells. It kills cancer cells that may have remained in the body after surgery, including cancer cells that have already spread to other parts of the body ('metastasised').
- Chemotherapy usually involves five different types of drug that can be used in combinations of two or more:³
 - 5-fluorouracil (5-FU)
 - Cyclophosphamide
 - Methotrexate
 - Anthracyclines (e.g. doxorubicin, epirubicin)
 - Taxanes (e.g. docetaxel, paclitaxel)

When chemotherapy is given, you will usually need to attend the day hospital or ambulatory care clinic as an outpatient. You will be checked by a doctor or nurse to ensure you have no signs of infection, and a blood sample will be taken. If your blood test is satisfactory, and there are no other reasons to delay or stop chemotherapy, then the treatment will be given (usually through a 'drip') before you go home.

Some types of chemotherapy need to be given over a longer period of time and you may go home with a small pump (about the same size as a small music personal stereo) to give the chemotherapy over a period of days.

Chemotherapy works on dividing cells (e.g. in your hair and digestive system) and therefore its side effects can occur in various parts of the body. The side effects that you may experience depend on the type of chemotherapy you receive and include:

- hair loss, feeling sick, being sick, tiredness, sore mouth, numbness, tingling or burning of the hands or feet, diarrhoea, joint or muscle pain, and increased risk of infection.⁴ Additional treatments to reduce these side effects may be given before chemotherapy, such as anti-emetics.

Chemotherapy may also prevent your ovaries from working, causing your periods to stop permanently ('amenorrhoea') when you have not yet reached menopause. When your periods stop you will be unable to get pregnant (infertile). You may also be at increased risk of osteoporosis (fragile bones) and heart problems. Some women, however, only experience their periods stopping temporarily and find they return in a few months or as long as a year or more. The chance of your periods returning depends on your age (less likely in women over 40 years of age), and on the type of chemotherapy you receive.⁴

If you want the chance of becoming pregnant after your treatment for breast cancer what are the options?

- to consider not having chemotherapy.
- to opt for a type of chemotherapy that may be less harmful to the ovaries.
- to receive drugs before your treatment starts that stimulate your ovaries to produce eggs, which are then collected and frozen until you are ready to have a baby.
- to consider egg donation after treatment.
- to have a small piece of your ovary taken away before chemotherapy, which is then put back after your treatment has finished. The small piece of ovary will be frozen to protect it during your course of chemotherapy. This technique is, however, in a very early stage of research.
- to receive a drug during chemotherapy to protect your eggs from damage. This is also currently under investigation.

You should discuss these options with your doctor before your treatment starts.

Side effects from chemotherapy are an important consideration and you need to discuss these thoroughly with your doctor before treatment begins.

Anti-emetic:

A drug used to control nausea and vomiting.

Osteoporosis:

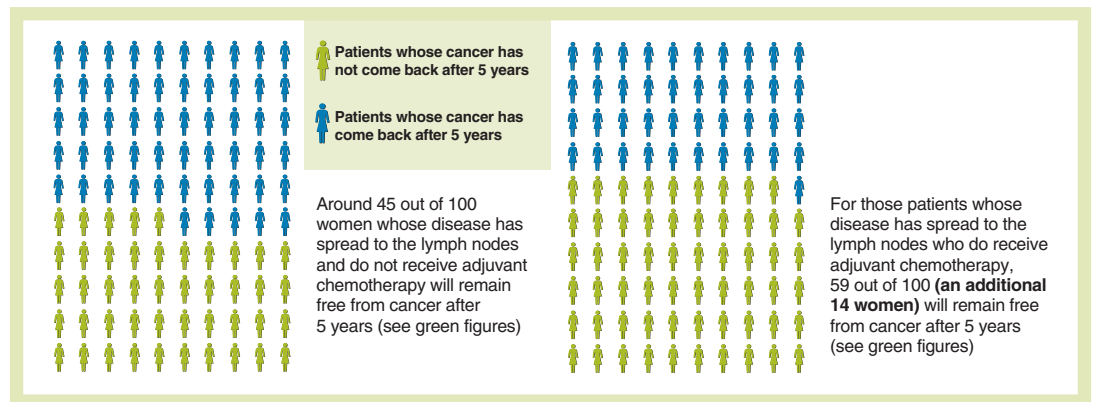
This is when your bones become thinner and more fragile. When this happens, your bones are more likely to break.

Chemotherapy: Clinical trial data

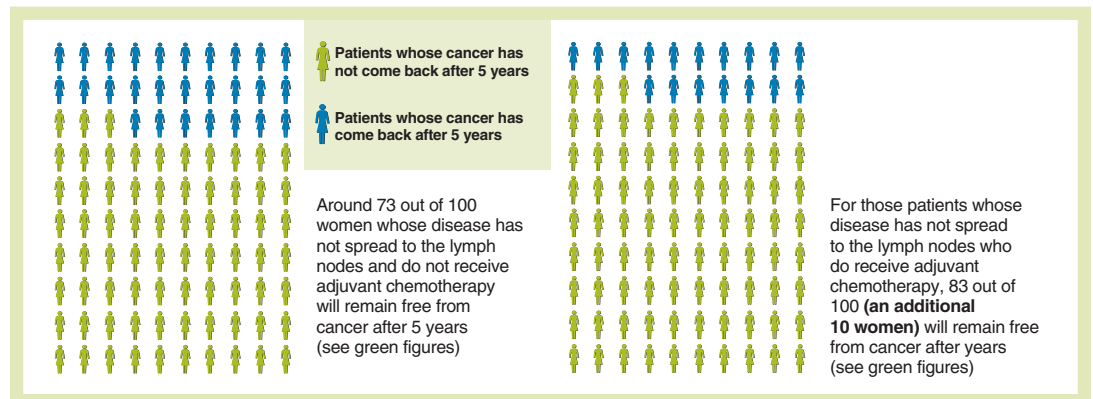
- Clinical trials have shown that chemotherapy reduces the risk of your disease coming back by about one-third, compared with if you had received no treatment after surgery.³

This means that for those patients whose disease has spread to other parts of the body (i.e. the lymph nodes), chemotherapy allows an **additional** 14 out of 100 patients to be free from cancer at 5 years following chemotherapy, compared with those that do not have any adjuvant treatment. If the disease has not spread to the lymph nodes, chemotherapy prevents the disease coming back within 5 years in an **additional** 10 out of 100 of patients compared with those that have received no adjuvant treatment.³

The risk of your disease coming back with and without adjuvant chemotherapy in women whose disease has spread to the lymph nodes



The risk of your disease coming back with and without adjuvant chemotherapy in women whose disease has not spread to the lymph nodes



Receptor:

For oestrogen to work, it must bind to a specific molecule inside the cell called a receptor. If oestrogen binds to its receptors in tumour cells, growth is encouraged and your cancer will increase in size. If oestrogen is stopped from binding to its receptors in tumour cells, then your cancer will be prevented from growing.

hormone receptor-positive:

Your tumour has a large number of oestrogen and/or progesterone receptors (also known as oestrogen receptor-positive and progesterone receptor-positive, respectively).

Hormone receptor test:

to determine whether you are hormone receptor-positive and may respond to hormonal therapy.

Surgery or radiotherapy to remove or destroy the ovaries

As some breast cancers require the natural female hormone oestrogen for growth, stopping oestrogen production will cause the cancer cells to die or stagnate.¹ In premenopausal women, oestrogen is mainly made in the ovaries. Therefore, permanently destroying the tissue of the ovaries, by using radiation or by removing them surgically (also known as 'oophorectomy'), will prevent oestrogen production and cause the cancer cells to die.

Preventing oestrogen production, however, may cause premature menopause. An early menopause may cause short-term symptoms such as hot flushes, sweats, vaginal dryness and loss of sex drive. In contrast to a natural menopause, these symptoms tend to come on rather abruptly and be more intense, and can increase your chance of developing osteoporosis and heart problems.

Another side effect of preventing oestrogen production is infertility. Permanent oestrogen blockade by radiation or surgery (and some chemotherapies) results in permanent menopause and a loss of fertility.

Adjuvant treatment choices with hormonal therapies

Hormonal therapy works by stopping your cancer from growing and blocking the production or action of oestrogen.¹

Hormonal therapy

- A 'hormone receptor' test will be performed on a sample of your tumour that has been removed to determine whether your cancer is hormone receptor-positive.
- The 'hormone receptor test' measures the presence of oestrogen and progesterone receptors in your tumour cells. The presence of these receptors is important because they indicate whether your cancer is likely to respond to hormonal therapies.
- Hormone therapy is recommended if your tumour is growing in response to hormones (i.e. hormone receptor-positive). Whether you receive hormonal therapy will also be dependent on the size and spread of the cancer as well as your own personal preference.
- If you have high levels of both oestrogen and progesterone receptors in your tumour, then it is likely that the risk of your cancer coming back will be reduced if you receive hormonal therapy. The fewer receptors you have, the less likely it is that hormonal therapy will work for you.
- Your doctor may present you with your oestrogen and progesterone receptor levels as a percentage. If you have a high percentage of oestrogen and progesterone receptors, your tumour is 'oestrogen receptor-positive' as well as 'progesterone receptor-positive' and will be called a 'hormone receptor-positive breast cancer'. In this instance your tumour is very likely to respond to hormonal therapy.

Tamoxifen

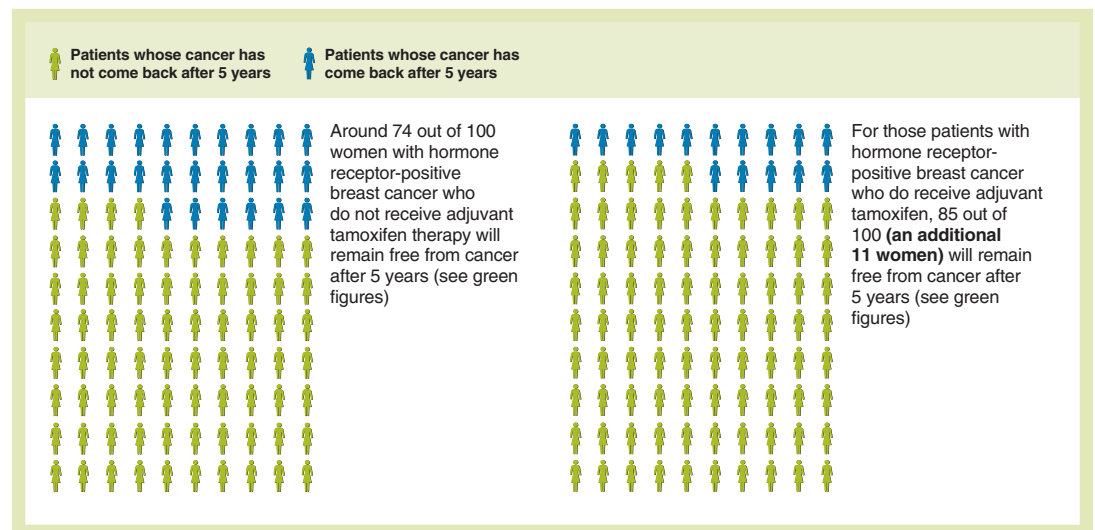
Tamoxifen is commonly used to treat hormone receptor-positive breast cancer. It is given as a once-daily tablet for 5 years. Tamoxifen works by blocking the action of oestrogen in the tumour cell, which starves the tumour and prevents it from growing.

Tamoxifen: clinical trial data

- 5 years of tamoxifen reduces the risk of your disease coming back compared with no treatment after surgery.³
- Tamoxifen appears to be at least as good as chemotherapy at preventing the disease returning if you have hormone receptor-positive disease.
- For premenopausal women, tamoxifen reduces the risk of your disease coming back by almost half compared with having no treatment.

This means that 5 years after surgery, an **additional** 11 out of 100 patients will still be free from cancer if they are treated with tamoxifen, compared with those that do not take tamoxifen. This benefit is the same for patients in whom the disease has spread to the lymph nodes and in those where it has not.³

The risk of your disease coming back with and without adjuvant tamoxifen in women with hormone receptor-positive breast cancer



Endometrial cancer:

Cancer of the lining of the womb.

Deep vein thrombosis:

Blood clotting in the veins of the inner thigh or leg.

Gonadotropin-releasing hormone analogue:

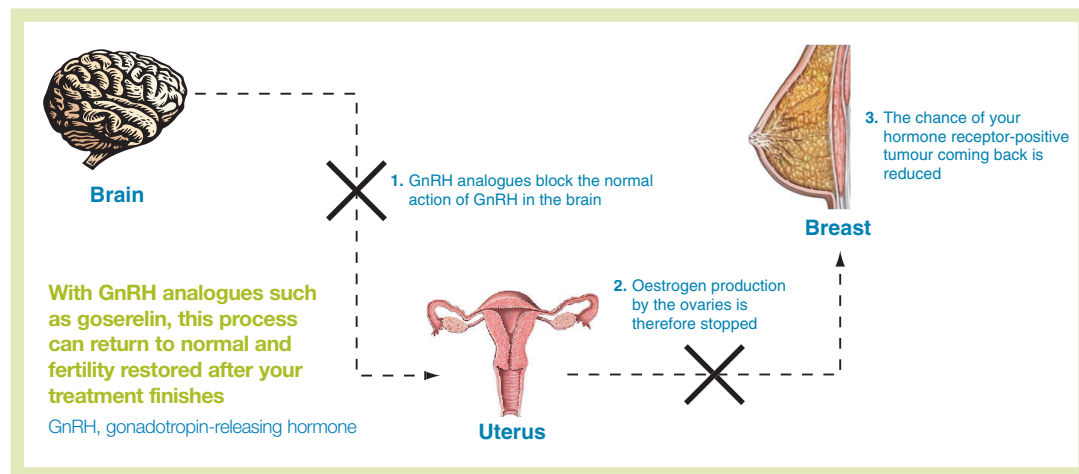
An artificially made hormone that blocks oestrogen production by the ovaries.

Side effects of tamoxifen therapy are associated with its oestrogen-blocking action, and include many of the side effects associated with the menopause such as hot flushes.⁴ In addition, tamoxifen is known to increase the risk of endometrial cancer (or cancer of the womb) by about 4 times the normal rate, although this is still a rare event. Patients are also slightly more likely to have a clot (deep vein thrombosis) and should stop tamoxifen for 4 weeks prior to any surgery.⁴

Gonadotropin-releasing hormones

A hormone in the brain called gonadotropin-releasing hormone (or GnRH) controls the production of oestrogen by the ovaries. Drugs that are artificial versions of GnRH are called 'GnRH analogues' and work by blocking the normal action of GnRH in the brain, which in turn blocks oestrogen production. Drugs such as goserelin act in this way and produce a 'reversible menopause' in the majority of premenopausal women. Goserelin is given as an injection once a month, usually for 2–3 years.¹

How GnRH analogues work



GnRH analogues

- GnRH analogues such as goserelin are another way to reduce the chance of your cancer returning and may be administered after surgery either*:
 - alone^{5,6}
 - in combination with tamoxifen instead of chemotherapy⁷
 - in combination with tamoxifen following chemotherapy.⁸

*indications for use may vary between countries

As highlighted in the 'What are my treatment choices with non-hormonal therapies' section, side effects of preventing oestrogen production are menopausal symptoms such as hot flushes, sweats, vaginal dryness and loss of sex drive. In contrast to a natural menopause, these symptoms tend to come on rather abruptly and be more intense, and may be associated with long-term side effects, such as increased risk of osteoporosis and heart disease. Infertility is also another side effect of preventing oestrogen production. Permanent oestrogen blockade by radiation, surgery and some chemotherapies results in permanent menopause and loss of fertility. If oestrogen production has been stopped using a GnRH analogue, however, infertility may be temporary.

Aromatase inhibitors

Aromatase inhibitors are a new class of drug that are effective for the treatment of breast cancer in *postmenopausal* women.⁹⁻¹² They work by blocking oestrogen production in fat, liver and muscle tissues (where the majority of oestrogen is made in postmenopausal women) but they do not block oestrogen production by the ovaries (where the majority of oestrogen is made in premenopausal women). This is why aromatase inhibitors are only appropriate for women whose ovaries are no longer producing oestrogen (see 'What is my tumour type' section). Currently, trials are ongoing to assess the benefits of giving aromatase inhibitors to patients who are receiving treatment with GnRH analogues, such as goserelin, to suppress ovarian oestrogen production.

Side effects of aromatase inhibitors include hot flushes, vaginal dryness, feeling sick, constipation or diarrhoea, hair thinning, tiredness, headaches, and joint and muscle pains.⁹⁻¹²

Summary of ways to stop oestrogen production in pre- and postmenopausal women

In premenopausal women oestrogen can be stopped by:

- blocking its action in breast cancer cells (e.g. with tamoxifen)
- radiation to the ovaries
- removal of the ovaries with surgery (oophorectomy)
- blocking the ovaries producing oestrogen (e.g. with GnRH analogues)

In postmenopausal women oestrogen can be stopped by:

- blocking its action in breast cancer cells (e.g. with tamoxifen)
- blocking its production by the fat, muscle, adrenal glands and liver cells (e.g. with aromatase inhibitors)

The right treatment for you should be decided upon consultation with your doctor

GnRH, gonadotropin-releasing hormone

Whichever adjuvant treatment you choose for your hormone receptor-positive breast cancer, you will require regular checkups by your doctor.

Summary

It is important to remember that even without additional treatment after surgery, about 60% of women with early breast cancer remain free from disease for more than 5 years.

The treatment that is appropriate for you will depend on a number of factors, for example, whether the disease has spread to your lymph nodes and the size and grade of the tumour. You may have either chemotherapy or hormonal treatment, or you may need a combination of treatments or even no treatment at all. You should discuss treatment options with your doctor and make a decision that best suits your needs.

How do I make my decision?

The variety of treatment options can be confusing; there are many factors to take into consideration, and you should discuss these options with your doctor.

There are important things that you, as the patient, may want to consider concerning your treatment. These factors vary from patient to patient, and it will help if you think about some of the following:

- How the treatment will impact on your daily life.
- How the treatment will impact on your family life.
- Which potential side effects of treatment may trouble you the most.
- How long will the treatment last.
- Whether you hope to have children in the future.

You have choices

Questions for your doctor

- What stage is my breast cancer?
- What are my options for treatment?
- Will I need radiotherapy? To what area of the body and for how long?
- Do I need chemotherapy?
- What type or combination of chemotherapy would be best for me?
- Is hormone therapy right for me? If so what are the options and how long will I need to take them for?
- What are the potential side effects of my treatment?
- How will this treatment affect my daily life? Will I be able to work, exercise, and perform my usual activities?
- How can I reduce the side effects before, during and after my treatments?
- Are there health and other risks of being pregnant once I am free from breast cancer?
- How quickly will my treatment begin?
- Can you talk to me about the risk of my disease coming back if I have no treatment?
- What is my nodal status and how does it affect the risk of my disease coming back?
- What is the risk of my disease coming back if I have treatment with chemotherapy or hormonal therapy?
- Where can I seek emotional support for me and/or my family if needed?

Questions for my doctor

Additional resources

WEBSITES

The following websites will provide you with additional information on the treatment of your breast cancer as well as provide online support groups:

Association Of Cancer Online Resources
www.acor.org

Breakthrough Breast Cancer
www.breakthrough.org.uk

Breast Cancer Source
www.breastcancersource.com

Lavender Trust At Breast Cancer Care
www.lavendertrust.org.uk

Cancer BACUP
www.cancerbacup.org.uk

Guide To Internet Resources For Cancer
www.cancerindex.org

National Cancer Institute
www.nci.nih.gov
www.cancer.gov

National Breast Cancer Awareness Month
www.nbcam.org

Susan Komen Breast Cancer Foundation
www.komen.org

The Young Survival Coalition
www.youngsurvival.org

Y-Me National Breast Cancer Organization
www.y-me.org

PATIENT FORUMS

The following patient forums will enable you, together with other breast cancer patients and survivors, to discuss the latest developments in breast cancer research and treatment.

Australia

Breast Cancer Network
www.bcna.org.au

Canada

Willow Breast Cancer Support &
Resource Services
www.willow.org

Quebec Breast Health Network
www.rqss.qc.ca/rqss

France

Europa Donna
www.europadonna.fr

Germany

Mamazone
www.mamazone.de/mamazone.html

Italy

Europa Donna
www.europadonna-italia.it

Japan

Akebonokai
www.akebono-net.org/contents/e_index.html

The Netherlands

Borstkanker Vereniging
www.kankerpatient.nl

Sweden

The Swedish Association of Breast Cancer
Societies
www.bro.org.se

United Kingdom

Breast Cancer Coalition
www.natlbcc.org

United States

Patient Advocate/Research Team (PART)
http://spores.nci.nih.gov/part/index_part.html

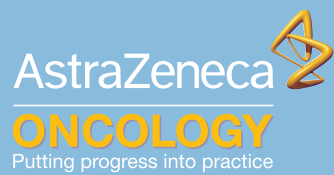
Breast Cancer Coalition
www.natlbcc.org

Worldwide

Europa Donna
www.cancerworld.org

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