

Advanced Breast Cancer: Treatment Overview

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1. Planning treatment with your medical support team

A team of specialists will work together to make sure you have the best treatment and care.

This medical team may include:

- A cancer doctor (oncologist) who specialises in treating cancer
- A specialist breast care nurse who provides information and support
- A specialist surgeon (if needed/beneficial)
- A doctor or nurse who specialises in controlling symptoms (pain and palliative care specialist)
- A radiation specialist who analyses x-rays and scans.

Your medical team:



The medical team may also include other healthcare professionals, such as a physiotherapist, dietitian, occupational therapist, psychologist, social worker or counsellor.

Your specialist doctor or nurse will discuss the benefits and disadvantages of different treatments with you. Remember to ask questions about anything you don't understand or feel worried about. ([See more in our document on questions to ask your doctor](#)).

2. Treatment overview

The main aim of treatment for advanced breast cancer is to improve symptoms and therefore quality of life. By slowing the growth of, or shrinking your tumors, treatment may allow you to live for longer and feel better.

You may have various single or combined treatments one after the other to keep your cancer under control. In between treatments, women often find they can get on with their day-to-day life.

Your cancer doctor (oncologist) and specialist breast cancer nurse will involve you in treatment decisions. They will support you and, if needed, they can refer you for more specialised help in coping with your day-to-day activities and emotions.

Types of treatment

Control of symptoms is very important at all stages of your illness. This can be managed by many of your care team, including your GP, oncologists, specialist breast care nurse and palliative care specialist.

In addition to hospital or private clinic visits, specialist nurses are available on the telephone and may even visit you at home.

Treatment for advanced breast cancer may include one or more of the following:

- Anticancer drug therapy
 - Anti-hormone/endocrine therapy
 - Targeted therapy
 - Chemotherapy
- Radiotherapy
- Surgery
- Other medicines to help manage symptoms



Your doctor can refer you to a specialist doctor or nurse who is an expert in symptom control at any time during or after treatment. This helps make sure that any uncomfortable symptoms you have are well controlled.

Many people are worried about having cancer treatment, particularly because of the possibility of side effects. Side effects can usually be controlled. A decision to switch or stop treatment can be made if side effects are unbearable.

In addition, treatment may be stopped or changed when it is not working. Making treatment decisions in these circumstances is always difficult, and you may want to talk it over carefully with your cancer doctor, specialist nurse and family.

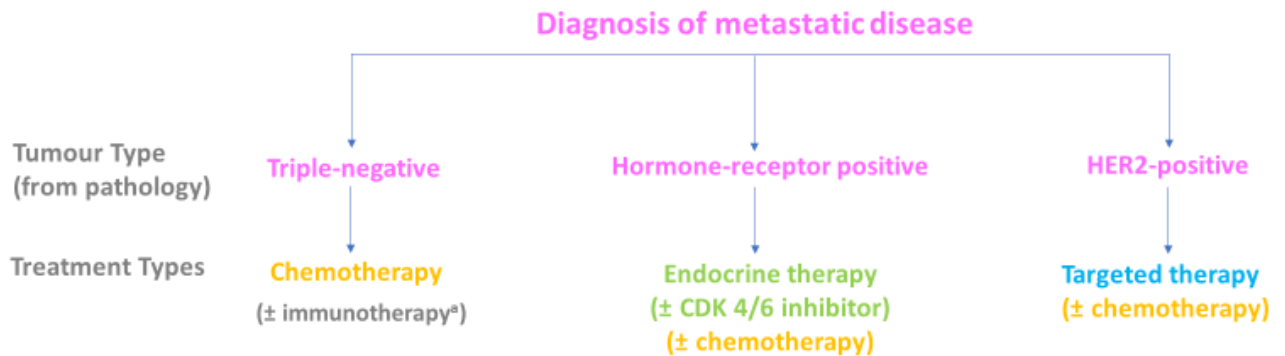
Should you decide not to have treatment or to stop treatment, you will be given supportive care, with medicines to control any symptoms. Experts in this area are sometimes called palliative care specialists.

2.1. Anticancer Drug Therapy

The treatment you have will depend on different factors such as:

1. Where the advanced cancer is in your body
2. Previous breast cancer treatments you have had and how long ago
3. Your symptoms and general health
4. Specific features of the cancer cells:
 - Hormone/oestrogen receptor (HR)-positive
 - Human epidermal growth factor receptor 2 (HER2)-positive
 - Triple-negative (not positive for either HR or HER2)

Overview of anti-cancer drug treatment options



^aImmunotherapy has proven beneficial in women with triple-negative breast cancer and is approved for use overseas. It is not currently funded in New Zealand.

Endocrine therapy for hormone receptor (HR)-positive disease

Hormones help control how healthy cells grow and what they do in the body. In hormone receptor-positive breast cancer, hormones, usually oestrogen, cause uncontrolled cell growth which leads to tumour formation.

Anti-oestrogen (endocrine) medications lower the level of oestrogen in the body or block it from acting on cancer cells. These medications only work for women who have hormone receptor-positive cancers.

Once your cancer has tested positive for hormone receptors, you will usually receive endocrine therapy as a first-line treatment. However, if you have tumours in your liver or lungs that are growing rapidly, you will receive chemotherapy and then endocrine therapy.

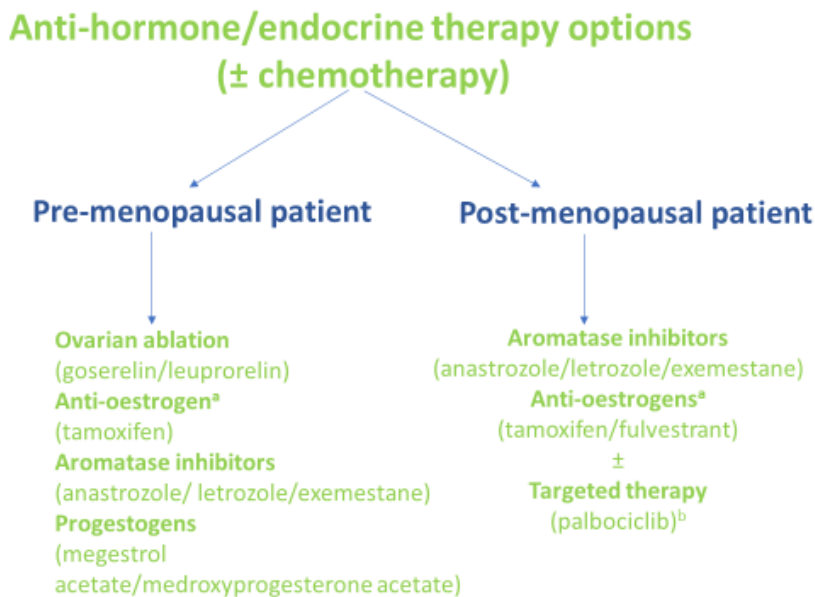
The type of endocrine therapy you will receive depends on:

- Whether you have been through menopause or not
- Other endocrine therapies you have already had, if any.

Endocrine therapies are usually given as tablets and are therefore easy to take. Any side effects are typically quite mild. A few things to be mindful of are as follows:

- Side effects may be more troublesome in the first few months, but they usually get better over time. If you continue to have problems, talk to your nurse or doctor. There are ways that side effects can be treated or managed.
- Some side effects are similar to menopausal symptoms and certain hormonal therapies cause a temporary or permanent menopause.

It takes a few weeks or months before your doctors can tell how well your treatment is working for you. If a treatment doesn't work, or stops working, your cancer doctor may prescribe another type.



^aAnti-oestrogens are also known as selective oestrogen receptor modulators (SERMs - tamoxifen) and oestrogen receptor downregulators (ERDs - fulvestrant)

^bPalbociclib (Ibrance[®]) is a targeted therapy which can be used in combination with hormone therapy to improve treatment response, there are several other drugs in this class which may be come available in New Zealand in years to come

Treatment options after the menopause (post-menopause)

Although the ovaries no longer produce oestrogen after the menopause, oestrogen is still produced in fat tissues/cells.

If you have been through menopause, you are post-menopausal, and your doctor may prescribe one of the following:

1. An aromatase inhibitor, such as anastrozole, letrozole or exemestane
2. An anti-oestrogen drug, such as tamoxifen or fulvestrant
3. A CDK 4/6 inhibitor (palbociclib)

Aromatase inhibitors

- Aromatase inhibitors block the aromatase enzyme which is responsible for making oestrogen in fatty tissue. These drugs are widely used in post-menopausal women. They are taken as a daily oral tablet. Side effects can include tiredness, joint and muscle pain, and hot flushes. They can also cause bone thinning (osteoporosis) so your doctor may prescribe drugs called bisphosphonates to protect your bones.

Anti-oestrogens

- Anti-oestrogens including tamoxifen and fulvestrant block the action of oestrogen at the cancer cell, thereby preventing tumor cell growth.
- Tamoxifen is the most widely used anti-oestrogen and is taken as a daily oral tablet.
 - Tamoxifen has been safely used in most patients for more than 50 years.
 - It may cause hot flushes and sweats, weight gain or tiredness.
 - There is a small increase in the risk of developing a blood clot in both pre- and post-menopausal women (similar to the risk with the oral contraceptive pill); however, this can be picked up early and is easily treated
 - The risk of developing endometrial cancer (cancer in the womb) is slightly increased by tamoxifen in postmenopausal women; however, this is very uncommon and easily detected.
 - It is important to be aware that when you take tamoxifen for advanced cancer in the bone, it may make the pain worse for the first few days, and then you will start to see an improvement.
- Fulvestrant is given as an injection once per month and has similar side effects to tamoxifen. Doctors may prescribe fulvestrant after other hormonal therapies have been tried.
- Whereas tamoxifen is also used in pre-menopausal women (see below), fulvestrant is only used in women who are post-menopausal.

CDK4/6 inhibitors – Palbociclib

- Recent research has shown that CDK4/6 inhibitors given together with endocrine therapy can reverse drug resistance that occurs in some people
- A CDK4/6 inhibitor given with either letrozole or fulvestrant can control the disease for several months longer than the endocrine/hormonal drug given alone
- Several CDK 4/6 inhibitors have been developed and, although only palbociclib is currently approved in New Zealand, others are likely to follow

Treatment options for women who are pre-menopausal

Before menopause, the ovaries produce oestrogen to support ovulation. Therefore, treatment options for premenopausal women are targeted at stopping oestrogen production in the ovaries.

If you haven't been through the menopause, you are pre-menopausal, and your doctor may prescribe one of the following treatments:

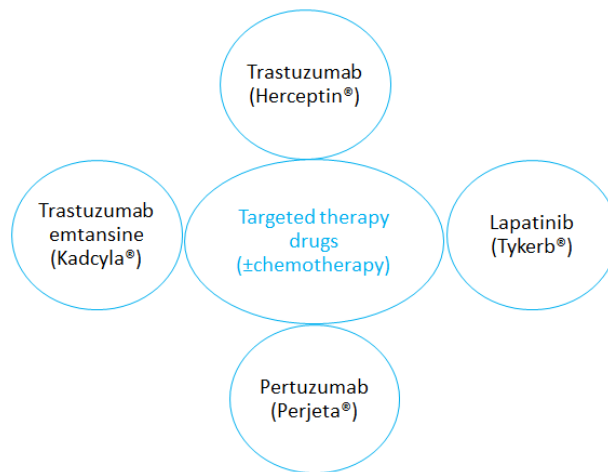
- Surgery to remove the ovaries (ovarian ablation)
 - Removing the ovaries is a small operation that will quickly lower the level of oestrogen in the body
 - You can usually have the operation with a short stay in hospital using keyhole surgery. A long thin tube called a laparoscope, that has a light and camera on the end, is used to remove the ovaries through small cuts made in the tummy area. You usually recover quickly from this type of operation. Your periods will stop straight away, and you will usually develop menopausal symptoms.
- Goserelin (Zoladex®) is a drug that stops the ovaries producing oestrogen (ovarian suppression)
 - Goserelin stops the pituitary gland in the brain from sending messages to the ovaries to produce oestrogen
 - The side effects are similar to menopausal symptoms and include hot flushes and sweats, joint pain, low sex drive
 - Your nurse will give you goserelin as a monthly injection under the skin of the tummy (abdomen).

- Tamoxifen (anti-oestrogen, described above), may also be given to block the action of oestrogen at the cancer cell and stop tumor growth.
- Progestogen therapy is another option that may be tried after other anti-hormone drugs. Progestogens are similar to the female hormone progesterone and are taken in tablet form. Megestrol acetate (Megace®) and medroxyprogesterone acetate (Farlutal®, Provera®) are the ones commonly used. Side effects may include increased appetite, weight gain, feeling sick, slight vaginal bleeding (spotting) and, rarely, breathlessness. Let your doctor know if this happens.

Premenopausal women usually also have tamoxifen in addition to ovarian suppression or ablation (surgery). If tamoxifen stops working, your doctor may then prescribe an aromatase inhibitor.

Targeted therapy for HER2-positive disease

Targeted therapy drugs (also called biological therapies) block the signals that are controlling cancer cell growth. HER2-targeted drugs block the HER2 signaling pathway which controls cell growth in some types of breast cancer. If your cancer cells are shown to contain the HER2 receptor, you will be given a HER2-targeted/blocking drug (usually with chemotherapy). HER2-targeted drugs are also occasionally given with hormonal therapy.



Several drugs are available that target the HER2 receptor pathway including trastuzumab, pertuzumab, lapatinib and trastuzumab emtansine.

- *Trastuzumab* blocks the binding of the HER-2 protein to its receptor on tumor cells which stops the cancer cells from dividing and growing. Trastuzumab is given every three weeks as a drip (infusion) or as a small injection under the skin. Side effects are

often mild, but some women may have flu-like symptoms, diarrhoea, headaches, an allergic reaction. Trastuzumab may cause damage to the heart; however, you will have tests to check your heart before and during treatment to monitor for any problems. If a heart problem does arise, your doctor may prescribe drugs to treat this or have you stop trastuzumab for a while.

- If trastuzumab is no longer controlling the cancer, your oncologist will consider other treatments for you.
- If your cancer spreads to the brain or spinal cord (central nervous system) while you are taking trastuzumab, you can usually continue taking it. Your doctor also will give you other treatments to control the cancer in the central nervous system (CNS).
- *Pertuzumab* is usually given with trastuzumab and the chemotherapy drug docetaxel. It is given as a drip every three weeks.
- *Trastuzumab emtansine (Kadcyla®)* is a combination of trastuzumab and a chemotherapy drug called emtansine. Trastuzumab delivers emtansine chemotherapy directly to the cancer cells. It is given as a drip every three weeks. In New Zealand, you need to have had previous treatment with trastuzumab and docetaxel or paclitaxel to have funded access.
- *Lapatinib (Tykerb®)* is taken as a tablet. It can be given in combination with the chemotherapy drug capecitabine (Xeloda®), or with an aromatase inhibitor.

Chemotherapy

The goal of chemotherapy is to destroy rapidly growing cancer cells. The drugs are carried in the blood and can reach cancer cells anywhere in the body.

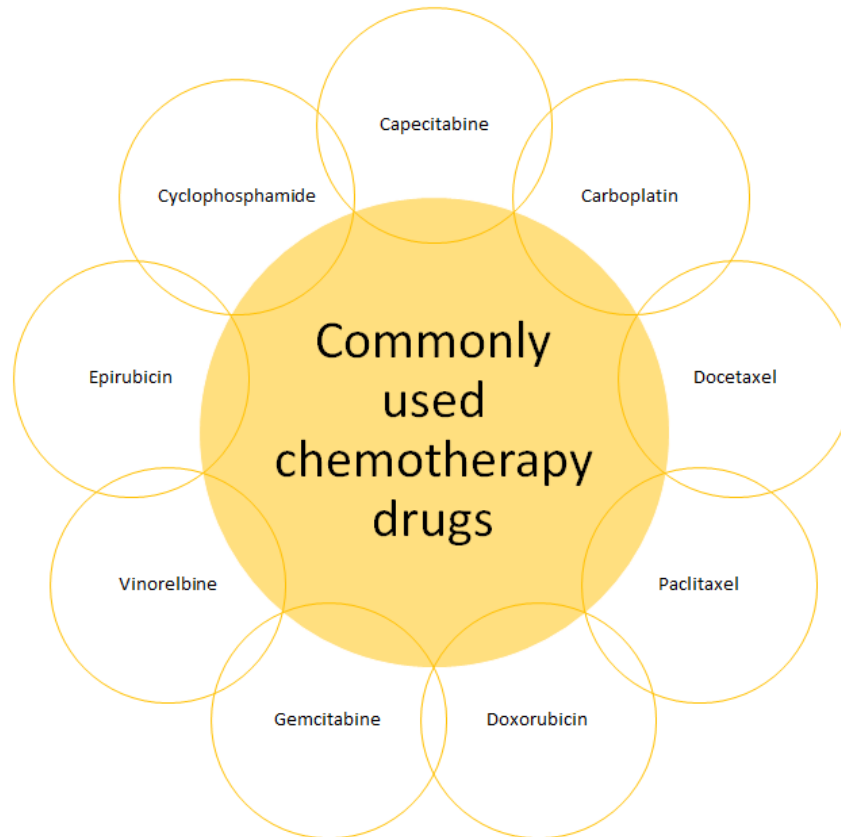
You usually have chemotherapy as your first line of treatment if:

1. The cancer does not have receptors for oestrogen (hormone receptor negative).
2. The cancer is in the liver or lungs.
3. The cancer is growing quickly.

If you have had chemotherapy before, your oncologist will choose a different drug or combination of drugs. Women with HER2-positive breast cancer may have chemotherapy in combination with a targeted therapy drug.

Drug options

Your oncologist or nurse will explain which drug or drugs are likely to be most beneficial for you.



Chemotherapy can be given as a single drug or a combination of 2 or 3 different drugs.

How chemotherapy is given

Chemotherapy drugs vary in how they are given. Some can be taken at home as a tablet whereas others require a visit to hospital where the drugs will be infused directly into a vein (intravenously). You will usually have your treatment in the chemotherapy day unit.

Occasionally, the drugs are given through a soft, plastic line called a central line into a vein in your chest, through a thin tube inserted into your upper arm (a PICC line), or an implanted device in your chest called a port-a-cath.

Chemotherapy is usually given in treatment cycles which include a few weeks of drug treatment (typically 3 weeks) followed by a 'rest' period to allow your body to recover from any side effects. Your oncologist or nurse will explain how many cycles of treatment are planned for you and how you will be given your chemotherapy.

Side effects of chemotherapy

The side effects of chemotherapy can vary greatly between individuals. Your oncologist or nurse will discuss possible side effects with you so that you know what you might experience and how to best manage it. Side effects become less troublesome when treatment finishes, and gradually go away.

2.2 Radiation therapy

Radiation therapy uses high-energy rays to specifically destroy cancer cells, causing as little harm as possible to surrounding healthy cells. It is used to relieve pain and other symptoms when breast cancer has spread to the bones or to the brain.

Radiation therapy is usually given as a series of short, daily treatments from Monday to Friday. The treatment will only take a few minutes. Radiation therapy is not painful, but the position you have to lie in during therapy may be uncomfortable. Taking a painkiller half an hour before your radiotherapy may help.

Radiation therapy does not make you radioactive. It is perfectly safe to be with other people, including children, after treatment. If you have any questions about radiation therapy, you can ask your doctor or the staff in the radiation therapy department.

Radiotherapy to the bones

Radiotherapy can shrink an advanced cancer in the bones, thereby strengthening the bone and reducing pain. It may take 3–4 weeks before it works so you need to carry on taking painkillers during this time.

Spinal cord compression

Doctors also use a short course of radiotherapy to the spine when a tumour is close to or pressing on the spinal cord. This is called spinal cord compression, and it can cause different symptoms including pain around the chest and difficulty walking. Spinal cord compression is not common but needs to be treated quickly to prevent permanent damage to the nerves.

Radiotherapy to the brain

Radiotherapy helps to shrink an advanced cancer in the brain and improve the symptoms. You may have up to two weeks of treatment. Occasionally a type of radiotherapy called stereotactic radiotherapy is used to treat small brain tumours. But it is only available in some specialist

hospitals and is not suitable for everyone. It delivers high doses of radiation accurately targeted to the tumour causing less damage to surrounding tissue.

Side effects of radiation therapy

When you have radiation therapy to improve symptoms, the side effects are not usually too troublesome. It can make you feel tired. This sometimes lasts for a few weeks after treatment finishes. Other side effects depend on the area of your body being treated and how much radiation you have. Always tell your nurse or radiographer about any side effects. There are usually ways in which they can be treated or managed. Side effects stop or improve gradually when treatment finishes. Try to pace yourself and get as much rest as you need. It helps to balance this with some gentle exercise, such as short walks, if possible.

You may feel sick if the area treated is close to your tummy, for example the ribs or spine. Your doctor can prescribe anti-sickness drugs to control any nausea or vomiting.

Radiation therapy to the brain causes some hair loss but this is usually temporary. Your hair should start to grow back within a few months after the treatment has finished. The skin on your scalp may also become dry and feel irritated. Your nurse or radiographer will give you advice on looking after your skin. You may feel very sleepy or drowsy for a few weeks. Tiredness can continue for weeks or months after treatment. Get plenty of rest but try to take regular short walks to help give you more energy. Radiation therapy to the brain may also make you feel sick or be sick. Your doctor can prescribe anti-sickness tablets or steroids to control this.

2.3 Surgery

Surgery is rarely used to remove tumors in patients with advanced breast cancer. This is because the cancer is not usually confined to one area. But it can occasionally be used in certain circumstances.

Surgery to strengthen a weakened bone

If an advanced breast cancer has weakened a bone, usually in the hip or leg, you may need an operation to strengthen it. The surgeon puts a metal pin into the centre of the bone with a metal plate to hold the bone permanently in place and prevent it from breaking. This surgery is performed under a general anaesthetic.

Surgery can also be used to replace a hip joint if it is affected. Occasionally it is used to treat advanced cancer in the spine.

You may need to stay in hospital for at least a week after the operation to allow a full recovery; however, most women can get up and start walking a couple of days after surgery.

Surgery is usually followed by radiation therapy to the bone to remove any other cancer cells.

Liver surgery

Very occasionally, it may be possible to remove a small cancer in a single area of the liver. This is major surgery that is carried out by a specialist liver surgeon.

Radiofrequency ablation may be used instead of surgery in some patients with liver tumors, but this is not a standard treatment. It destroys cancer cells using heat generated from needle electrodes placed in the liver.

Brain surgery

Occasionally, it may be possible to have surgery to the brain. This is usually if there is only a single tumour in the brain in an area where it is possible to operate.

You will be referred to a specialist brain surgeon (neurosurgeon) to assess whether surgery is possible. The surgeon and specialist nurse will tell you what to expect before and after your operation. You will usually be in hospital for at least a week.

Your doctor will prescribe steroids to reduce the swelling around the tumour and improve your symptoms. You take them before your operation and for a few weeks afterwards, depending on your symptoms. You usually have radiotherapy to the brain after you have recovered from the operation.

2.4 Drugs to improve bone strength, relieve bone pain, and prevent hypercalcaemia

Bisphosphonates are drugs that are used to strengthen the bones (preventing breaks, fractures) and to relieve bone pain. In addition, they may be used to treat high levels of calcium in the blood (hypercalcaemia).

Your doctor may prescribe a bisphosphonate to protect your bones from the spread of your breast cancer. Bisphosphonates are usually given in a drip (infusion). The main bisphosphonate used is zoledronic acid (Zometa®), which is given every 3 to 4 weeks.

An option to bisphosphonates is the monoclonal antibody Denosumab (Xgeva®, Prolia®) which can also strengthen bones and relieve bone pain. Denosumab is given by injection. It is licensed in New Zealand, but is not funded by Pharmac for use in patients with cancer.

Bisphosphonate side effects

Side effects are usually mild. They can include feeling sick, headaches, and flu-like symptoms such as chills and muscle aches. If you have bisphosphonates by drip, you may find the pain in your bones get worse for a short time. Your doctor can prescribe painkillers until this wears off. Even if you get significant side effects from the first dose of a bisphosphonate, it is extremely rare to get them with subsequent doses so you should still be able to continue with treatment.

Very rarely, bisphosphonates can damage the bone (osteonecrosis) in the jaw. It is important to tell your doctor straight away if you have any problems with your teeth or jaw. You will be asked to have a dental check-up before starting treatment with bisphosphonates. Dental treatment or dental problems can increase the risk of osteonecrosis of the jaw. Always tell your dentist that you are taking bisphosphonates.

Too much calcium in the blood (hypercalcaemia)

Advanced cancer in the bones can cause calcium leak from the damaged bone into the blood.

High levels of calcium in the blood can make you feel very tired and thirsty, and you may pass lots of urine. You may also feel sick or become irritable and confused. Tell your doctor or nurse if you have these symptoms. It is important that hypercalcaemia is diagnosed quickly so that it can be treated.

You will be given fluids (infused through a drip) to flush out the extra calcium from your body as well as bisphosphonates to lower the calcium levels. Your symptoms should go away within a couple of days.

3. Palliative care

Palliative care offers patients comfort and support to help them live as well as possible with an incurable disease. There is a popular misconception that palliative care is only for end of life, but its provision is appropriate at any stage of advanced cancer.

Palliative care nurses and doctors not only work with physical discomforts (such as pain and nausea) but also provide support for the family and coordinate services with your medical team, GP, social services, and community groups to provide patients with comprehensive care.

Palliative care can be provided within the home, hospital or Hospice and referrals for such care can be made by your medical team or GP. For a list of Hospice services in New Zealand, please see our Community Services Directory.

4. Well-being choices

Complementary medicines and therapies

Complementary medicines are best used in conjunction with conventional care rather than in place of. These medicines sit outside of conventional medical interventions (such as chemotherapy and radiotherapy) but can offer significant benefits to those living with advanced breast cancer, helping to improve quality of life. It is very important to discuss the use of complementary medicines with your GP and/or cancer specialist as these medicines can sometimes affect conventional medical treatments. This is particularly true of hormonally-based complementary medicines which can reverse the benefit from hormonal chemotherapy drugs. In addition, some Chinese herbal remedies may contain hormones.

A combination of conventional medical treatments and some complementary therapies can be coordinated to improve and enhance overall well-being and quality of life. Some patients find that meditation and prayer provide good coping strategies too. Discuss the inclusion of complementary therapies in your care plan with your team.

Wellbeing choices that can improve health and bring comfort and relaxation:



Examples of complementary therapies:



5. Research – clinical trials

Clinical trials are carried out in patients to try to find new and better treatments for cancer.

Clinical trials may have the following goals:

1. Test new treatments, such as new chemotherapy drugs, targeted therapies and immunotherapies and compare them to existing therapies.
2. Look at new combinations of existing treatments or change the way they are given to make them more effective or reduce side effects.
3. Compare the effectiveness of drugs used to control symptoms.

Trials are the only reliable way to find out if a different type of surgery, radiotherapy, drug therapy or other treatment is better than what is already available.

Participation in clinical trials

New drugs are continually under development for the treatment of cancer. Some clinical trials are conducted internationally while others are conducted locally within certain countries. Your doctor will discuss your participation in a clinical trial if there is one recruiting patients in New Zealand and if you fit the study eligibility criteria.

In 'randomized clinical trials' patients are selected at random to receive either the best existing treatment or the new treatment.

The decision to take part is always yours and if you agree to join a trial, be sure you understand the reasons for the trial and the implications for you of your participation.

Blood and tumour samples

Blood and tumour samples may be taken to help make the right diagnosis. You may be asked for your permission to use some of your samples for further research. If you take part in a trial, you may also give other samples, which may be frozen and stored for future use when new research techniques become available. Your name will be removed from the samples so you can't be identified.

The research may be carried out at the hospital where you are treated, or at another one. This type of research takes a long time, and results may not be available for many years. The samples will be used to increase knowledge about the causes of cancer and its treatment, which will hopefully improve the outlook for future patients.