

Understanding Immunotherapy

A guide for people affected by cancer

This fact sheet has been prepared to help you understand more about immunotherapy, a treatment offered to some people with cancer. The main type of immunotherapy for cancer uses drugs known as checkpoint inhibitors. Most of the information in this fact sheet relates to checkpoint inhibitors.

What is immunotherapy?

Immunotherapy is a treatment that uses the body's own immune system to fight cancer. There are several types of immunotherapy, and each works differently. Checkpoint inhibitors remove barriers that stop the immune system from finding and attacking cancer. Other types stimulate the immune system to help it work better against cancer.

In this fact sheet, the term “immunotherapy” means the use of checkpoint inhibitors. Examples of checkpoint inhibitors include pembrolizumab, nivolumab, ipilimumab, atezolizumab, durvalumab and avelumab. To read more about how checkpoint inhibitors work, see the next page. For information about other types of immunotherapy, see page 7.

Immunotherapy may be used on its own or with other cancer treatments. It is most often given when cancer has not responded to or has come back after initial treatment. In some cases, it may be available as part of the first treatment plan.

About the immune system

The immune system is a network of cells, chemicals, tissues and organs. It includes the lymph nodes, spleen, thymus, tonsils and bone marrow, as well as white blood cells known as lymphocytes. Together, this network tries to protect the body from infections and from abnormal cells such as cancer cells.

When a germ enters the body, or when a cell becomes abnormal, the immune system usually recognises and then attacks the germ or cell so that it does not harm the body. This process is known as an immune response.

The immune system can remember every germ or abnormal cell it has attacked so it can easily recognise them if they appear in the body again.

The role of the immune system

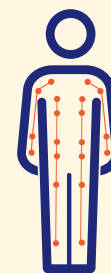
To keep you healthy, the immune system needs to be carefully balanced. If it is too weak, you will be prone to infection and disease. If it is too active, it can start to attack normal cells and lead to autoimmune diseases such as rheumatoid arthritis and lupus.

Tipping the balance



Cancers find ways to disrupt the balance of the immune system so that it does not see cancer cells as abnormal. Immunotherapy manipulates the immune system to restore the balance and allow it to attack the cancer.

Immune side effects



If immunotherapy makes the immune system overactive, you can get side effects anywhere in the body (see pages 4–6).

After treatment



Because the immune system has a “memory”, immunotherapy sometimes keeps working long after treatment finishes. This means side effects can also appear months or even years after treatment.

Cancer and the immune system

Cancer starts when abnormal cells begin growing out of control. The immune system usually stops new cancers from developing because it recognises abnormal cells and destroys them. In some cases, the body's immune response is not able to kill all abnormal cells and they develop into cancer.

Cancer cells find ways to stop the immune system from destroying them – for example, by setting up barriers (“checkpoints”) so the immune system can't recognise them, or by changing over time (mutating) to avoid being found by the immune system. This is why treating cancer isn't as simple as boosting the immune system. Modern immunotherapy drugs try to help the immune system in very specific ways.

Some people with cancer wonder if they should try special diets or supplements to boost the immune system so it can fight the cancer. While having a healthy diet is always important, extreme diets are not proven to be effective and can be harmful. Talk to your doctors before starting any special diets or supplements during cancer treatment.

How cancer is treated

Because each cancer is unique, people may have different treatment plans, even if their cancer type is the same. The three main cancer treatments are:

- surgery
- chemotherapy
- radiation therapy (also called radiotherapy).

Other treatments used for some types of cancer in some people include:

- immunotherapy
- targeted therapy
- hormone therapy.

Chemotherapy, targeted therapy, immunotherapy and hormone therapy are all drug therapies. They are known as systemic treatment because the drugs circulate throughout the body.

Cancer treatments may be used on their own or in combination. For example, you may have surgery

to remove a tumour, followed by immunotherapy to stop the cancer returning. Doctors will recommend the best treatment for you based on the type and stage of cancer, its genetic make-up, your age and your general health.

- ▶ See our publications on surgery, chemotherapy, radiation therapy and targeted therapy.

How checkpoint inhibitors work

The white blood cells known as lymphocytes are an important part of the immune system. There are two main types of lymphocytes – T-cells and B-cells. They travel throughout the body looking for germs and abnormal cells and work together to destroy them.

Checkpoint inhibitors help T-cells to recognise and attack cancer. The table below gives a simplified explanation of this process.

T-cells and checkpoint inhibitors

What T-cells usually do

Your immune system's T-cells circulate throughout the body looking for abnormal cells to destroy. The T-cells carry “checkpoints”, special proteins with names such as PD-1, PD-L1 and CTLA-4.

What checkpoints usually do

Checkpoints act as natural brakes to stop T-cells destroying healthy cells.

How some cancer cells use checkpoints

In some people, cancer cells use checkpoints to stop T-cells from seeing the cancer cells as abnormal.

What checkpoint inhibitors do

Checkpoint inhibitors are drugs that block these checkpoints so that the T-cells can once again find and attack the cancer. This is like taking the brakes off the immune system.

See pages 4–7 for more information about having checkpoint inhibitors as part of your cancer treatment, including common and rare side effects.

Is immunotherapy right for me?

Immunotherapy using checkpoint inhibitors has worked well for some people, but it does not help everyone. It is available for some types of cancer, including bladder cancer, head and neck cancer, Hodgkin and non-Hodgkin lymphoma, kidney cancer, liver cancer, lung cancer, melanoma and Merkel cell carcinoma.

So far, most people who have been treated with checkpoint inhibitors have had advanced cancer. Advanced cancer means either the cancer has come back and spread after the initial treatment, or it was at an advanced stage when first diagnosed. For some cancer types, such as melanoma, immunotherapy is starting to become available for earlier-stage cancers.

To work out if immunotherapy is an option for you, your cancer specialist will consider the type and stage of cancer, your treatment history, your future treatment options and your overall health.

Even if immunotherapy is recommended as a treatment, it is difficult to predict whether it will work. The rate of success varies greatly depending on the type of cancer and many individual factors. You can ask your specialist how successful the treatment has been for people with the same type of cancer as you.

Challenges of immunotherapy

Some media reports have claimed that checkpoint inhibitors are “miracle drugs” that can cure cancer. This means that people often have very high expectations when starting immunotherapy, or they may be confused and upset if they aren’t offered it.

Will it work? – The most challenging issue is that checkpoint inhibitors don’t work for everyone. If you are thinking about trying immunotherapy, ask your specialist how likely the cancer is to respond to the treatment and what other treatments are available. To make immunotherapy available to more people in the future, researchers are trying to understand why some people’s cancers respond better than others.

How long will it take to work? – Like most other cancer treatments, immunotherapy usually takes a

while to work, so you and your family may experience anxiety waiting to see whether you’ll respond to the treatment. If it does work, you may worry about how long immunotherapy will control the cancer or whether the cancer will come back.

How will I feel? – You may feel it is hard to make plans about work, relationships and travel. Many people find comfort in everyday activities; others focus on doing things they’ve always wanted to do. Let your cancer nurse or specialist know how you’re feeling. They may connect you with a psychologist who can help you work through your thoughts.

▶ See our *Emotions and Cancer* booklet for more information on coping with uncertainty.



If immunotherapy doesn’t work or stops working, ask your cancer specialist about your other treatment options. You may be able to try another type of checkpoint inhibitor or join a clinical trial. A clinical trial is a research study that tests new or modified treatments to see if they are better than current approaches.

How much will it cost? – Checkpoint inhibitors are expensive (often several thousand dollars per dose), but the Australian Government covers most of this cost for some drugs for some types of cancer through the Pharmaceutical Benefits Scheme (PBS). Other cancer types and new drugs may be added to the PBS in the future. Your specialist can give you the latest information about which drugs are on the PBS.

What if it’s not on the PBS? – You may be able to get checkpoint inhibitors through clinical trials or, sometimes, through a compassionate access program or cost-share program offered by the pharmaceutical company. Some people choose to pay the entire cost themselves, but this can involve major financial decisions.

Before deciding to pay for any cancer treatment, it is important to fully understand the total cost, as well as the likely rates of success and the possible risks and benefits of the treatment. Take the time to discuss these questions with your cancer specialist and your family or close friends.

How immunotherapy is given

Checkpoint inhibitors are usually prescribed by a medical oncologist or haematologist. They are given as a liquid through a drip inserted into a vein (intravenous infusion). Sometimes two or more drugs may be given together, such as two checkpoint inhibitors, or a checkpoint inhibitor with one or two chemotherapy drugs or a targeted therapy drug.

You will usually have immunotherapy as an outpatient, which means you visit the hospital or treatment centre for the infusion and then go home again. Checkpoint inhibitors are commonly given in repeating cycles, with rest periods of 2–6 weeks in between.

How often and how long you have the treatment depends on the type of cancer and how advanced it is; the type of checkpoint inhibitor; how the cancer responds to the treatment; and what side effects you experience. Many people stay on immunotherapy for up to two years. Clinical trials are now testing if the treatment can be given for a shorter period of time once it has started working or whether ongoing treatment is needed.

Checkpoint inhibitors can take weeks or months to start working, depending on how your immune system and the cancer respond. Sometimes they keep working long after treatment stops, but this varies from person to person.

Most cancers have treatment protocols that set out which drugs to have, how much and how often. You can find information about protocols for checkpoint inhibitors and other cancer drugs at [eviQ Cancer Treatments Online](http://eviQ.org.au) (visit eviQ.org.au). Your specialist may need to tailor the protocols to your individual situation.

Like many other cancer treatments, immunotherapy drugs are often not safe to use if you are pregnant or breastfeeding. Ask your doctor for advice about contraception. If you become pregnant, let your medical team know immediately.

What if I have an autoimmune disease? – It is important to tell your cancer specialist if you have an autoimmune disease such as rheumatoid arthritis, lupus, ulcerative colitis and Crohn's disease. You may

still be able to have immunotherapy, but there will be extra issues to consider.

Autoimmune diseases make the body's immune system overactive so it attacks normal cells, causing redness, swelling and pain (inflammation). The extra immune system activity caused by immunotherapy can make these symptoms worse.

What if I've had an organ transplant? – If you have had an organ transplant, you will probably be taking medicines that suppress the immune system and stop your body from rejecting the new organ. Talk to your specialists, as they will need to carefully balance these medicines with the extra immune system activity caused by immunotherapy.



Let your treatment team know about any over-the-counter medicines, vitamins, supplements or herbal therapies you are thinking about using. Some may affect how the immunotherapy works or make side effects worse.

Side effects of immunotherapy

Like all treatments, checkpoint inhibitors can cause side effects. These are sometimes called immune-related adverse effects (IRAEs).

Immunotherapy side effects are different to the side effects of other cancer treatments and need to be managed differently. The diagram on the next page shows some possible side effects of immunotherapy, but you are unlikely to have all of the side effects shown.

When to expect side effects

You may have side effects within days of starting treatment, but more commonly they occur several weeks or months after starting treatment. In some rare cases, new side effects can appear months after finishing treatment.

Most people have mild side effects. Side effects are likely to be more severe if you are having higher doses or a combination of immunotherapy drugs, or if you are having immunotherapy with other cancer treatments.

Common and rare side effects of immunotherapy

Checkpoint inhibitors trigger an immune response that can lead to redness, swelling or pain (inflammation) anywhere in the body. Side effects will depend on which part of the body becomes inflamed. The diagram below shows examples of common and rare side effects. The side effects you have will depend on the drug and how your body responds. While some people have serious side effects, others have just one or two mild side effects.

Common side effects

Fatigue

tiredness that does not go away with rest, caused by inflammation throughout your body

Dry eyes

could be inflammation of the eyes or tear glands

Changes in weight and body temperature

could be inflammation causing the thyroid to work too fast (hyperthyroidism, leading to weight loss and feeling warm) or too slow (hypothyroidism, leading to weight gain and feeling cold)

Skin rash and itching

could be dermatitis, which makes skin red, bumpy and itchy

Diarrhoea, abdominal pain and bloating

could be inflammation of the bowel (colitis)

Pain in the joints

could be inflammation of the joints (arthralgia), especially if you already have arthritis or a similar condition

Rare side effects

Headache or blurred vision

could be inflammation of the pituitary gland (hypophysitis) or the membranes around the brain and spinal cord (meningitis)

Breathlessness, coughing, fainting or chest pain

could be a lung or heart problem – rare but serious

Yellowing of the eyes, severe abdominal pain and dark urine

could be inflammation of the liver (hepatitis)

Excessive thirst or urination

could be inflammation of the pancreas affecting the production of insulin

Reduced urination or blood in the urine

could indicate problems in the kidneys – very rare but serious

Muscle pain

could be inflammation of the muscles (myositis)

Confusion, seizures

could be nerve problems – very rare but serious



Other rare side effects can occur, and some side effects can be life-threatening. Let your treatment team know about any new or worsening side effects during or after treatment. Do not try to treat side effects yourself. Most immunotherapy side effects can be managed and reversed if they are reported early.

Managing side effects

Because immunotherapy works differently from other cancer treatments, it's important to work closely with your treatment team to monitor any side effects and how the cancer responds.

Before starting immunotherapy, discuss the potential side effects with your cancer specialist. Ask which side effects to watch out for or report, who to report them to, and who to contact after hours. You can read about the side effects of specific checkpoint inhibitors at eviq.org.au.

Before treatment begins, you will usually have some tests to check that you are well enough to have immunotherapy. Throughout treatment, the team will regularly test your blood and ask you questions to check for early signs of side effects. New side effects can appear months after having immunotherapy, so ask your cancer specialist how long you need to keep watching for side effects.

Reporting side effects

Side effects can be better managed if reported early, so it is important to let your cancer care team know about new or worsening symptoms, even if they seem minor or you're not sure if they are related to your treatment. If left untreated, side effects can become serious and may even be life-threatening.

Sometimes it can be tricky to know whether your symptoms are related to the cancer or the treatment. Make sure to discuss this with your cancer care team.

Because immunotherapy is a newer cancer treatment, general practitioners (GPs) and other health professionals may not yet be familiar with the side effects. Your team may give you a card with information about your immunotherapy treatment and potential side effects. You can show this card to other health professionals you see and ask them to consult with your cancer specialist. Do not start any new medicines, including anti-inflammatory steroids, herbal therapies or over-the-counter medicines, until your cancer specialist has been consulted. If you become unwell, even years later, it is important to tell any health professionals you see that you have had immunotherapy.

Treating side effects

Side effects are graded on a scale of 1–4. Your doctor will tell you how to manage mild to moderate side effects (grades 1–2). For example, you may be given a moisturising cream to treat a skin rash. Moderate to severe side effects (grades 2–4) are often treated with steroid tablets, such as prednisolone. In some cases of severe side effects (grades 3–4), people may need to stay in hospital and/or have intravenous steroids or other medicines, and immunotherapy may be stopped until the side effects are better controlled.

If side effects become too severe, you may have to stop immunotherapy permanently. In this case, the immunotherapy that you have already received may have “trained” your immune system to recognise cancer cells, so you may continue to benefit.

Although there is a risk of severe side effects, it may be reassuring to know that many people experience only mild side effects.



If you have had immunotherapy, it is important to check with your cancer specialist before having vaccinations, including for flu or COVID-19.

How will I know whether the immunotherapy is working?

You will have regular check-ups with your cancer specialist, blood tests and different types of scans to check whether the cancer has responded to the treatment. It may take some time to know if immunotherapy has worked because people often have a delayed response. In some cases, the cancer may appear to get worse before improving.

You may wonder whether having side effects means the immunotherapy is working. Side effects are a sign that the treatment is affecting your immune system in some way, but this may or may not mean the treatment is affecting the cancer. Many people with mild side effects have still seen improvements.

A good response from immunotherapy will make the cancer shrink or disappear. In some cases, the cancer remains stable, which means it does not

grow but also does not shrink or disappear. People with stable disease often continue to have a good quality of life.

What if immunotherapy doesn't work?

Unfortunately, checkpoint inhibitors do not work for everyone. Some cancers will not respond to the treatment at all, or the cancer cells can become resistant to the treatment even if it works at first. This can be very disappointing, but your cancer specialist will help you explore other treatment options if this happens.

How do I get immunotherapy?

To access immunotherapy, talk to your cancer specialist. Ask if any checkpoint inhibitors would be a suitable treatment for you and whether they are reimbursed through the PBS for your type of cancer (see page 3).

It may be possible to have immunotherapy treatments through clinical trials. Speak with your treatment team for more information.

► See our *Understanding Clinical Trials and Research* booklet.

Other types of immunotherapy

While checkpoint inhibitors are the main type of immunotherapy, there are some other types of immunotherapy that work in different ways. A few have been approved to treat particular cancers, but most are still being tested in clinical trials. Your cancer specialist can give you the latest information.

| Type | How it works | Examples |
|--------------------------------|--|---|
| immune stimulants | These treatments stimulate the immune system to attack cancer. | <ul style="list-style-type: none"> • Bacillus Calmette–Guérin (BCG) – a vaccine put directly into the bladder to prevent bladder cancer coming back or spreading • imiquimod – a cream applied directly to some skin cancers |
| CAR T-cell therapy | Chimeric antigen receptor (CAR) T-cell therapy boosts the ability of T-cells to fight cancer. T-cells are removed from the blood and altered so they can better recognise cancer cells. The altered T-cells are then returned to the blood through an intravenous drip (infusion). | <ul style="list-style-type: none"> • used for some types of leukaemia and lymphoma that have come back or not responded to treatment • clinical trials are testing whether CAR T-cell therapy works well for other types of cancer • available only in a few public hospitals at this stage |
| oncolytic virus therapy | This therapy uses viruses that infect cancer cells, causing the cells to die and stimulating the immune system to attack the cancer. | <ul style="list-style-type: none"> • melanoma is sometimes treated with an oncolytic virus therapy known as talimogene laherparepvec or T-VEC, which is injected directly into the melanoma • clinical trials are testing oncolytic virus therapies for brain cancer and some other cancer types, but research is still in its early stages |

Vaccines to prevent cancer

Some vaccines are not used to treat cancer, but can help prevent it. They do this by training the immune system to attack viruses that have been linked to certain cancers. The human papillomavirus (HPV) vaccine helps prevent cervical cancer and also offers some protection against anal and penile cancers and some head and neck cancers. You can read more about the HPV vaccine at hpvaccine.org.au. Vaccines against the hepatitis B virus help prevent liver cancer. Visit health.gov.au and search for “hepatitis B immunisation” for more information.

Question checklist

It is important to ask your specialist questions, especially if you feel confused or uncertain about your treatment. You may want to make a list of your questions before your appointments and include some of the questions below.

- Is immunotherapy available as part of my treatment plan? If not, why not? Would other treatment options be better for me?
- How do I find out about clinical trials? Are there any nearby that might be right for me?
- Which immunotherapy drug are you recommending? Does it have different names?
- What percentage of people with this type of cancer respond to immunotherapy?
- How often have you prescribed this treatment? Has it worked well for your other patients?
- What do you expect the immunotherapy to do to the cancer? Will it be my only treatment?
- How much will immunotherapy cost? Is there any way to reduce the cost if I can't afford it?
- How often will I receive immunotherapy?
- How long will I have treatment?
- Where will I have treatment?
- What side effects should I watch out for or report? Can I get some written information about them?
- Am I likely to get all of the side effects on the list?
- Who do I contact if I get side effects?
- How can side effects be managed?
- Will I have to pay for extra medicines to help manage side effects?
- Can I take my other medicines while I am having immunotherapy?
- Can I have the flu, COVID-19 or other vaccines?
- How will I know if the treatment is working?

Where to get help and information

Call Cancer Council 13 11 20 for more information about immunotherapy. Our experienced health professionals can listen to your concerns, put you in touch with local services and send you our free booklets. You can also visit your local Cancer Council website:

| | |
|-----------|--|
| ACT | actcancer.org |
| NSW | cancercouncil.com.au |
| NT | cancer.org.au/nt |
| QLD | cancerqld.org.au |
| SA | cancersa.org.au |
| TAS | cancer.org.au/tas |
| VIC | cancervic.org.au |
| WA | cancerwa.asn.au |
| Australia | cancer.org.au |

Other useful websites

You can find many useful resources online, but not all websites are reliable. These websites are good sources of support and information.

| | |
|---------------------------------|--|
| Cancer Council Online Community | cancercouncil.com.au/OC |
| Cancer Council podcasts | cancercouncil.com.au/podcasts |
| Australian Cancer Trials | australiancancertrials.gov.au |
| eviQ Cancer Treatments Online | eviq.org.au |
| Peter MacCallum Cancer Centre | petermac.org (search for "immunotherapy videos") |
| Cancer Research Institute (US) | cancerresearch.org |

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Note to reader

Always consult your doctor about matters that affect your health. This fact sheet is intended as a general introduction and is not a substitute for professional medical, legal or financial advice. Information about cancer is constantly being updated and revised by the medical and research communities. While all care is taken to ensure accuracy at the time of publication, Cancer Council Australia and its members exclude all liability for any injury, loss or damage incurred by use of or reliance on the information provided in this fact sheet.

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Cancer Council acknowledges Traditional Custodians of Country throughout Australia and recognises the continuing connection to lands, waters and communities. We pay our respects to Aboriginal and Torres Strait Islander cultures and to Elders past, present and emerging.

