

# Understanding Immunotherapy

A guide for people affected by cancer

This fact sheet has been prepared to help you understand more about checkpoint immunotherapy, a treatment offered to some people with cancer. We hope this fact sheet will help you, your family and friends understand how immunotherapy may help treat cancer.

## What is immunotherapy?

Immunotherapy is a type of drug treatment that uses the body's own immune system to fight cancer. It is different to chemotherapy, which works by killing cancer cells.

Different types of immunotherapy work in different ways. Some stimulate the immune system so it works better against cancer. Others remove barriers that stop the immune system attacking the cancer.

Checkpoint immunotherapy is currently available in Australia for some types of cancer. It has worked well for some people, but it does not help everyone.

## Is immunotherapy right for me?

Surgery, chemotherapy and radiation therapy are still the main treatments for many cancers. However, some people with particular types of cancer may benefit from checkpoint immunotherapy.

To work out if checkpoint immunotherapy is suitable 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 depending on the type of cancer (see box below).

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

## Who benefits from checkpoint immunotherapy?

The main type of immunotherapy uses drugs known as checkpoint inhibitors. Checkpoint immunotherapy has different rates of success with different types of cancer:



Advanced melanoma – about 5 in 10 people (50%) benefit from checkpoint immunotherapy



Advanced kidney cancer, bladder cancer, lung cancer, head and neck cancer or Hodgkin lymphoma – 2–3 in 10 people (20–30%) benefit from checkpoint immunotherapy



Most other types of advanced cancer – less than 1 in 10 people (1–10%) benefit from checkpoint immunotherapy

## Understanding Immunotherapy

### About the immune system

The immune system protects the body from infections. When a foreign organism such as a germ enters the body, or when a cell becomes abnormal, the immune system usually recognises and then attacks it so that it doesn't harm the body. This process is called an immune response.

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

### The parts of the immune system

The immune system is made up of a network of cells, chemicals, tissues and organs. White blood cells known as lymphocytes are part of the immune system. They travel throughout the body looking for germs and abnormal cells. There are two main types of lymphocytes:

**T-cells** – recognise and destroy germs and abnormal cells. T-cells also help control and direct the activity of the immune system.

**B-cells** – make proteins called antibodies. An antibody can lock onto the surface of the invading germ. This helps T-cells recognise the germ.

The organs of the immune system help to make, filter and process lymphocytes. These organs include the:

- lymph nodes – small structures found in groups throughout the body and linked by lymph vessels
- spleen – a large organ in the abdomen
- thymus – a gland behind the breastbone
- tonsils – two small organs at the back of the throat
- bone marrow – the spongy material inside bones.

### Cancer and the immune system

Cancer starts when abnormal cells begin growing out of control. The immune system usually prevents cancers from developing because it recognises abnormal cells and destroys them. In some cases, the natural immune response is not strong enough to kill all abnormal cells and they develop into cancer.

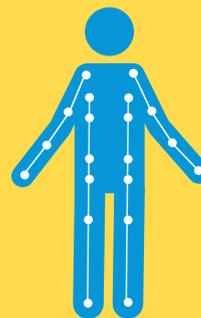
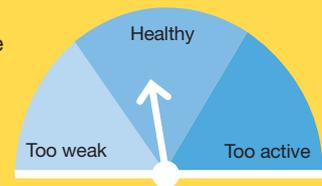
Cancer cells also find ways to stop the immune system destroying them – for example, by setting up barriers (“checkpoints”) so the immune system can't reach them, or by changing over time (mutating) to avoid being recognised by T-cells and antibodies.

### The role of the immune system

The immune system has to be carefully balanced to keep you healthy – 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 (as in autoimmune diseases such as rheumatoid arthritis).

#### Tipping the balance

Cancers find ways to tip the balance of the immune system so that it does not attack the cancer. Immunotherapy tips the balance back in favour of the immune system, helping it to fight the cancer.



#### Immune side effects

If immunotherapy tips the balance of the immune system too far and makes it too active, you can get side effects anywhere in the body (see page 5–7).

#### Over time

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



**Conditions affecting immune response** – It is important to tell your cancer specialist if you have an autoimmune disease such as rheumatoid arthritis or lupus or if you've had an organ transplant. You may still be able to have immunotherapy, but it could be more difficult. Autoimmune diseases make the body's immune system overactive so it attacks normal cells, leading to symptoms such as inflammation, swelling and pain. The extra immune system activity caused by immunotherapy can make these symptoms worse. After an organ transplant, most people take drugs that suppress the immune system to stop the body rejecting the new organ. Your specialists will need to carefully balance these drugs with the extra immune system activity caused by immunotherapy.

## Understanding Immunotherapy

### How checkpoint immunotherapy works

The drugs known as checkpoint inhibitors are the most widely used form of immunotherapy for cancer. They work by helping the immune system to recognise and attack the cancer.

#### T-cells and checkpoint inhibitors

##### What T-cells usually do

The immune system's T-cells circulate throughout the body looking for abnormal cells to destroy. The T-cells carry proteins known as "checkpoints".

##### 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, the cancer cells use these checkpoints to stop T-cells recognising 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 recognise and destroy the cancer. This is like taking the brakes off the immune system.

See pages 4–8 for more information about having checkpoint immunotherapy as part of your cancer treatment, including common and rare side effects.

### Other types of immunotherapy

There are other types of immunotherapy. A few are available now as approved treatment for cancer, but most are still being tested in clinical trials and may be more widely available in future.

#### Immune stimulants

Some treatments are used to stimulate the immune system to attack the cancer. These are known as immune stimulants.

In non-muscle-invasive bladder cancer, the vaccine Bacillus Calmette-Guérin (BCG) may be used as

an immune stimulant. It is given into the bladder through a catheter. The BCG stimulates the immune system to stop or delay bladder cancer coming back or becoming invasive.

In some types of skin cancers, a cream called imiquimod is applied directly to the affected area to stimulate a local immune response.

#### Adoptive cell transfer

This experimental type of immunotherapy is used to boost the ability of T-cells to fight cancer. Chimeric antigen receptor (CAR) T-cell therapy is a type of adoptive cell transfer that is being tested in Australian clinical trials. It is showing good results for some types of leukaemia and lymphoma.

In CAR T-cell therapy, the T-cells are removed from the blood, and a new gene is introduced into the T-cells to enable them to recognise cancer cells. The T-cells are then returned to the blood by an intravenous drip (infusion). The altered T-cells multiply and trigger a number of immune responses that attack the cancer cells.

#### Oncolytic viruses

These viruses directly infect tumour cells and cause an immune response against the infected cells. An oncolytic virus therapy known as talimogene laherparepvec or T-VEC (brand name Imlygic) is sometimes used for melanoma. It is injected directly into the melanoma both to kill the melanoma cells and to stimulate the immune system to attack melanoma cells.

Oncolytic virus therapies for brain cancer and some other types of cancer are being tested in clinical trials, but the research is still in its early stages.

#### How vaccines help prevent cancer

Vaccines help train the immune system to prevent some types of cancer. The human papillomavirus (HPV) vaccine is used to prevent cervical cancer, and it is hoped it will also prevent anal and penile cancers and some cancers of the head and neck. Vaccines against hepatitis B and hepatitis C viruses help prevent liver cancer.

## Understanding Immunotherapy

### How is immunotherapy different from other cancer treatments?

Immunotherapy works in a different way to other cancer treatments and has different side effects. Other treatments for cancer include:

**Surgery** – removes cancer from a specific area of the body. This can be effective if the cancer is found before it has spread to other parts of the body. However, surgery on its own is rarely able to treat cancer that has spread. The main side effects of surgery are pain and risk of infection.

**Radiation therapy** – uses targeted radiation (usually x-ray beams) to kill or damage cancer cells so they cannot grow, multiply or spread. The treatment focuses on a specific area at a time and is most effective when the cancer has not spread to other parts of the body. It can also be used to treat symptoms such as pain. Radiation therapy can cause fatigue, as well as side effects at or near the treatment site (e.g. skin problems, nausea, bowel problems).

**Chemotherapy** – uses drugs to kill or damage rapidly dividing cells anywhere in the body. It can work for many types of cancer because cancer cells divide rapidly. Chemotherapy also damages healthy cells that divide rapidly, such as hair follicles, blood cells and cells inside the mouth and bowel. This can cause a range of side effects, such as nausea, fatigue, hair loss, and low white blood cell counts (making you more prone to infections). Unlike cancer cells, normal cells can recover, so most side effects are temporary.

**Targeted therapy** – uses drugs to attack specific features of cancer cells, known as molecular targets, that are causing the tumour to grow uncontrollably. While targeted therapy is designed to affect only the cancer cells, it can still cause side effects in some people.

As researchers learn more about cancer, treatments change. Immunotherapy is not a new idea, but older types were less effective. Checkpoint immunotherapy is having better results in some cancers. Like all treatments, checkpoint immunotherapy sometimes causes side effects. The extra activity of the immune system can cause inflammation anywhere in the body, leading to a

variety of possible side effects, such as skin rash, diarrhoea and breathing problems. See pages 5–7 for more information about side effects.

### The challenges of immunotherapy

You may have several questions and concerns about having immunotherapy. There have been media reports of how immunotherapy is a “miracle drug” and how it can cure cancer. This means that people’s expectations can be very high when starting treatment, or they may be confused and upset if they aren’t offered immunotherapy as part of their treatment.

**Will it work?** – The most challenging issue is that checkpoint immunotherapy doesn’t work for everyone (see page 1). If you are thinking about trying immunotherapy, ask your cancer specialist how likely you are 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 respond better than others.



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 immunotherapy drug or join a clinical trial.

**How long will it take to work?** – Like most other cancer treatments, checkpoint 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.

These uncertainties can make it challenging 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 recommend seeing a psychologist to help you work through your thoughts.

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

## Understanding Immunotherapy

**How much will it cost?** – The cost of checkpoint immunotherapy drugs is high (often several thousand dollars per dose).

As at June 2019, the Australian Government covers most of this cost for some types of advanced cancer through the Pharmaceutical Benefits Scheme (PBS). Reimbursement for some other types of cancer may be added in the future. Your specialist can give you the latest information.

Advanced cancer type	Checkpoint inhibitors available on the PBS*
melanoma	pembrolizumab (brand name Keytruda), nivolumab (Opdivo), ipilimumab (Yervoy)
lung cancer	pembrolizumab, nivolumab, atezolizumab (Tecentriq)
kidney cancer	nivolumab, ipilimumab
bladder cancer	pembrolizumab
head and neck cancer	nivolumab
Hodgkin lymphoma	pembrolizumab
Merkel cell carcinoma	avelumab (Bavencio)

\* As at June 2019

**What if it's not on the PBS?** – You may be able to access checkpoint immunotherapy through clinical trials or, sometimes, through a compassionate access program or cost-share program offered by the pharmaceutical company.

Some people choose to make significant financial decisions to cover the costs of immunotherapy for cancers that are not on the PBS. Before deciding to pay for these drugs, it is important to fully understand the financial costs, as well as the possible risks and benefits for your type of cancer. Take the time to discuss these questions with your cancer specialist and your family.

### How immunotherapy is given

Checkpoint immunotherapy is usually given directly into a vein through an intravenous drip. Sometimes two checkpoint inhibitor drugs are given together, or a checkpoint inhibitor drug is given with a chemotherapy or targeted therapy drug.

You will usually have checkpoint immunotherapy as an outpatient, which means you visit the hospital or treatment centre for the day. You may have treatment every 2–4 weeks in a repeating cycle.

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/s; how you respond to treatment; and what side effects, if any, you experience. Many people stay on immunotherapy for up to two years, but 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 necessary.

Because immunotherapy drugs act directly on the body's own immune system, how long they keep working will vary from person to person. Sometimes, they keep working long after treatment stops.

### Side effects of immunotherapy

Checkpoint immunotherapy can cause side effects anywhere in the body. These are different to the side effects of other cancer treatments and need to be managed differently. The side effects of immunotherapy are sometimes called immune-related adverse effects (IRAEs).

The diagram on the next page shows some possible side effects of immunotherapy. You may have side effects within days of starting treatment, but more commonly they occur many weeks or months after starting treatment. In some rare cases, new side effects can appear months after treatment.

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

## Understanding Immunotherapy

### Common and rare side effects of immunotherapy

Immunotherapy can cause inflammation, which may lead to different side effects depending on which part of the body becomes inflamed. The diagram below shows examples of both common and rare side effects. The side effects you might experience will depend on the type of immunotherapy you receive and how your body responds. Most people have mild side effects. Side effects are likely to be more severe if you are taking a combination of immunotherapy drugs or having immunotherapy with other cancer treatments.

#### Common side effects

##### Fatigue

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

##### Changes in weight and 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), less commonly may lead to bloody stools

##### 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, change in vision

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

##### Dry eyes

could be inflammation of the eyes or tear glands

##### Breathlessness and coughing

could be inflammation of the lungs

##### Yellowing of the eyes, severe abdominal pain and dark urine

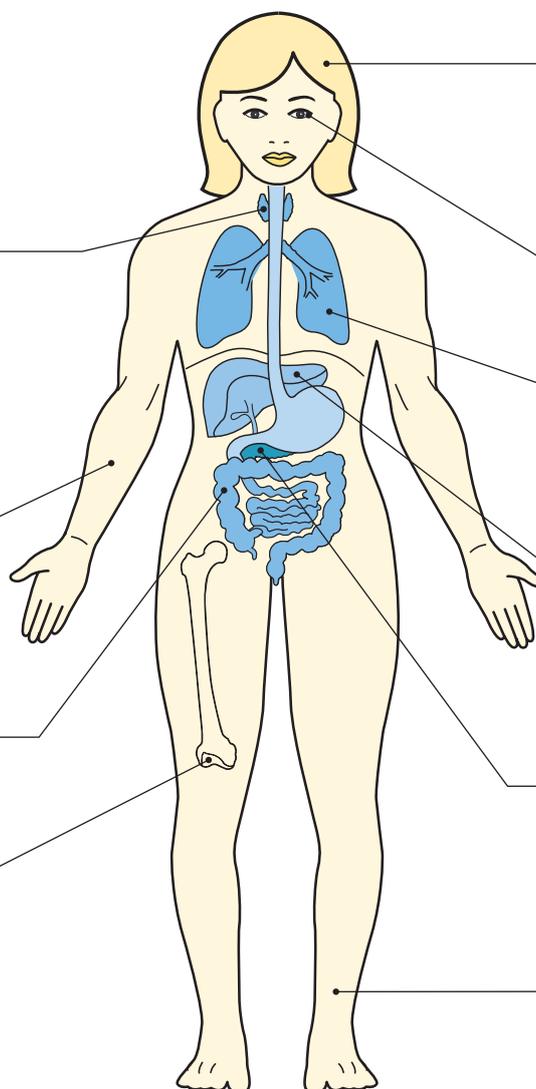
could be inflammation of the liver (hepatitis)

##### Excessive thirst or urination

could be inflammation of the pancreas affecting the production of insulin

##### Muscle pain

could be inflammation of the muscles (myositis)



Other rare side effects can occur. 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.

## Understanding Immunotherapy

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### Managing side effects

Because immunotherapy works differently from other cancer treatments, it's important to work closely with your treatment team to monitor your response.

Before starting immunotherapy, discuss the potential side effects with your cancer specialist. They can give you a Consumer Medicine Information leaflet about the immunotherapy drug that you are having. Ask which side effects to watch out for or report, and who to contact after hours. Throughout treatment, the team will regularly test your blood and ask you questions to check for early signs of side effects.

Because new side effects can appear months after having immunotherapy, ask your cancer specialist how long you need to look out 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.

Because immunotherapy is still a new 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 give this card to any other health professionals you see and ask them to consult with your cancer specialist. Do not start any new medicines, including anti-inflammatory steroids, 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 will be graded on a scale of 1–4 to help decide how to treat them. Moderate to severe side effects (grades 2–4) are often treated with steroid tablets, such as prednisone. In some cases of severe side effects (grades 3–4), people may be hospitalised and/or treated with intravenous steroids or other medicines, and immunotherapy may need to be stopped until the side effects are better controlled.

If side effects become too severe, immunotherapy must be stopped permanently. In this case, the immunotherapy that you have already received may have “trained” the 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.

### 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 treatment.

It may take some time to know if immunotherapy has worked because some people have a delayed response. Rarely, the cancer may appear to get worse before improving.

You may wonder whether having side effects means the treatment is working. Immunotherapy side effects do indicate that the treatment is affecting your immune system in some way, but the link with treatment success is unclear. Many people who have had no side effects have still seen improvements in the cancer.

Sometimes it can be tricky to know which of your symptoms may be related to the cancer and which may be side effects of the immunotherapy. Make sure to discuss this with your cancer care team.

A good response from immunotherapy will make the cancer shrink. In some cases, the cancer remains stable, which means it doesn't increase in size on scans but also does not shrink or disappear. People with stable disease can continue to have a good quality of life.

**What if it doesn't work?** – Unfortunately, immunotherapy does not work for everyone, and some people who have immunotherapy will not respond to the treatment. This can be very disappointing, but your cancer specialist will help you explore other treatment options if this happens.

# Understanding Immunotherapy

## How do I access immunotherapy?

Ask your cancer specialist if immunotherapy is a suitable treatment for you and whether it is reimbursed through the PBS for your type of cancer (see page 5). It may be possible to access immunotherapy treatments through clinical trials. Speak with your treatment team for more information.

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

## Question checklist

- 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?
- What do you expect the immunotherapy to do to the cancer?
- What percentage of people with this type of cancer respond to immunotherapy?
- Which immunotherapy are you recommending?
- Will it be my only treatment, or will I also have other treatments?
- How often will I receive immunotherapy? Can you give me the Consumer Medicine Information for it?
- How long will I have treatment?
- Where will I have treatment?
- What side effects should I watch out for or report?
- Who do I contact if I get side effects?
- How can side effects be managed?
- How will I know if the treatment is working?
- How much will immunotherapy cost?
- Can I take my other medicines while having immunotherapy? Can I have the flu vaccine?

## Where to get help and information

Call Cancer Council **13 11 20** for more information about immunotherapy. Our 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](http://actcancer.org)  
 NSW ..... [cancercouncil.com.au](http://cancercouncil.com.au)  
 NT ..... [nt.cancer.org.au](http://nt.cancer.org.au)  
 QLD ..... [cancerqld.org.au](http://cancerqld.org.au)  
 SA ..... [cancersa.org.au](http://cancersa.org.au)  
 TAS ..... [cancertas.org.au](http://cancertas.org.au)  
 VIC ..... [cancervic.org.au](http://cancervic.org.au)  
 WA ..... [cancerwa.asn.au](http://cancerwa.asn.au)  
 Australia..... [cancer.org.au](http://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.

- Peter MacCallum Cancer Centre  
[petermac.org](http://petermac.org)  
(search for “immunotherapy videos”)
- American Cancer Society  
[cancer.org](http://cancer.org)
- Cancer Research Institute  
[cancerresearch.org](http://cancerresearch.org)
- ECPC (European Cancer Patient Coalition) Immuno Oncology Portal  
[iop.ecpc.org](http://iop.ecpc.org)
- Society for Immunotherapy of Cancer (SITC)  
[sitcancer.org](http://sitcancer.org)
- Understanding immuno-oncology for kidney cancer  
[10forio.info](http://10forio.info)

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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.



For information and support on cancer-related issues, call Cancer Council **13 11 20**. This is a confidential service.