Cancer Immunotherapy.

Immunotherapy is treatment that uses your body’s own immune system to help fight cancer. Get information about the different types of immunotherapy and the types of cancer they are used to treat.

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What Is Cancer Immunotherapy?

Immunotherapy is treatment that uses certain parts of a person’s immune system to fight diseases such as cancer. This can be done in a couple of ways:

- Stimulating your own immune system to work harder or smarter to attack cancer cells
- Giving you immune system components, such as man-made immune system proteins
Some types of immunotherapy are also sometimes called \textit{biologic therapy} or \textit{biotherapy}.

In the last few decades immunotherapy has become an important part of treating some types of cancer. Newer types of immune treatments are now being studied, and they'll impact how we treat cancer in the future.

Immunotherapy includes treatments that work in different ways. Some boost the body’s immune system in a very general way. Others help train the immune system to attack cancer cells specifically.

Immunotherapy works better for some types of cancer than for others. It’s used by itself for some of these cancers, but for others it seems to work better when used with other types of treatment.

\textbf{What the immune system does}

Your immune system is a collection of organs, special cells, and substances that help protect you from infections and some other diseases. Immune cells and the substances they make travel through your body to protect it from germs that cause infections. They also help protect you from cancer in some ways.

The immune system keeps track of all of the substances normally found in the body. Any new substance that the immune system doesn’t recognize raises an alarm, causing the immune system to attack it. For example, germs contain substances such as certain proteins that are not normally found in the human body. The immune system sees these as “foreign” and attacks them. The immune response can destroy anything containing the foreign substance, such as germs or cancer cells.

The immune system has a tougher time targeting cancer cells, though. This is because cancer starts when cells become altered and start to grow out of control. The immune system doesn’t always recognize cancer cells as foreign.

Clearly there are limits on the immune system’s ability to fight cancer on its own, because many people with healthy immune systems still develop cancer. Sometimes the immune system doesn’t see the cancer cells as foreign because the cells aren’t different enough from normal cells. Sometimes the immune system recognizes the cancer cells, but the response might not be strong enough to destroy the cancer. Cancer cells themselves can also give off substances that keep the immune system in check.
To overcome this, researchers have found ways to help the immune system recognize cancer cells and strengthen its response so that it will destroy them.

Types of cancer immunotherapy

The main types of immunotherapy now being used to treat cancer include:

- **Monoclonal antibodies**: These are man-made versions of immune system proteins. Antibodies can be very useful in treating cancer because they can be designed to attack a very specific part of a cancer cell.
- **Immune checkpoint inhibitors**: These drugs basically take the ‘brakes’ off the immune system, which helps it recognize and attack cancer cells.
- **Cancer vaccines**: Vaccines are substances put into the body to start an immune response against certain diseases. We usually think of them as being given to healthy people to help prevent infections. But some vaccines can help prevent or treat cancer.
- **Other, non-specific immunotherapies**: These treatments boost the immune system in a general way, but this can still help the immune system attack cancer cells.

Immunotherapy drugs are now used to treat many different types of cancer. For more information about immunotherapy as a treatment for a specific cancer, please see our information on that type of cancer.

Many newer types of immunotherapy are now being studied for use against cancer. Some of these are discussed in [What’s new in cancer immunotherapy research?](#)

Last Medical Review: July 23, 2015 Last Revised: August 8, 2016

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**Monoclonal antibodies to treat cancer**

One way the immune system attacks foreign substances in the body is by making large numbers of antibodies. An antibody is a protein that sticks to a specific protein called an antigen. Antibodies circulate throughout the body until they find and attach to the antigen. Once attached, they can recruit other parts of the immune system to destroy the cells containing the antigen.
Researchers can design antibodies that specifically target a certain antigen, such as one found on cancer cells. They can then make many copies of that antibody in the lab. These are known as *monoclonal antibodies* (mAbs).

Monoclonal antibodies are used to treat many diseases, including some types of cancer. To make a monoclonal antibody, researchers first have to identify the right antigen to attack. For cancer, this is not always easy, and so far mAbs have proven to be more useful against some cancers than others.

Over the past couple of decades, the US Food and Drug Administration (FDA) has approved more than a dozen mAbs to treat certain cancers. As researchers have found more antigens linked to cancer, they have been able to make mAbs against more and more cancers. Clinical trials of newer mAbs are now being done on many types of cancer.

**Types of monoclonal antibodies**

Different types of monoclonal antibodies are used in cancer treatment.

**Naked monoclonal antibodies**

Naked mAbs are antibodies that work by themselves. There is no drug or radioactive material attached to them. These are the most common type of mAbs used to treat cancer.

Most naked mAbs attach to antigens on cancer cells, but some work by binding to antigens on other, non-cancerous cells, or even free-floating proteins.

Naked mAbs can work in different ways.

- Some boost a person’s immune response against cancer cells by attaching to them and acting as a marker for the body’s immune system to destroy them. An example is **alemtuzumab (Campath®)**, which is used to treat some patients with **chronic lymphocytic leukemia** (CLL). Alemtuzumab binds to the CD52 antigen, which is found on cells called *lymphocytes* (which include the leukemia cells). Once attached, the antibody attracts immune cells to destroy these cells.
- Some naked mAbs boost the immune response by targeting immune system checkpoints. (See Immune checkpoint inhibitors to treat cancer.)
- Other naked mAbs work mainly by attaching to and blocking antigens on cancer cells (or other nearby cells) that help cancer cells grow or spread. For example,
trastuzumab (Herceptin®) is an antibody against the HER2 protein. Breast and stomach cancer cells sometimes have large amounts of this protein on their surface. When HER2 is activated, it helps these cells grow. Trastuzumab binds to these proteins and stops them from becoming active.

Conjugated monoclonal antibodies

Monoclonal antibodies (mAbs) joined to a chemotherapy drug or to a radioactive particle are called conjugated monoclonal antibodies. The mAb is used as a homing device to take one of these substances directly to the cancer cells. The mAb circulates throughout the body until it can find and hook onto the target antigen. It then delivers the toxic substance where it is needed most. This lessens the damage to normal cells in other parts of the body.

Conjugated mAbs are also sometimes referred to as tagged, labeled, or loaded antibodies.

Radiolabeled antibodies: Radiolabeled antibodies have small radioactive particles attached to them. Ibritumomab tiuxetan (Zevalin®) is an example of a radiolabeled mAb. This is an antibody against the CD20 antigen, which is found on lymphocytes called B cells. The antibody delivers radioactivity directly to cancerous B cells and can be used to treat some types of non-Hodgkin lymphoma.

Treatment with this type of antibody is sometimes known as radioimmunotherapy (RIT).

Chemolabeled antibodies: These mAbs have powerful chemotherapy (or other) drugs attached to them. They are also known as antibody-drug conjugates (ADCs). (The drug is often too powerful to be used on its own – it would cause too many side effects if not attached to an antibody.)

Chemolabeled antibodies used to treat cancer include:

- Brentuximab vedotin (Adcetris®), an antibody that targets the CD30 antigen (found on lymphocytes), attached to a chemo drug called MMAE. This drug is used to treat Hodgkin lymphoma and anaplastic large cell lymphoma.
- Ado-trastuzumab emtansine (Kadcyla®, also called TDM-1), an antibody that targets the HER2 protein, attached to a chemo drug called DM1. It’s used to treat some breast cancer patients whose cancer cells have too much HER2.
A related drug known as **denileukin diftitox (Ontak®)** is an immune system protein known as interleukin-2 (IL-2) attached to a toxin from the germ that causes diphtheria. Although it’s not an antibody, IL-2 normally attaches to certain cells in the body that contain the CD25 antigen, which makes it useful for delivering the toxin to these cells. Denileukin diftitox is used to treat **lymphoma of the skin**⁶ (also known as cutaneous T-cell lymphoma). It’s also being studied for use against a number of other cancers.

**Bispecific monoclonal antibodies**

These drugs are made up of parts of 2 different mAbs, meaning they can attach to 2 different proteins at the same time. An example is **blinatumomab (Blincyto)**, which is used to treat some types of acute lymphocytic leukemia (ALL). One part of blinatumomab attaches to the CD19 protein, which is found on some leukemia and lymphoma cells. Another part attaches to CD3, a protein found on immune cells called T cells. By binding to both of these proteins, this drug brings the cancer cells and immune cells together, which is thought to cause the immune system to attack the cancer cells.

**Possible side effects of monoclonal antibodies**

Monoclonal antibodies are given intravenously (injected into a vein). The antibodies themselves are proteins, so giving them can sometimes cause something like an allergic reaction. This is more common while the drug is first being given. Possible side effects⁷ can include:

- Fever
- Chills
- Weakness
- Headache
- Nausea
- Vomiting
- Diarrhea
- Low blood pressure
- Rashes

Compared with chemotherapy drugs, naked mAbs tend to have fewer serious side effects. But they can still cause problems in some people. Some mAbs can have side effects that are related to the antigens they target. For example:

- **Bevacizumab (Avastin®)** is an mAb that targets a protein called **VEGF** that affects tumor blood vessel growth. It can cause side effects such as high blood pressure,
bleeding, poor wound healing, blood clots, and kidney damage.

- **Cetuximab (Erbitux®)** is an antibody that targets a cell protein called *EGFR*, which is found on normal skin cells (as well as some types of cancer cells). This drug can cause serious rashes in some people.

Conjugated antibodies can be more powerful than naked mAbs, but they can also cause more side effects. The side effects depend on which type of substance they’re attached to.

### Hyperlinks


Last Medical Review: July 23, 2015 Last Revised: August 8, 2016

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### CAR T-Cell Therapies

**Chimeric antigen receptor (CAR) T-cell therapy**

Your immune system helps keep track of all the substances normally found in your body. Any new substance the immune system doesn’t recognize raises an alarm, causing the immune system to attack it. CAR T-cell therapy is a promising new way to get immune cells called **T cells (a type of white blood cell)** to fight cancer by changing them in the lab so they can find and destroy cancer cells. CAR T-cell therapies are sometimes talked about as a type of gene or cell therapy, or an adoptive cell transfer therapy.

**Cancer and the Immune System**

To better understand how CAR T-cell therapies work, it can help to know a little more
about the immune system and cancer. Your immune system has many different kinds of cells that work together to destroy foreign substances. First, the immune system has to recognize that these substances do not belong in the body. It does this by finding proteins on the surface of those cells, called antigens. Some immune cells, like T-cells, have their own proteins (called receptors) that attach to foreign antigens and help trigger other parts of the immune system to destroy the foreign substance. The relationship between antigens and immune receptors is like a lock and key. Just as every lock can only be opened with the right key, each foreign antigen has a unique immune receptor that is able to bind to it. Cancer cells also have antigens, but the immune system has a tougher time knowing cancer cells are foreign. If your immune cells do not have the right receptor (protein) to find a cancer cell's antigen, they cannot attach to it and help destroy the cancer cell.

The T-cells used in CAR T-cell therapies get changed in the lab to spot specific cancer cells by adding a man-made receptor (called a chimeric antigen receptor or CAR). This helps them better identify specific cancer cell antigens. Since different cancers have different antigens, each CAR is made for a specific cancer's antigen. For example, certain kinds of leukemia or lymphoma will have an antigen on the outside of the cancer cells called CD19. The CAR T-cell therapies to treat those cancers are made to connect to the CD-19 antigen and will not work for a cancer that does not have the CD19 antigen. The patient’s own T-cells are used to make the CAR T-cells.

**CAR T-cell Therapy Steps**

The process for CAR T cell therapy can take a few weeks. First, T cells are removed from the patient’s blood using a procedure called leukapheresis. During this procedure, patients usually lie in bed or sit in a reclining chair. Two IV lines are needed because blood is removed through one IV, and then is returned to the body through the other. Sometimes a special type of IV line is used called a central venous catheter, that has both IV lines built in. The patient needs to remain still for 2 to 3 hours during the procedure. During leukapheresis, sometimes calcium levels can drop and cause numbness and tingling or muscle spasms. This can be easily treated with calcium, which may be given by mouth or through an IV.

After the white cells are removed from the patient, the T-cells are separated, sent to the lab, and genetically altered by adding the specific chimeric antigen receptor (CAR). This makes them CAR T-cells. It can take a few weeks to finish making CAR T-cells because a very large number of CAR T-cells are needed for this therapy. Once there are enough CAR T-cells, they will be given back to the patient to launch a precise attack against the cancer cells.

A few days before a CAR T-cell infusion, a patient might receive chemotherapy to help
lower the number of other immune cells so the CAR T-cells have a better chance to get activated to fight the cancer. This chemotherapy is usually not very strong because CAR T-cells work best when there are some cancer cells to attack. Once the CAR T-cells start binding with cancer cells, they start to increase in number and can destroy even more cancer cells.

Approved CAR T-cell Therapies

Currently, there are three CAR T-cell therapies approved for use in the United States. One is for advanced or recurrent acute lymphoblastic leukemia in children and young adults. The other two are for certain types of advanced or recurrent large B-cell lymphoma. This type of lymphoma is one of several types of non-Hodgkin’s lymphoma. This technique has shown very encouraging results in clinical trials against these cancers. In many patients, the cancer could not be found after treatment, although it’s not yet clear if these therapies will result in a long-term cure. In some patients, the CAR T-cells seem to go away after the cancer has been in remission for a while, and researchers are studying whether those patients have a higher risk of their cancer coming back. Researchers are also studying long-term side effects of this kind of treatment. Other CAR T-cell therapies to treat different types of cancer are being studied and are currently only available in clinical trials. For more information, see What’s New in Cancer Immunotherapy Research?

CAR T-cell Side Effects

Some people have had serious side effects from this treatment, especially as the CAR T-cells multiply in the body to fight the cancer. Serious side effects can include very high fevers and dangerously low blood pressure in the days after it’s given. This is called cytokine release syndrome, or CRS. Doctors are learning how to manage these side effects. Other serious side effects include neurotoxicity or changes in the brain that cause confusion, seizures, or severe headaches. Some patients have also developed serious infections, low blood cell counts, and a weakened immune system. These side effects can be life threatening and it is important for patients to know what to watch for and to tell the cancer care team if any of these symptoms develop.

Hyperlinks

2. www.cancer.org/treatment/treatments-and-side-effects/treatment-
Immune checkpoint inhibitors to treat cancer

An important part of the immune system is its ability to tell between normal cells in the body and those it sees as “foreign.” This lets the immune system attack the foreign cells while leaving the normal cells alone. To do this, it uses “checkpoints” – molecules on certain immune cells that need to be activated (or inactivated) to start an immune response.

Cancer cells sometimes find ways to use these checkpoints to avoid being attacked by the immune system. But drugs that target these checkpoints hold a lot of promise as cancer treatments.

Drugs that target PD-1 or PD-L1

PD-1 is a checkpoint protein on immune cells called T cells. It normally acts as a type of “off switch” that helps keep the T cells from attacking other cells in the body. It does this when it attaches to PD-L1, a protein on some normal (and cancer) cells. When PD-1 binds to PD-L1, it basically tells the T cell to leave the other cell alone. Some cancer cells have large amounts of PD-L1, which helps them evade immune attack.

Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells. These drugs have shown a great deal of promise in treating certain cancers.

**PD-1 inhibitors:** Examples of drugs that target PD-1 include:

- Pembrolizumab (Keytruda)
• Nivolumab (Opdivo)
• Cemiplimab (Libtayo)

These drugs have been shown to be helpful in treating several types of cancer, including melanoma of the skin, non-small cell lung cancer, kidney cancer, bladder cancer, head and neck cancers, and Hodgkin lymphoma. They are also being studied for use against many other types of cancer.

**PD-L1 inhibitors:** Examples of drugs that target PD-L1 include:

• Atezolizumab (Tecentriq)
• Avelumab (Bavencio)
• Durvalumab (Imfinzi)

These drugs have also been shown to be helpful in treating different types of cancer, including bladder cancer, non-small cell lung cancer, and Merkel cell skin cancer (Merkel cell carcinoma). They are also being studied for use against other types of cancer.

One concern with all of these drugs is that they can allow the immune system to attack some normal organs in the body, which can lead to serious side effects in some people. Common side effects of these drugs can include fatigue, cough, nausea, loss of appetite, skin rash, and itching. Less often they can cause more serious problems in the lungs, intestines, liver, kidneys, hormone-making glands, or other organs.

Many other drugs that target either PD-1 or PD-L1 are now being tested in clinical trials as well, both alone and combined with other drugs (see [What's new in cancer immunotherapy research?](#)).

**Drugs that target CTLA-4**

CTLA-4 is another protein on some T cells that acts as a type of “off switch” to keep the immune system in check.

**Ipilimumab (Yervoy)** is a monoclonal antibody that attaches to CTLA-4 and stops it from working. This can boost the body’s immune response against cancer cells.

This drug is used to treat melanoma of the skin and some other cancers.

Because ipilimumab affects the immune system, it can sometimes cause serious or
Cancer vaccines

Most of us know about vaccines given to healthy people to help prevent infections, such as measles and chicken pox. These vaccines use weakened or killed germs like viruses or bacteria to start an immune response in the body. Getting the immune system ready to defend against these germs helps keep people from getting infections.

Most cancer vaccines work the same way, but they make the person’s immune system attack cancer cells. The goal is to help treat cancer or to help keep it from coming back after other treatments. But there are also some vaccines that may actually help prevent certain cancers.

Vaccines to help prevent cancer

Many people might not realize it, but some cancers are caused by viruses. Vaccines that help protect against infections with these viruses might also help prevent some of these cancers.

- Some strains of the human papilloma virus (HPV)\(^1\) have been linked to cervical, anal, throat, and some other cancers. Vaccines against HPV may help protect against some of these cancers.
- People who have chronic (long-term) infections with the hepatitis B virus (HBV) are at higher risk for liver cancer\(^2\). Getting the vaccine to help prevent HBV infection may therefore lower some people’s risk of getting liver cancer.

These are traditional vaccines that target the viruses that can cause certain cancers. They may help protect against some cancers, but they don’t target cancer cells directly.

These types of vaccines are only useful for cancers known to be caused by infections. But most cancers, such as colorectal, lung, prostate, and breast cancers, are not thought to be caused by infections. Doctors are not yet sure if it’s possible to make
vaccines to prevent these other cancers. Some researchers are now trying, but this research is still in very early stages. Even if such vaccines prove to be possible, it will be many years before they become available.

**Vaccines to help treat cancer**

Cancer treatment vaccines are different from the vaccines that work against viruses. These vaccines try to get the immune system to mount an attack against cancer cells in the body. Instead of preventing disease, they are meant to get the immune system to attack a disease that already exists.

Some cancer treatment vaccines are made up of cancer cells, parts of cells, or pure antigens. Sometimes a patient’s own immune cells are removed and exposed to these substances in the lab to create the vaccine. Once the vaccine is ready, it’s injected into the body to increase the immune response against cancer cells.

Vaccines are often combined with other substances or cells called *adjuvants* that help boost the immune response even further.

Cancer vaccines cause the immune system to attack cells with one or more specific antigens. Because the immune system has special cells for memory, it’s hoped that the vaccine might continue to work long after it’s given.

**Sipuleucel-T (Provenge®)**

This is the only vaccine approved in the US to treat cancer so far. It’s used to treat advanced prostate cancer that is no longer being helped by hormone therapy.

For this vaccine, immune system cells are removed from the patient’s blood and sent to a lab. There they are exposed to chemicals that turn them into special immune cells called *dendritic cells*. They are also exposed to a protein called *prostatic acid phosphatase* (PAP), which should produce an immune response against prostate cancer cells.

The dendritic cells are then given back to the patient by infusion into a vein (IV). This process is repeated twice more, 2 weeks apart, so that the patient gets 3 doses of cells. Back in the body, the dendritic cells help other immune system cells attack the prostate cancer.

Although the vaccine doesn’t cure prostate cancer, it has been shown to help extend patients’ lives by several months on average. Studies to see if this vaccine can help
men with less advanced prostate cancer are now being done.

Side effects are usually mild and can include fever, chills, fatigue, back and joint pain, nausea, and headache. A few men may have more severe symptoms, including problems breathing and high blood pressure.

**Other vaccines**

Many different types of cancer vaccines have shown some promise in clinical trials, but they are not yet approved in the United States to treat cancer. For more information on some these newer vaccines, see [What’s new in cancer immunotherapy research?](#)

**Hyperlinks**


_Last Medical Review: July 23, 2015 Last Revised: August 8, 2016_

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**Non-specific cancer immunotherapies and adjuvants**

Non-specific immunotherapies don’t target cancer cells specifically. They stimulate the immune system in a more general way, but this can still sometimes lead to a better immune response against cancer cells.

Some non-specific immunotherapies are given by themselves as cancer treatments. Others are used as adjuvants (along with a main treatment) to boost the immune system to improve how well another type of immunotherapy (such as a vaccine) works. Some are used by themselves against some cancers and as adjuvants against others.

**Cytokines**

Cytokines are chemicals made by some immune system cells. They are crucial in controlling the growth and activity of other immune system cells and blood cells.
Cytokines are injected, either under the skin, into a muscle, or into a vein. The most common ones are discussed here.

**Interleukins**

Interleukins are a group of cytokines that act as chemical signals between white blood cells.

**Interleukin-2 (IL-2)** helps immune system cells grow and divide more quickly. A man-made version of IL-2 is approved to treat advanced kidney cancer\(^1\) and metastatic melanoma\(^2\).

IL-2 can be used as a single drug treatment for these cancers, or it can be combined with chemotherapy or with other cytokines such as interferon-alfa. Using IL-2 with these treatments might help make them more effective against some cancers, but the side effects of the combined treatment are also increased.

Side effects of IL-2 can include flu-like symptoms such as chills, fever, fatigue, and confusion. Most people gain weight. Some have nausea, vomiting, or diarrhea. Many people develop low blood pressure, which can be treated with other medicines. Rare but potentially serious side effects include an abnormal heartbeat, chest pain, and other heart problems. Because of these possible side effects, if IL-2 is given in high doses, it must be done in a hospital.

Other interleukins, such as IL-7, IL-12, and IL-21, are now being studied for use against cancer too, both as adjuvants and as stand-alone agents.

**Interferons**

Interferons are chemicals that help the body resist virus infections and cancers. The types of interferon (IFN) are named after the first 3 letters of the Greek alphabet:

- IFN-alfa
- IFN-beta
- IFN-gamma

Only **IFN-alfa** is used to treat cancer. It boosts the ability of certain immune cells to attack cancer cells. It may also slow the growth of cancer cells directly, as well as the blood vessels that tumors need to grow.

IFN-alfa can be used to treat these cancers:
- Hairy cell leukemia
- Chronic myelogenous leukemia (CML)
- Follicular non-Hodgkin lymphoma
- Cutaneous (skin) T-cell lymphoma
- Kidney cancer
- Melanoma
- Kaposi sarcoma

Side effects of interferons can include:

- Flu-like symptoms (chills, fever, headache, fatigue, loss of appetite, nausea, vomiting)
- Low white blood cell counts (which increase the risk of infection)
- Skin rashes
- Thinning hair

These side effects can be severe and can make treatment with interferon hard for many people to tolerate. Most side effects don’t last long after the treatment stops, but fatigue can last longer. Other rare long-term effects include damage to nerves, including those in the brain and spinal cord.

Other drugs that boost the immune system

Some other drugs boost the immune system in a non-specific way, similar to cytokines. But unlike cytokines, these drugs are not naturally found in the body.

Immune checkpoint inhibitors

These drugs target molecules like PD-1, PD-L1, and CTLA-4, which normally help keep the immune system in check. While these checkpoint proteins are important in stopping the immune system from attacking normal cells, they can also stop it from attacking cancer cells. These drugs help boost the immune response against some cancers. For more on these drugs, see Immune checkpoint inhibitors to treat cancer.

Thalidomide, lenalidomide, and pomalidomide

Thalidomide (Thalomid®), lenalidomide (Revlimid®), and pomalidomide (Pomalyst®) are known as immunomodulating drugs (or IMiDs). They are thought to work in a general way by boosting the immune system, although it’s not exactly clear how they do this.
These drugs are used to treat multiple myeloma\(^3\) and some other cancers.

The drugs can cause side effects such as drowsiness, fatigue, constipation, low blood cell counts, and neuropathy (painful nerve damage). There is also an increased risk of serious blood clots (that start in the leg and can travel to the lungs). These tend to be more likely with thalidomide than with the other drugs.

These drugs can also cause severe birth defects if taken during pregnancy.

**Bacille Calmette-Guérin**

Bacille Calmette-Guérin (BCG) is a germ that doesn’t cause serious disease in humans, but it does infect human tissues and helps activate the immune system. This makes BCG useful as a form of cancer immunotherapy. BCG was one of the earliest immunotherapies used against cancer and is still being used today.

BCG is used to treat early stage bladder cancer\(^4\). It is a liquid put into the bladder through a catheter. BCG attracts the body’s immune system cells to the bladder, where they can attack the bladder cancer cells. Treatment with BCG can cause symptoms that are like having the flu, such as fever, chills, and fatigue. It can also cause a burning feeling in the bladder.

BCG can also be used to treat some melanoma skin cancers\(^5\) by injecting it directly into the tumors.

**Imiquimod**

Imiquimod (Zyclara\(^\circledR\)) is a drug that is applied to the skin as a cream. It stimulates a local immune response against skin cancer cells. It is used to treat some very early stage skin cancers (or pre-cancers), especially if they are in sensitive areas such as on the face.

The cream is applied anywhere from once a day to twice a week for several months. Some people have serious skin reactions to this drug.

**Hyperlinks**

What’s new in cancer immunotherapy research?

Immunotherapy is a very active area of cancer research. Many scientists and doctors around the world are studying new ways to use immunotherapy to treat cancer. Some of these are discussed here.

Newer monoclonal antibodies

Monoclonal antibodies (mAbs) have already become an important part of the treatment for many cancers. As researchers have learned more about what makes cancer cells different from normal cells, they have developed mAbs to exploit these differences. They have also developed newer forms of mAbs, attaching them to drugs or other substances to make them more powerful.

Researchers are also studying other ways of making monoclonal antibodies safer and more effective. For example, because mAbs are proteins, they can actually make the body’s immune system react against them. This can lead to side effects, as well as destroying the mAbs. Newer forms of mAbs are less likely to cause immune reactions. Researchers are also looking to see if using only parts of antibodies can make these drugs work better.

Another new approach is to combine parts of two antibodies together (known as a bispecific antibody). One part attaches to a cancer cell, while the other attaches to an immune cell, bringing the two together and leading to an immune response.

New types of mAbs are now being studied for use against many types of cancer. For information on newer treatments for a particular type of cancer, please see our information on that type of cancer.

Treatments that target immune system checkpoints
As mentioned in Immune checkpoint inhibitors to treat cancer, the immune system has checkpoint proteins (such as PD-1 and CTLA-4) that help keep it from attacking other normal cells in the body. Cancer cells sometimes take advantage of these checkpoints to avoid being attacked by the immune system.

Targeting these checkpoints is quickly becoming an important part of the treatment for some cancers, including melanoma and non-small cell lung cancer. Researchers have also found promising early results against a number of other cancer types. Unlike most other cancer drugs, these checkpoint inhibitors seem to be helpful against many different types of cancer.

Only a handful of these treatments have been approved for use so far, but many others are now being studied in clinical trials.

A newer approach being studied is to combine treatments that have different targets (such as nivolumab, which targets PD-1, and ipilimumab, which targets CTLA-4) to see if this might work better. In melanoma, this combined approach has been shown to work better than using either treatment alone, but the combination also comes with an increased risk of serious side effects.

Other studies are looking at combining checkpoint inhibitors with other types of drugs used to treat cancer.

**Newer cancer vaccines**

Vaccines are not yet a major type of treatment for cancer. Researchers have been trying to develop vaccines to fight cancer for decades, but this has proven to be harder than was first thought. As researchers have learned over the years, the immune system is very complex. It has also become clear that cancer cells have different ways of eluding the immune system, which makes creating effective vaccines difficult.

Researchers are using the knowledge gained in recent years to improve how they develop cancer vaccines. For example, vaccines are now often given along with other substances (called adjuvants) that help boost the body’s immune response, which might help the vaccines work better.

Researchers are also studying the best way to give vaccines, looking to see if they work better when used alone or with other types of cancer treatments.

**Types of cancer vaccines**
Many different types of vaccines are now being studied to treat a variety of cancers.

**Tumor cell vaccines:** These vaccines are made from actual cancer cells that have been removed from the patient during surgery. The cells are altered (and killed) in the lab to make them more likely to be attacked by the immune system and then injected back into the patient. The patient’s immune system then attacks these cells and any similar cells still in the body.

Most tumor cell vaccines are *autologous*, meaning the vaccine is made from killed tumor cells taken from the same person in whom they will later be used. Other vaccines are *allogeneic*, meaning the cells for the vaccine come from someone other than the patient being treated. Allogeneic vaccines are easier to make than autologous vaccines, but it’s not yet clear if one type works better than the other.

**Antigen vaccines:** These vaccines boost the immune system by using only one antigen (or a few), rather than whole tumor cells. The antigens are usually proteins or pieces of proteins called *peptides*.

Antigen vaccines can be specific for a certain type of cancer, but they are not made for a specific patient like autologous tumor cell vaccines are.

**Dendritic cell vaccines:** These vaccines have shown the most success so far in treating cancer. Sipuleucel-T (Provenge), which is approved for the treatment of advanced *prostate cancer*[^4], is an example of a dendritic cell vaccine.

Dendritic cells are special immune cells in the body that help the immune system recognize cancer cells. They break down cancer cells into smaller pieces (including antigens), and then hold out these antigens so other immune cells called T cells can see them. The T cells then start an immune reaction against any cells in the body that contain these antigens.

Dendritic cell vaccines are made from the person in whom they will be used. The process used to create this type of vaccine (known as an *autologous* vaccine) is complex and expensive. Doctors remove some immune cells from the patient’s blood and expose them in the lab to cancer cells or cancer antigens, as well as to other chemicals that turn the immune cells into dendritic cells and help them grow. The dendritic cells are then injected back into the patient, where they should cause an immune response to cancer cells in the body.

**Vector-based vaccines:** These vaccines use special delivery systems (called *vectors*) to make them more effective. They aren’t really a separate category of vaccine; for example, there are vector-based antigen vaccines.
Vectors are special viruses, bacteria, yeast cells, or other structures that can be used to get antigens into the body. The vectors are often germs that have been altered to make sure they can no longer cause disease.

Vectors can be helpful in making vaccines for a number of reasons. First, they can be used to deliver more than one cancer antigen at a time, which might make the body’s immune system more likely to mount a response. Second, vectors such as viruses and bacteria might trigger their own immune responses from the body, which could help make the overall immune response even stronger. Finally, these vaccines might be easier and less expensive to make than some other vaccines.

Some common cancers in which vaccines are being tested

Some of the more common types of cancer in which vaccines are now being studied include:

- Brain tumors (especially glioblastoma)
- Breast cancer
- Cervical cancer
- Colorectal cancer
- Kidney cancer
- Lung cancer
- Lymphoma
- Melanoma
- Pancreas cancer
- Prostate cancer

This is not a complete list – vaccines are being studied in other types of cancer as well. For information on newer treatments for a particular type of cancer, please see our information on that type of cancer.

Oncolytic viruses

Viruses are a type of germ that can infect and kill cells. Some viruses can be altered in the lab so that they infect and kill mainly cancer cells. These are known as oncolytic viruses. Along with killing the cells directly, the viruses can also alert the immune system to attack the cancer cells.

An example is talimogene laherparepvec (Imlygic), which is an oncolytic virus that has been modified to make GM-CSF, a protein that boosts the immune response. This
virus can be used to treat melanomas in the skin or lymph nodes that can’t be removed with surgery. It is injected directly into the tumors, typically every 2 weeks. This treatment can sometimes shrink these tumors, but it has not been shown to shrink tumors in other parts of the body.

Other ways to boost the immune system

Some other forms of immunotherapy are being studied to try to boost specific parts of the immune system. These types of treatments show a lot of promise, but they are complex and so far are available only through clinical trials being done at major medical centers.

Chimeric antigen receptor (CAR) T-cell therapy

This is a promising new way to get immune cells called T cells to fight cancer. For this technique, T cells are removed from the patient’s blood and genetically altered in the lab to have specific antigen receptors (called chimeric antigen receptors, or CARs) on their surface. These receptors will attach to proteins on the surface of cancer cells. The T cells are then multiplied in the lab and given back to the patient, where they can now seek out the cancer cells and launch a precise attack against them.

Currently, there are only few CAR T-cell therapies approved for use in the United States for certain types of advanced, hard-to-treat leukemias and lymphomas. These approvals are based on the results of clinical trials showing that in many patients the cancer could no longer be found after treatment. It is not yet clear if these treatments will result in a long-term cure. Researchers are also still learning about long-term side effects of these treatments. See CAR T-cell Therapies for more information about approved CAR T-cell treatments.

Doctors are still improving how they make the T cells and are learning the best ways to use them for different types of cancer. CAR T-cell therapies being studied are only available in clinical trials for patients whose cancer is not responding to treatment or has returned after treatment.

Some common cancers in which CAR T-cell Therapies are being tested

Some of the more common types of cancer in which CAR T-cell therapies are now being studied include:

- Brain tumors (especially glioblastoma)
- Breast cancer
• Acute Myeloid Leukemia
• Multiple Myeloma
• Hodgkin’s Lymphoma
• Neuroblastoma
• CLL
• Pancreas cancer

Tumor-infiltrating lymphocytes and interleukin-2 (IL-2)

Researchers have found immune system cells deep inside some tumors and have named these cells *tumor-infiltrating lymphocytes* (TILs). These T cells can be removed from tumor samples taken from patients and multiplied in the lab by treating them with IL-2. When injected back into the patient, these cells can be active cancer fighters.

Treatments using TILs are being tested in clinical trials in people with melanoma, kidney cancer, ovarian cancer, and other cancers. Early studies of this approach by researchers from the National Cancer Institute have been promising, but its use may be limited because doctors might not be able to get TILs from all patients.

Hyperlinks


Last Medical Review: July 23, 2015 Last Revised: October 31, 2017

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Last Medical Review: July 23, 2015 Last Revised: August 8, 2016

Written by

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