Immunotherapy

Immunotherapy is treatment that uses a person's own immune system to fight cancer. Immunotherapy can boost or change how the immune system works so it can find and attack cancer cells. If your treatment plan includes immunotherapy, knowing how it works and what to expect can often help you prepare for treatment and make informed decisions about your care.

Related Topics

- Intravenous (IV) Lines, Catheters, and Ports Used in Cancer Treatment
- Tubes, Catheters, and Drains Used in Cancer Treatment and Care
- Compassionate Drug Use
- Off-label Drug Use

Video

This short video provides answers to some of the most common questions that people with cancer have about immunotherapy.

Watch this video on YouTube

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 normal, healthy cells become changed or altered and start to grow out of control. Because cancer cells actually start in normal cells, the immune system doesn’t always recognize them 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 from finding and attacking them.

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. In this way, your own body is actually getting rid of the cancer, with some help from science.

Types of cancer immunotherapy

There are several main types of immunotherapy used to treat cancer, and many are being studied. **For more information about immunotherapy as a treatment for a specific cancer, please choose a cancer type[1].**

- Checkpoint inhibitors**:** These drugs basically take the ‘brakes’ off the immune system, which helps it recognize and attack cancer cells.
- Chimeric antigen receptor (CAR) T-cell therapy**:** This therapy takes some T-cells from a patient's blood, mixes them with a special virus that makes the T-cells learn how to attach to tumor cells, and then gives the cells back to the patient so they can find, attach to, and kill the cancer.
- **Cytokines**: This treatment uses *cytokines* (small proteins that carry messages between cells) to stimulate the immune cells to attack cancer.
- **Immunomodulators**: This group of drugs generally boosts parts of the immune system to treat certain types of cancer.
- 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.

- Monoclonal antibodies **(mAbs or MoAbs):** These are man-made versions of immune system proteins. mAbs can be very useful in treating cancer because they can be designed to attack a very specific part of a cancer cell.
- **Oncolytic viruses**: This treatment uses viruses that have been modified in a lab to infect and kill certain tumor cells.

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Monoclonal Antibodies and Their Side Effects

One way the immune system protects the body from germs and other foreign substances 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 help 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 or Moabs).

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. Finding the right antigens for cancer cells is not always easy, and so far mAbs have proven to be more useful against some cancers than others.

NOTE: Some monoclonal antibodies used to treat cancer are sometimes considered to be a type of targeted therapy[1] because they work by attaching to a specific target on a cancer cell and stopping it from functioning. But other monoclonal antibodies act like immunotherapy because they help the immune system find and attack cancer cells more effectively.

What mAbs are made of

Monoclonal antibodies are man-made proteins that act like human antibodies in the immune system. There are 4 different ways they can be made and are named based on what they are made of.

- **Murine:** These are made from mouse proteins, and the names of the treatments end in -omab.
- **Chimeric:** These proteins are a combination of part mouse and part human, and the names of the treatments end in -ximab.
- **Humanized:** These are made from small parts of mouse proteins attached to human proteins, and the names of the treatments end in -zumab
- **Human:** These are fully human proteins, and the names of the treatments end in -umab.

Types of mAbsused to treat cancer

Naked monoclonal antibodies

Naked mAbs are antibodies that have no drug or radioactive material attached to them. They work by themselves. 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 rituximab (Rituxan), which is used to treat some types of non-Hodgkin lymphoma (NHL) and other cancers.Rituxi20mab binds to the CD antigen, which is found on cells called *B lymphocytes* (which include some types of lymphoma 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 and Their Side Effects.)
- Other naked mAbs work mainly by attaching to and blocking proteins 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, which helps these cells grow. Trastuzumab binds to these proteins and stops them from becoming active.

Conjugated monoclonal antibodies

Conjugated mAbs are connected to a chemotherapy drug or a radioactive particle. These mAbs are 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. Conjugated mAbs are also sometimes referred to as *tagged*, *labeled*, or *loaded* antibodies.

Antibody-drug conjugates (ADCs): These mAbs have powerful chemotherapy (or other) drugs attached to them. Examples include:

- Brentuximab vedotin (Adcetris), an ADC made up of an antibody that targets the CD30 antigen (found on lymphocytes), attached to a chemo drug called *MMAE*
- Ado-trastuzumab emtansine (Kadcyla, also called TDM-1), an ADC made up of an antibody that targets the HER2 protein, attached to a chemo drug called DM1

Radiolabeled antibodies: Radiolabeled antibodies have small radioactive particles attached to them. The antibody delivers radioactivity directly to cancer cells. Treatment with this type of antibody is sometimes known as **radioimmunotherapy (RIT)**. The drug and radiation are delivered directly to the target cells because the mAb looks for the target, and then the radiation affects the target and nearby cells to a certain extent.

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.

T-cell engagers (TCEs): In these drugs, one part attaches to a protein on cancer cells, and the other sticks to a protein on immune cells called *T cells*. This brings the immune cells into contact with the cancer cells, which helps the immune system mount a more effective response against them. TCEs are becoming an important part of treatment for some types of cancer.

Possible side effects of monoclonal antibodies

Monoclonal antibodies are given intravenously (injected into a vein). The antibodies themselves are proteins, and giving them can sometimes cause an **infusion reaction**,

which is something like an allergic reaction. This is more common while the drug is first being given. Possible symptoms 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.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html

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Last Revised:

CAR T-cell Therapy and Its Side Effects

Chimeric antigen receptor (CAR) T-cell therapy is a 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 therapy is also sometimes talked about as a type of *cell-based gene therapy*, because it involves altering the genes inside T cells to help them attack the cancer.

This type of treatment can be very helpful in treating some types of cancer, even when other treatments are no longer working.

How CAR T-cell therapy works

Immune receptors and foreign antigens

The immune system recognizes foreign substances in the body by finding proteins called *antigens* on the surface of those cells. Immune cells called *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 a lock can only be opened with the right key, each foreign antigen has a unique immune receptor that can bind to it.

Cancer cells also have antigens, but if your immune cells don't have the right receptors, they can't attach to the antigens and help destroy the cancer cells.

Chimeric antigen receptors (CARs)

In CAR T-cell therapies, T cells are taken from the patient's blood and are changed in the lab by adding a gene for a receptor (called a **chimeric antigen receptor** or **CAR**), which helps the T cells attach to a specific cancer cell antigen. The CAR T cells are then given back to the patient.

Since different cancers have different antigens, each CAR is made for a specific cancer's antigen. For example, in certain kinds of leukemia or lymphoma, the cancer cells have an antigen called CD19. Many of the CAR T-cell therapies to treat these cancers are made to attach to the CD19 antigen and will not work for a cancer that does not have the CD19 antigen.

Examples of CAR T-cell therapies currently approved include:

- **Tisagenlecleucel**, also known as **tisa-cel (Kymriah)**
- **Axicabtagene ciloleucel**, also known as **axi-cel (Yescarta)**
- **Brexucabtagene autoleucel**, also known as **brexu-cel (Tecartus)**
- **Lisocabtagene maraleucel**, also known as **liso-cel (Breyanzi)**
- **Idecabtagene vicleucel**, also known as **ide-cel (Abecma)**
- **Ciltacabtagene autoleucel**, also known as **cilta-cel (Carvykti)**
- **Obecabtagene autoleucel**, also known as **obe-cel (Aucatzyl)**

Many other CAR T-cell therapies (and similar types of treatment) are now being studied in clinical trials, in the hope of treating other types of cancer as well.

Possible CAR T-cell therapy side effects

CAR T-cell therapy can be very effective against some types of hard-to-treat cancers, but it can also sometimes cause serious or even life-threatening side effects. Because of this, it needs to be given in a medical center that is specially trained in its use, and patients need to be watched closely for several weeks after getting the CAR T cells.

Cytokine release syndrome (CRS): As CAR T cells multiply, they can release large amounts of chemicals called *cytokines* into the blood, which can ramp up the immune system. Serious side effects from this release can include:

- High fever and chills
- Trouble breathing
- Severe nausea, vomiting, and/or diarrhea
- Feeling dizzy or lightheaded
- Headaches
- Fast heartbeat
- Feeling very tired
- Muscle and/or joint pain

As doctors are gaining more experience with CAR T-cell therapy, they are learning how to recognize CRS early, as well as how to treat it.

Nervous system problems: This treatment can sometimes have serious effects on the nervous system, leading to a condition known as **immune effector cell-associated neurotoxicity syndrome (ICANS)**. This can result in symptoms such as:

- Headaches
- Changes in consciousness
- Confusion or agitation
- Seizures
- Shaking or twitching (tremors)
- Trouble speaking and understanding
- Loss of balance

Because of the risk of these side effects, adult patients are typically advised not to drive, operate heavy machinery, or do any other potentially dangerous activities for at least several weeks after getting treatment.

Other serious side effects: Other possible serious side effects of CAR T-cell therapy can include:

- Allergic reactions during the infusion
- Abnormal levels of minerals in the blood, such as low potassium, sodium, or phosphorous levels
- A weakened immune system, with an increased risk of serious infections
- Low blood cell counts, which can increase the risk of infections, fatigue, and bruising or bleeding
- An increased risk of getting another type of blood cancer

If you are getting CAR T-cell therapy, it's very important to report any side effects to your health care team right away, as there are often medicines that can help treat them.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html
2. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html

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American Society of Clinical Oncology

Immune Checkpoint Inhibitors and Their Side Effects

inhibitors).

Checkpoint inhibitors don't kill cancer cells directly. They work by helping the immune system to better find and attack the cancer cells, wherever they are in the body.

Medicines that target different checkpoint proteins are now used to treat many types of cancer.

All of these drugs can be given as an infusion into a vein (IV). Some of them can now be given as an injection under the skin (subcutaneously) over several minutes as well.

PD-1 and PD-L1 inhibitors

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 hide from an immune attack.

Monoclonal antibodies that target either PD-1 or PD-L1 can block this binding and boost the immune response against cancer cells.

PD-1 inhibitors

Examples of drugs that target PD-1 include:

- **Pembrolizumab (Keytruda)**
- **Nivolumab (Opdivo** and **Opdivo Qvantig)**
- **Cemiplimab (Libtayo)**

PD-L1 inhibitors

Examples of drugs that target PD-L1 include:

- **Atezolizumab (Tecentriq** and **Tecentriq Hybreza)**
- **Avelumab (Bavencio)**
- **Durvalumab (Imfinzi)**

Both PD-1 and PD-L1 inhibitors have been shown to be helpful in treating many

different types of cancer.

CTLA-4 inhibitors

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

Ipilimumab (Yervoy) and **tremelimumab (Imjuno)** are monoclonal antibodies that attach to CTLA-4 and stop it from working. This can help boost the body’s immune response against cancer cells.

These drugs are typically used along with a PD-1 or PD-L1 inhibitor. These combinations can be used to treat several types of cancer.

LAG-3 inhibitors

LAG-3 is a checkpoint protein on some types of immune cells that normally acts as a type of “off switch” to help keep the immune system in check.

Relatlimab is a monoclonal antibody that attaches to LAG-3 and stops it from working. This can help boost the body’s immune response against cancer cells.

This drug is given along with the PD-1 inhibitor nivolumab (in a combination known as **Opdualag**). It can be used to treat melanoma of the skin, and it’s being studied for use

Other, more serious side effects occur less often:

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It’s important to tell your doctor or nurse right away if you have any of these symptoms while getting one of these drugs.

Autoimmune reactions: By targeting a checkpoint protein, these drugs remove one of the safeguards on the body's immune system. Sometimes the immune system responds by attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It’s very important to report any new side effects to someone on your health care team as soon as possible. If serious side effects do occur, treatment may need to be stopped and you might be given high doses of corticosteroids to suppress your immune system.

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Vaccines to 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 (certain proteins on the cancer cells). 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):

Hyperlinks

1. www.cancer.org/cancer/risk-prevention/hpv.html
2. www.cancer.org/cancer/risk-prevention/hpv/hpv-vaccine.html
3. www.cancer.org/cancer/types/liver-cancer.html
4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Cytokines and Their Side Effects

Cytokines are small proteins that are crucial in controlling the growth and activity of other immune system cells and blood cells. When released, they signal the immune system to do its job. Cytokines affect the growth of all blood cells and other cells that help the body's immune and inflammation responses. They also help to boost anti-cancer activity by sending signals that can help make abnormal cells die and normal cells live longer.

- Interleukins
- Interferons

One specific type of cytokine is called a *chemokine*. A chemokine can make immune cells move toward a target. There are different kinds of chemokines, including *interleukins, interferons, tumor necrosis factors,* and *growth factors*.

Some cytokines can be made in a lab and are used to treat cancer. Some are used to help prevent or manage chemotherapy side effects. They are injected, either under the skin, into a muscle, or into a vein. The most common ones are interleukins and interferons.

Interleukins

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-alfais used to treat cancer. It boosts the ability of certain immune cells to

Hyperlinks

1. www.cancer.org/cancer/types/kidney-cancer.html
2. www.cancer.org/cancer/types/melanoma-skin-cancer.html
3. www.cancer.org/cancer/managing-cancer/side-effects.html

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Immunomodulators and Their Side

Effects

Immunomodulators are a group of drugs that mainly target the pathways that treat multiple myeloma and a few other cancers. They have many ways to work, including working on the immune system directly by turning down some proteins and turning up others.

- Thalidomide, lenalidomide, and pomalidomide
- Bacillus Calmette-Guérin
- Imiquimod

Thalidomide, lenalidomide, and pomalidomide

Imiquimod 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.

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Immunotherapy Safety

Much is known about the need to protect others from exposure to traditional or standard chemotherapy[1] because it is hazardous. This is why there are safety rules and recommendations for people who handle chemo drugs. However, because

immunotherapy drugs are newer, there is not as much information about long-term effects of exposure.

To be safe, many experts recommend treating immunotherapy drugs as hazardous and taking the same precautions. This is especially true when immunotherapy drugs are given to treat cancer in combination with other drugs that are known to be hazardous, so your cancer care team will take precautions to protect themselves and others from exposure to them.

Precautions the cancer care team might take

You may notice special clothing and protective equipment being worn by the nurses and other members of your cancer care team. Pharmacists and nurses who prepare drugs to treat cancer use a special type of pharmacy that must meet certain regulations. If you are being cared for in a treatment center, the nurses and others who give treatment and help take care of patients afterwards wear protective clothing, such as 2 pairs of special gloves and a gown, and sometimes goggles or a face shield. If you're getting immunotherapy through an IV, there might be a disposable pad under the infusion tubing to protect the surface of the bed or chair.

Special precautions when taking oral or topical immunotherapy

Oral immunotherapy that you take by mouth and swallow, or topical immunotherapy that you rub on your skin, is usually taken at home. Some are considered hazardous. There might be special precautions for storing and handling an immunotherapy drug. You might be told to be careful not to let others come into contact with it or your body fluids while taking it and for a time after taking it. Sometimes you need to wear gloves when touching the pills or capsules. Some drugs have to be kept in the bottle or box they came in. And some drugs and the packages they come in need to be disposed of in a certain way. Some might have to be taken back to the drug store to be thrown away safely. If you are taking an oral drug, talk to your cancer care team about whether special precautions are needed at home.

Keeping family and friends safe

Unless your health care team tells you differently, you can usually be around family and

friends during the weeks and months you're getting immunotherapy. If you're getting treatment at a center, family and friends can often come with you. However, some treatment centers only allow patients in the infusion area and visitors may need to stay in the waiting room.

You are the only person who should be exposed to the drug you are getting, but any spilled IV drug, and any powder or dust from a pill or capsule, or any liquid from oral or topical immunotherapy might be hazardous to others if they are around it.

It's important to talk to your cancer care team and be aware of any special precautions that might be needed while you are taking an immunotherapy drug.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html

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Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as editors and translators with extensive experience in medical writing.