



This booklet gives an overview of immunotherapy and explains how this type of treatment uses the body's natural defenses to identify, attack, and kill cancer cells.

Researchers have wanted to use the body's natural defense system to fight cancer for over 100 years. Recent findings have helped scientists understand how this process works. Today, immunotherapy is being used for several common cancer

types. It is estimated that more than half of current cancer clinical trials include some form of immunotherapy. While immunotherapy helps some patients live longer and better, it may not currently be an option for every patient or cancer type.



What is Immunotherapy?

Immunotherapy is a type of cancer treatment that uses the body's natural defenses to identify, attack, and kill cancer cells. The immune system is designed to attack any cell it sees as unhealthy or abnormal. Most immunotherapies are biologic therapies — made by living organisms.

Today, there are multiple kinds of immunotherapy treatments. They help fight cancer by:

- Boosting the immune system. A “revved up” immune system can be better at fighting the cancer.
- “Marking” cancer cells so that your immune system can better find and destroy them. This keeps the cancer from being able to hide from the immune system.
- Helping the immune system find cancer cells and delivering treatment (like chemotherapy, radiation, or even T cells) directly to the cancer cells.

How is Immunotherapy Given?

The use of immunotherapy is rapidly increasing as more immunotherapies are approved to treat people with more types of cancer. Most immunotherapy is given using an IV (through a vein). You may receive immunotherapy in a doctor's office, in a clinic, or as a day patient in a hospital. Different immunotherapies are given on different schedules. Some may be given in combination with other therapies or with a different immunotherapy.

IMMUNE SYSTEM: A network of cells, tissues, and organs that work together to protect the body from bacteria, viruses, parasites, fungi, and abnormal cells like cancer.

T CELLS: A type of white blood cell. T cells are the immune system's “soldiers.” They help protect the body from infection and can help fight cancer. They are also called T lymphocytes.

ANTIBODY: A protein made by your body's immune cells to attach to a specific foreign invader, such as bacteria, viruses, and potentially cancerous cells.

TUMOR ANTIGEN: A substance produced by a tumor cell that can cause the body to create a specific immune response.

BIOMARKER: A molecule in your body that your doctors can measure. Biomarkers give your doctor specific information about your cancer. Biomarkers can let doctors know if your tumor has a good chance of responding to a certain treatment.

HOW IMMUNOTHERAPY COMPARES

Some of the most common cancer treatments include:



SURGERY

Surgery is an operation to remove the cancer (or part of it) from your body. It is not always possible or helpful. When it is thought that the cancer can be completely removed, it is often the first treatment. The most common side effects of surgery are pain, fatigue, bleeding, swelling around the surgical site, and infection.



CHEMOTHERAPY

Chemotherapy (also called chemo) uses drugs to attack and kill cancer cells. These very strong drugs only attack fast-growing cells like cancer. Chemo can cause side effects like hair loss, nausea, and low white blood cell counts.



RADIATION THERAPY

Radiation therapy (also called radiotherapy) uses strong energy beams, such as x-rays or protons, to kill cells and shrink tumors where the beam is pointed. If your cancer hasn't spread far, radiation can be used to try to control or cure it. Side effects occur when normal tissue or organs are damaged from radiation exposure.



TARGETED THERAPY

Targeted therapy is a type of cancer treatment that targets a specific change in some cancers that helps them grow, divide, and spread. Currently, targeted therapy can only be used to treat certain types of cancer. Targeted drugs are designed to block cancer growth 'driven' by these changes to the tumor's gene. Doctors decide to use it based on the findings of biomarker tests, including mutation testing of your tumor. Diarrhea and skin problems, including rashes, are the most common side effects of targeted therapy. Some research suggests targeted therapy works better in younger patients than in older patients.



IMMUNOTHERAPY

Immunotherapy works by making the immune system stronger so it can fight cancer better. The immune system helps your body fight infections and other diseases. Immunotherapy side effects are different from side effects of other cancer treatments (like the ones listed above). Not everyone gets side effects. Most side effects are mild, but some can be severe. Ask your doctor what to expect. Some research suggests immunotherapy works better in older patients than in younger patients.

KEY THINGS TO KNOW

- It is very important that anyone receiving immunotherapy let their health care team know right away if they develop any side effects.
- Although there are promising results, immunotherapy does not work for every patient who tries it.
- There is still a lot that researchers don't know about immunotherapy.

Here are some questions researchers are trying to answer about immunotherapy treatments:

- Why do they work so well in some people and not at all in others?
- How can they be combined with other treatments?
- When is the best time to use them?
- What are the long-term side effects?

Is Immunotherapy Right for Me?

Most people who receive immunotherapy today have cancers that are advanced (metastatic, or stage 4). Their cancers have either returned and spread after initial treatment or were diagnosed in an advanced stage. Researchers are now beginning new clinical trials with people with earlier-stage cancers who are at high risk for having their cancers return or spread. Some people cannot receive immunotherapy because of health problems (like autoimmune disorders) that make it impossible to take these drugs safely. Ask your health care team if immunotherapy is right for you.

What Does it Cost?

Many new treatments, including immunotherapy, are very expensive. Patients who are being treated on clinical trials may have those costs covered. Cost will likely be an issue for many patients. Talk to your health care team upfront about the financial issues involved in your treatment. Many centers have resources to help patients obtain insurance coverage or access programs designed to help cover costs of treatment.

“Keep pushing until you get the answers you are looking for, because they are out there.”

— Steve, immunotherapy clinical trial patient

Types of Immunotherapy

CHECKPOINT INHIBITORS

The immune system has safeguards in place to prevent it from attacking healthy cells. These safeguards are called checkpoints. They slow down or stop the immune system from attacking healthy tissue. Some cancers have learned how to activate these checkpoints to avoid being killed by the immune system. They trick the body into turning its own defenses off. Checkpoint inhibitors turn off these checkpoints, helping the body fight cancer.

Most patients who receive immunotherapy today are on one of two kinds of checkpoint inhibitors. However, not all cancers can be treated with these drugs. Currently, checkpoint inhibitors only work for up to a third of patients who are given them. These drugs may be given in combination with other therapies, such as chemotherapy or other immunotherapy drugs. Researchers are also studying giving checkpoint inhibitors in combination with radiation therapy.

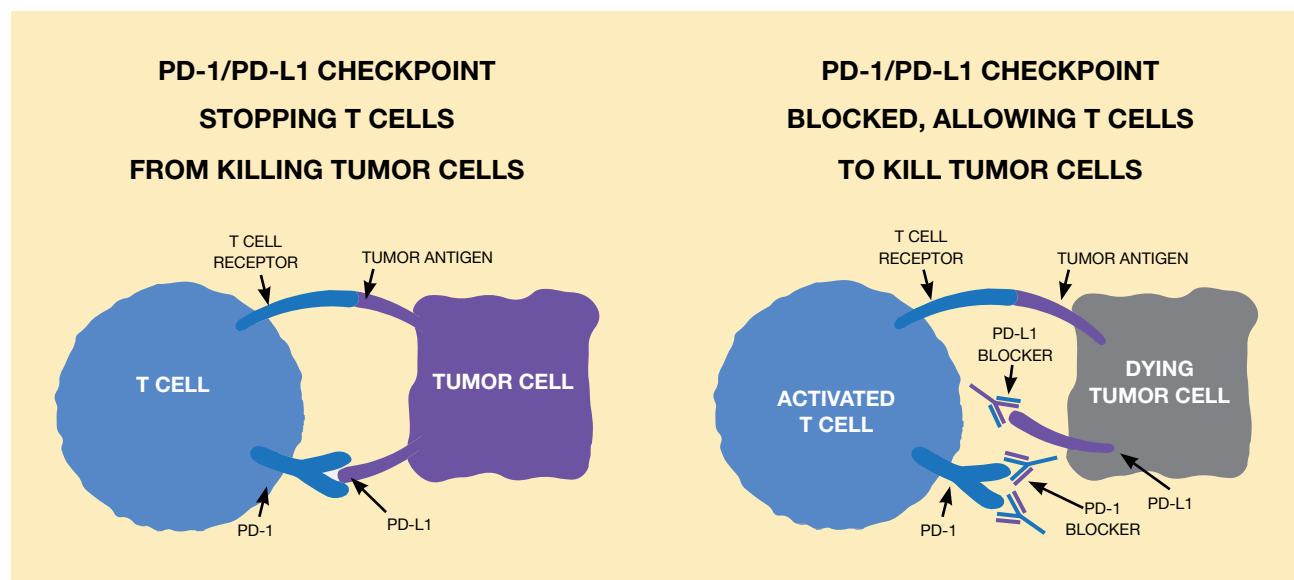
PD-1 AND PD-L1 INHIBITORS

These drugs work by stopping the tumor from turning off T cells (the immune system's "soldiers"). When cancer cells use the PD-1/PD-L1 checkpoint to shut down T cells, they can "hide" from the immune system. These drugs block cancer cells from using this checkpoint, so they aren't "hidden." This allows your T cells to kill the cancer cells.

Checkpoint inhibitors targeting the PD-1/PD-L1 checkpoint include:

- atezolizumab (Tecentriq[®])
- avelumab (Bavencio[®])
- cemiplimab (Libtayo[®])
- durvalumab (Imfinzi[®])
- nivolumab (Opdivo[®])
- pembrolizumab (Keytruda[®])

These drugs have been shown to successfully treat a growing number of cancers, such as melanoma, Hodgkin lymphoma, Merkel cell



and cutaneous squamous cell carcinoma, head and neck cancer, triple negative breast cancer, and lung, colorectal, kidney, and bladder cancers. Pembrolizumab (Keytruda[®]) is approved to treat any solid tumor that tests positive for MSI-H or dMMR.

CTLA-4 INHIBITOR

CTLA-4 inhibition works by activating T cells that can search for and destroy cancer cells. Ipilimumab (Yervoy[®]) is approved to treat advanced melanoma, and, in combination with Opdivo, advanced colorectal and kidney cancers.

Checkpoint Inhibitor Side Effects

We tend to think of immunotherapy as “natural” — as our body’s own defense system. However, immunotherapy can still have side effects. These effects are generally different from those caused by chemotherapy or radiation therapy. In many cases, they are not severe and may be short-lived or easy to manage. Less often, side effects can be very severe and even life-threatening.

COMMON SIDE EFFECTS

- Flu-like symptoms (fever, chills, headache, nausea, cough, loss of appetite)
- Fatigue (some people get extreme fatigue)
- Rashes, redness, or itching
- Pain or soreness
- Muscle or joint pain
- Drops in blood pressure

LESS COMMON SIDE EFFECTS

- Colitis or other gastrointestinal problems (stomach pain, diarrhea)
- Thyroid problems
- Lung problems (cough, shortness of breath)
- Other serious autoimmune conditions (such as pituitary disorders or diabetes)

Sometimes the side effects do not occur right after treatment is given. They may show up



“It is important to call your health care team even with the slightest change of the person’s symptoms, because symptoms can escalate very quickly. No question or call is wrong, so always call.”

— Heather DiFilippo, Nurse Practitioner
(Abramson Cancer Center, Hospital of the University of Pennsylvania)

several months later. Little is known at this time about whether there are any long-term side effects. **If you are on immunotherapy, it is important to let your health care team know immediately if you notice any change in side effects or symptoms. Most side effects can be managed if they are treated early.**

OTHER MONOCLONAL ANTIBODIES

Checkpoint inhibitors are one type of monoclonal antibody (mAb). Other types let the immune system find and destroy cancer cells using targets that aren't checkpoints. Still others take radiation or chemotherapy drugs directly to cancer cells. Each mAb is made to find and attach to a specific protein that occurs in cancer cells. Not all mAbs are immunotherapies, some are targeted therapies. Most mAb treatments that aren't checkpoint inhibitors are used in blood cancers. To learn more, see our Immunotherapy and Blood Cancers page at www.CancerSupportCommunity.org/IOBlood.

ADOPTIVE T CELL THERAPY

In adoptive T cell therapy, T cells are removed from a person with cancer, taken to a lab, and modified. Once returned to the person, these modified T cells find and destroy cancer cells. It is now being tested in several types of cancers.

One type of adoptive cell therapy, CAR T cell therapy, is approved to treat certain types of leukemia and lymphoma. Tisagenlecleucel (Kymriah[®]) and axicabtagene ciloleucel (Yescarta[®]) are only available in a few dozen major cancer

centers. These centers have the expertise and technical ability to modify the T cells and provide this treatment to patients. For more information on CAR T cell therapy, visit: www.CancerSupportCommunity.org/CART.

BACILLUS CALMETTE-GUERIN (BCG)

therapy used in bladder cancer can cause a general immune response when put directly into the bladder with a catheter. This type of therapy helps prevent cancer from returning in about 70 percent of patients with early-stage bladder cancer.

CYTOKINES have been used for years.

They work by speeding up the growth of T cells and activating other immune cells. Interleukins and interferon are examples of cytokines that have shown some success in treating cancer. High dose interleukin 2 (IL2) leads to great responses in a small percentage of people with advanced melanomas and kidney cancers.

TREATMENT VACCINES are designed to “teach” T cells to respond to specific cancer antigens. Currently, there is only one approved cancer vaccine, sipuleucel-T (Provenge[®]), which treats advanced prostate cancer. Provenge[®] is made from the patient's own white blood cells. These cells are sent to a lab where their ability to recognize and fight prostate cancer cells is boosted. They are then re-infused into the patient. Researchers are also studying possible vaccines for other cancers like blood cancers and breast cancer.

RADIOIMMUNOTHERAPY uses an antibody combined with a radioactive substance to send radiation directly to cancer cells. Ibritumomab tiuxetan (Zevalin[®]) is the only radioimmunotherapy that is approved by the FDA and available in the U.S. This type of therapy lets doctors target cancer cells with higher doses of radiation without hurting normal cells. It is used to treat certain types of lymphomas.

ONCOLYTIC VIRUS THERAPY is an experimental form of immunotherapy. Oncolytic viruses infect both cancer and normal cells, but they have little effect on normal cells. Oncolytic viruses multiply inside cancer cells and cause the cancer cells to die. Several viruses are currently being tested in clinical trials. The only oncolytic virus therapy approved in the U.S. is talimogene laherparepvec (Imlygic[®]), which is used to treat very specific types of melanoma.

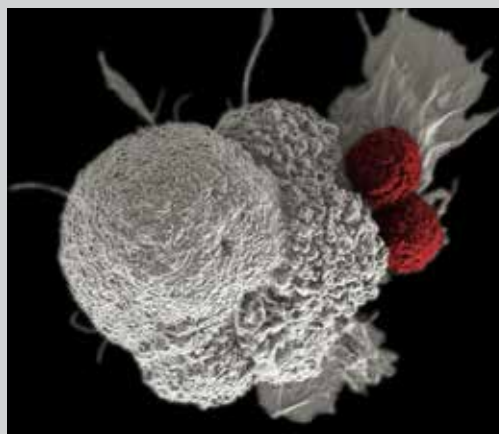
Is a Clinical Trial Right for Me?

Be sure to ask your health care team about clinical trials. Clinical trials are research studies to test new treatments or learn how to use existing treatments better.

- A clinical trial may be the only way to get some of the newest, most promising treatments. Talk with your health care team about clinical trial options.
- The U.S. FDA and local review boards oversee all U.S. clinical trials to keep patients safe. Participating in a clinical trial means that you will receive the best available standard of care for your

cancer or a new approach that may offer improved outcomes.

- Almost no one receives a placebo or “sugar pill,” and you will be specifically told if this is a possibility.
- If you join a clinical trial, you can leave the trial at any time and continue to get standard treatment by your doctor.
- Every doctor does not have the same trials. Even if another doctor is in charge of the trial, your doctor may still help with your care.
- Most often, the trial pays the costs of the drug being studied, and your health insurance only has to pay for “standard” treatment costs. However, your health insurance may not pay for everything. Be sure to ask your health care team.



An oral squamous cancer cell (white) is attacked by two T cells (red) as part of a natural immune response.



QUESTIONS TO ASK YOUR HEALTH CARE TEAM

■ What type of immunotherapy treatments do you recommend? _____

■ Has my tumor been sent for biomarker testing? If so, what do the results mean for me?

■ Was my tumor tested for the PD-L1, MSI-H, or dMMR biomarkers? If so, does that give me more treatment options? _____

■ Are there any clinical trials for immunotherapy that would be right for me? How do I find out more about them? _____

For each treatment or clinical trial that is recommended:

■ Why are you recommending this type of therapy for me? _____

■ What is the goal of this treatment? What are the risks? _____

■ How will I receive this treatment? _____

■ How often will I receive this treatment? How long will each session take? _____

■ Where will I go to receive treatment? _____

■ What side effects should I expect (short and long term)? _____



QUESTIONS TO ASK YOUR HEALTH CARE TEAM (CONTINUED)

- What can I do to prepare for immunotherapy treatment? _____

- Will I need someone to drive me home after treatment? _____

- Can/should I eat before or after treatment? _____

- How long will I need to be on this treatment? _____
- How will we know if this therapy is working? _____

- How much will this therapy cost? _____

- Will I need other cancer treatments at the same time? _____

- How will this treatment impact my daily routine? Will I be able to do my usual daily activities? _____

- Whom should I call if I have questions or problems during office hours?
Name: _____
Phone Number: _____

- After hours and weekends? _____
Name: _____
Phone Number: _____



KARL PRITCHARD

Karl's Story: Ask About Immunotherapy

At age 76, Karl was diagnosed with bladder cancer in February of 2014. After his surgery, Karl began to research new treatments. That's how he learned about immunotherapy. When Karl asked his doctor, the doctor had never heard of immunotherapy. Karl got a second opinion. When he asked his new doctor about immunotherapy, Karl says, she responded, "I'm glad you asked."

In January 2015, Karl became the last patient enrolled in an international clinical trial. He received his first infusion of the drug in February 2015. Two months later, scans showed no evidence of the cancer. He continues to receive an infusion of the drug every three weeks. "It's a good thing I asked about immunotherapy," says Karl. "Asking that question saved my life."

General Cancer Information, Survivorship, and Support

Cancer Support Community • 888-793-9355 • www.CancerSupportCommunity.org

American Cancer Society • 800-227-2345 • www.cancer.org

CancerCare • 800-813-4673 • www.cancercare.org

Cancer.net • 888-651-3038 • www.cancer.net

National Cancer Institute (NCI) • 800-422-6237 • www.cancer.gov

NCI Clinical Trial Information • 800-422-6237 • www.cancer.gov/ClinicalTrials

Patient Advocate Foundation • 800-532-5274 • www.patientadvocate.org

Cancer Support Community Resources

Cancer Support Helpline® — Have questions, concerns or looking for resources? Call CSC's toll-free Cancer Support Helpline (888-793-9355), available in 200 languages Mon - Fri 9am - 9pm ET.

Open to Options® — Need help making a cancer treatment decision? Our trained specialists can help you create a list of questions to share with your doctor. Make an appointment by calling 888-793-9355 or by contacting your local CSC or Gilda's Club.

Frankly Speaking About Cancer® — Trusted information for cancer patients and their loved ones is available through publications, online, and in-person programs.

Services at Local CSCs and Gilda's Clubs — With the help of 170 locations, CSC and Gilda's Club affiliates provide services free of charge to people touched by cancer. Attend support groups, educational sessions, wellness programs, and more at a location near you. www.CancerSupportCommunity.org/FindLocation

Cancer Experience Registry® — Help others by sharing your cancer patient or cancer caregiver experience via survey at www.CancerExperienceRegistry.org.

MyLifeLine — CSC's private, online community allows patients and caregivers to easily connect with friends and family to receive social, emotional, and practical support throughout the cancer journey and beyond. Sign up at www.MyLifeLine.org.

Grassroots Network — Make sure your voice is heard by federal and state policy makers on issues affecting cancer patients and survivors by joining our Network at www.CancerSupportCommunity.org/become-advocate.

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