FRANKLY SPEAKING ABOUT CANCER

Immunotherapy and Lung Cancer

This booklet explains how immunotherapy uses the body's own natural defenses to treat lung cancer. So far, immunotherapy is approved for non-small cell lung cancer (NSCLC) and is being studied in small cell lung cancer (SCLC). Learning how the immune system and cancer interact is helping researchers create new immunotherapy treatments that are changing the outlook for many people with advanced or metastatic lung cancer. Many therapies are still being tested. They don't work for everyone. There is still a lot to learn. Researchers are studying these therapies to see which are the safest and most effective, how to tell which patients will benefit, and when to use them.

CANCER SUPPORT COMMUNITY

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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 cells 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.

Immunotherapy for Lung Cancer

Immunotherapy is the newest approach to treating lung cancer. There are many different types of lung cancer. There are also big differences between individual tumors, even within the same cancer type. Some lung cancers respond to immunotherapy better than others, and some don't respond at all. Immunotherapy treatments are showing promising results for some people with advanced lung cancers. In lung cancer, immunotherapy has only been approved for non-small cell lung cancer (NSCLC). There are also promising data for using immunotherapy in small cell lung cancer (SCLC).

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.

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.

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.

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 at 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.

How is Immunotherapy Given?

Immunotherapy use 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 time schedules. Some may be given in combination with other therapies (like chemotherapy) or immunotherapies.

Is it Working?

The results of chemotherapy or radiation therapy are usually seen fairly quickly. The benefits of immunotherapy can occur quickly, but results can also take weeks longer to be seen. Sometimes, cancers actually appear to get bigger before they shrink or disappear. Many doctors wait to do a first scan to measure results at 12 weeks, rather than earlier. While the goal of treatment is to shrink tumors, some people who are benefitting from immunotherapy see their cancers remain stable, neither shrinking nor growing. Some people benefit from this for long periods of time.

> *"Even if we don't see a response right away, we may continue the immune therapy and look again for a delayed response if the patient continues to do well and feel well and handle the treatment."*
>
> *— Dr. Tara Gangadhar (Abramson Cancer Center, Hospital of the University of Pennsylvania)*

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. Talk to your health care team upfront about the financial issues involved in your treatment. Many centers have resources dedicated to helping patients obtain insurance coverage or access programs designed to help cover costs of treatment.

MARY PROUGH

Mary's Story: Getting A Second Opinion

Mary was initially diagnosed with lung cancer in 1983, when her children were ages 9 and 11. Thirty years later, following a bout with pneumonia, she learned her cancer had not only recurred but was now stage IV—and that there were no treatment options. When she told her older brother the news, he suggested she get a second opinion. The second doctor also told her there were no standard treatments. The conversation might have ended there, but Mary asked about clinical trials. Two weeks later, she entered a phase II trial of an experimental immunotherapy drug. In October 2016, the drug she was using, an anti-PD-L1 immunotherapy, was approved to treat metastatic non-small cell lung cancer. Mary is still on the drug—and will likely be on it the rest of her life.

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?

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 an immune system attack when healthy tissue is threatened. Some cancers have learned how to activate these checkpoints to avoid being killed by the immune system. Cancer cells trick the body into turning its own defenses off. New drugs, called checkpoint inhibitors, are designed to turn off these checkpoints, helping the body fight cancer. Most patients who receive immunotherapy today are on one of two kinds of checkpoint inhibitors.

PD-1 and PD-L1 Inhibitors

These drugs stop the tumor from turning off T cells (the immune system's "soldiers"). When cancer cells use the 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.

- In 2015, nivolumab (Opdivo®) was the first PD-1 inhibitor approved for lung cancer. This treatment is used for patients with non-small cell lung cancer (NSCLC) who no longer respond after chemotherapy and EGFR or ALK targeted therapy (if their tumor has those genetic mutations). It is also approved for bladder cancer, melanoma, kidney cancer, and head and neck cancer.
- Pembrozulimab (Keytruda®) is approved for patients with NSCLC whose tumors

have high levels (at least 50%) of the PD-L1 marker, and are negative for EGFR and ALK. It is also approved in combination with chemotherapy for treating nonsquamous NSCLC, even if there is no sign of the PD-L1 marker. This therapy is also approved for any tumors with MSI-H or dMMR biomarkers, head and neck cancer, Hodgkin lymphoma, and melanoma.

- Atezolizumab (Tencentriq®) is used for patients with NSCLC whose disease progressed after chemotherapy and EGFR or ALK targeted therapy (if their tumor has those genetic mutations). It is also approved to treat bladder cancer.
- Avelumab (Bavencia®) was approved in 2017 to treat Merkel cell carcinoma and bladder cancer. It is being studied as a treatment for NSCLC.
- Durvalumab (Imfinzi™) was approved in 2017 to treat bladder cancer. It is also being studied as a treatment for NSCLC.

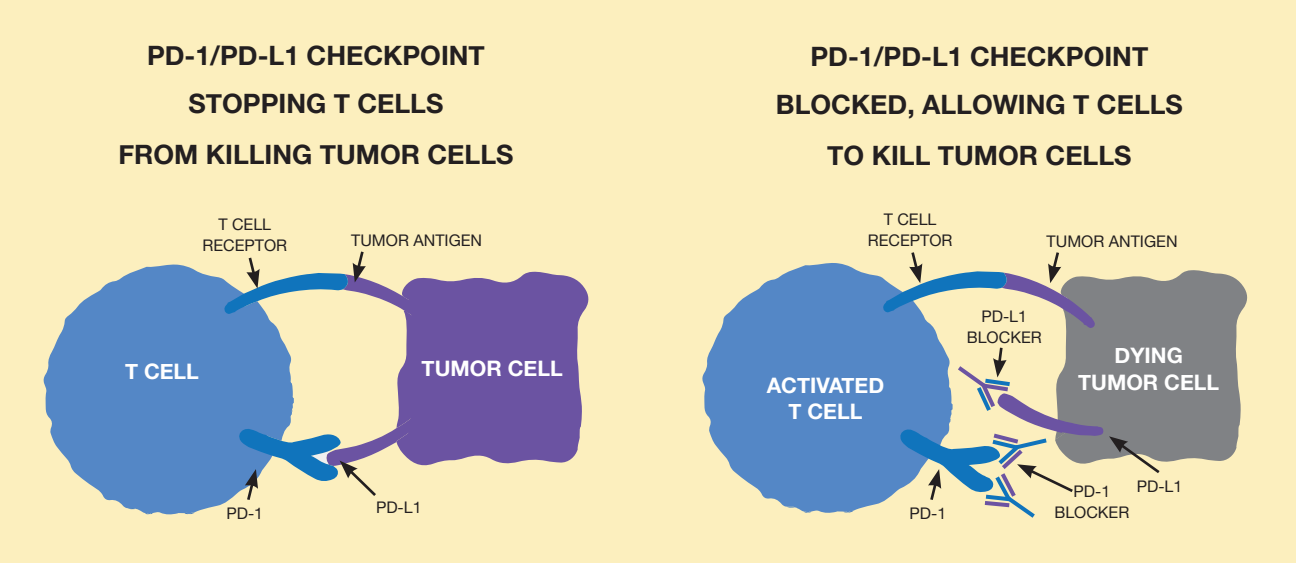
CTLA-4 Inhibitors

These drugs work by activating T cells that can search for and destroy cancer cells. Ipilimumab (Yervoy®) is approved to treat advanced melanoma. It's also being studied in a number of other tumors, including non-small cell lung cancer (NSCLC) and small cell lung cancers. In NSCLC, it is being studied in combination with chemotherapy and other immunotherapies. Tremelimumab is another CTLA-4 inhibitor being tested.

Other Monoclonal Antibodies

Checkpoint inhibitors are one type of monoclonal antibody. 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. Not all monoclonal antibodies are immunotherapies. Some are targeted therapies such as bevacizumab (Avastin®), ramucirumab (Cyramza®), and necitumumab (Portrazza®).

To learn more, see our lung cancer book at www.CancerSupportCommunity.org/LungBook.



"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)

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. The side effects listed below are commonly seen with checkpoint inhibitor immunotherapy drugs.

Common side effects are:

- 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 are:

- 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 several months later. Little is known about whether there are any long-term side effects. Having one or more side effects does not always mean that you will have to stop taking drugs that are working for you. Most side effects can be managed if they are treated early. **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.**

QUESTIONS TO ASK YOUR HEALTH CARE TEAM

- What type of immunotherapy treatments are available for my lung cancer type?

_____

_____

- Which treatment would you recommend, and why? _____

_____

- Has my tumor been sent for biomarker testing, both gene mutation and immunotherapy tests? If so, what do the results mean for me? _____

_____

- 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:

- 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: _____

Types of Immunotherapy Still Being Studied for Lung Cancer

LUNG CANCER VACCINES

Vaccines are designed to "teach" T-cells to respond to specific tumor antigens. Several are being tested in lung cancer clinical trials. Current trials are seeing if vaccines can delay or prevent cancer from returning. This could help people with lung cancer who are at high risk for it to return or spread. There are also trials to treat people with advanced disease. As with other types of immunotherapy, vaccines are still a new approach. If you are interested in being treated with a lung cancer vaccine, talk to your doctors about clinical trial options.

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. This is now being tested in several types of cancer, including lung. One type of adoptive cell therapy, CAR T cell therapy, is approved to treat certain types of leukemia and lymphoma. For information on CAR T, see our booklet at: www.CancerSupportCommunity.org/CART.

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.

Lung Cancer Information, Survivorship, & Support

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

Bonnie J. Addario Lung Cancer Foundation • 650-779-8286 • www.lungcancerfoundation.org

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

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

Free to Breathe • 844-835-4325 • www.freetobreathe.org

LUNGevity Foundation • 844-360-5864 • www.LUNGevity.org

National Cancer Institute • 800-422-6237 • www.cancer.gov/ClinicalTrials

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

Cancer Support Community Resources

The Cancer Support Community's (CSC) resources and programs are available free of charge. To access any of these resources below call 888-793-9355 or visit www.CancerSupportCommunity.org

Cancer Support Helpline® Whether you are newly diagnosed with cancer, a longtime cancer survivor, caring for someone with cancer, or a health care professional looking for resources, CSC's toll-free Cancer Support Helpline (888-793-9355) is staffed by licensed CSC Helpline Counselors available to assist you Mon-Fri 9am - 9pm ET.

Open to Options® If you are facing a cancer treatment decision, this research-proven program can help you. In less than an hour, our trained specialists can help you create a written list of specific questions about your concerns for your doctor. Appointments can be made by calling 888-793-9355, visiting www.CancerSupportCommunity.org or by contacting your local CSC or Gilda's Club providing this service.

Cancer Experience Registry® The Registry is a community of people touched by cancer. The Registry works to collect, analyze, and share information about the experience and needs of patients and their families. To join, go to www.CancerExperienceRegistry.org.

Frankly Speaking about Cancer® CSC's landmark cancer education series provides trusted information for cancer patients and their loved ones. Information is available through publications, online, and in-person programs.

Services at Local CSCs and Gilda's Clubs Almost 50 locations plus 120 satellite locations around the country offer on-site support groups, educational workshops, and healthy lifestyle programs specifically designed for people affected by cancer at no cost to the member.

The Living Room, Online Here you will find support and connection with others on discussion boards, a special space for teens, and personal web pages to keep your family and friends up-to-date.

FRANKLY SPEAKING ABOUT CANCER: IMMUNOTHERAPY AND LUNG CANCER PROGRAM PARTNERS:

LUNGEVITY Find it. Treat it. Live. · free to breathe a partnership for lung cancer survival · BONNIE J. ADDARIO LUNG CANCER FOUNDATION

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