A fishing net is stretched across the frame, with a bright sun setting in the background, creating a warm, golden glow. The net's mesh is visible, and the sun is partially obscured by the net's structure.

IMMUNOTHERAPY FOR LUNG CANCER

Patient and
Caregiver Guide

GO₂
FOUNDATION
FOR LUNG
CANCER



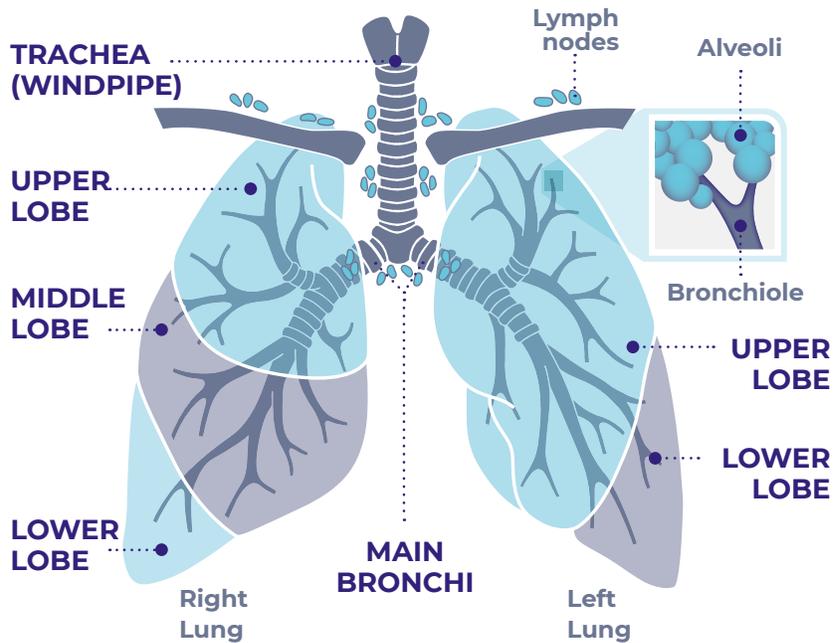
IMMUNOTHERAPY

FOR LUNG CANCER

Patient and Caregiver Guide

TABLE OF CONTENTS

Lung Cancer Basics.....	2
Immunotherapy.....	3
FDA Approved Immunotherapies.....	4
Monoclonal Antibodies.....	4
Checkpoint Inhibitors.....	5
PD-1/PD-L1 Checkpoint Inhibitors.....	6
Important Information about Immunotherapy.....	8
Biomarker Testing.....	9
Other Immunotherapies Being Studied.....	10
Other Checkpoint Inhibitors.....	10
Vaccines.....	11
Adoptive Cell Therapy.....	12
Oncolytic Viruses.....	12
About GO ₂ Foundation for Lung Cancer.....	13



WHY IMMUNOTHERAPY?

Until the mid-2000s, lung cancer treatment choices were mostly limited to surgery, chemotherapy and radiation. Now, people living with the disease often have newer treatment options.

The goal of immunotherapy is to help the body's own immune system fight cancer. This brochure will help you understand immunotherapies and what they mean to you.

Knowing the type and subtype of your lung cancer is important. That information guides treatment choices.

LUNG CANCER

Cancer that starts in the lungs – lung cancer – is one of the most common cancers in the United States. But lung cancer is not one disease.

THE BASICS

There are two main types of lung cancer based on how the cancer looks under a microscope:

NON-SMALL CELL LUNG CANCER

(NSCLC), the most common type. Two subtypes of NSCLC found most often are:

- Adenocarcinoma
- Squamous Cell Carcinoma

SMALL CELL LUNG CANCER (SCLC),

less commonly diagnosed and made up of cells that are smaller in size than most other cancer cells.



IMMUNOTHERAPY

Immunotherapy, also called immuno-oncology or “IO”, is a kind of treatment that helps the body’s own immune system fight cancer.

The job of the body’s immune system is to fight off infections and other foreign invaders that can make us sick. Without help, the immune system does not fight against cancer for a few reasons:

- Cancer comes from normal cells that have changed so the immune system may not see the cancer as an invader.
- The immune system may not be strong enough to fight the cancer.
- Cancer cells can fool the immune system so it cannot work to fight the cancer in the right way.

The goal of immunotherapy is to help the body’s normal defenses find and attack the cancer. Immunotherapies help the immune system work better against the cancer.

Some immunotherapies are being used to treat lung cancer and others are being tested in research studies.

Learn more about immunotherapy and if it makes sense for you. Call our Treatment and Trial Navigators at 1-800-298-2436 or visit www.lungmatch.org.

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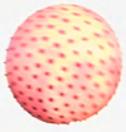
IMMUNOTHERAPIES APPROVED BY THE FOOD AND DRUG ADMINISTRATION (FDA)

MONOCLONAL ANTIBODIES

Antibodies are proteins made in blood to fight toxins or foreign substances in the body. Monoclonal antibodies (mAbs) are proteins made in a laboratory that act like normal antibodies, but are designed to attack a specific target on a cell. mAbs can be used alone or with other drugs to aim at defects in the cancer cell. They can also make the cancer cells more open to the body's immune system. mAbs are most often used as therapies

to fight cancers with a specific gene change. They can also carry other drugs or substances directly to the cancer to fight it.

Some approved mAbs are immunotherapies called PD-1/PD-L1 checkpoint inhibitors. Others are not immunotherapies but are targeted therapies like Avastin (bevacizumab) and Cyramza (ramucirumab). Please see our *Targeted Therapies* brochure for more information on those therapies.



CHECKPOINT INHIBITORS

When the immune system is working well, it attacks invaders and not normal cells. If it went after all the normal cells in the body, we would all have auto-immune diseases, like lupus or type 1 diabetes. The normal immune system has “checkpoints” to stop the immune cells from attacking everything. When checkpoints are turned on, they stop the immune system from attacking.

Cancer can trick the body’s natural defenses into not attacking. Then the cancer cells keep growing without

being slowed down or stopped. The cancer makes proteins that turn on the checkpoints. With those checkpoints turned on, the immune system does not fight the cancer well.

Some treatments work to fix the problem at the checkpoint. Treatments called “checkpoint inhibitors” block the checkpoint so the cancer cannot turn it on. This keeps the immune system active and working against the cancer. Many of these checkpoint inhibitors are mAbs. They target a specific protein in the checkpoint.

PD-1/PD-L1 CHECKPOINT

Cancer sometimes makes a protein called PD-L1. This protein can bind (attach) to a protein called PD-1 that is found on a normal immune cell. When these two proteins bind, it turns on a checkpoint. This slows the immune system and allows the cancer to continue to grow.

Some drugs target either the PD-1 or PD-L1 protein. The drugs keep them from binding. This “takes the brakes off” the immune system by turning off the checkpoint. Your immune system stays active and keeps working to fight the cancer.

▶ FDA Approved Drugs for Stage IV or metastatic Non-Small Cell Lung Cancer (cancer that has spread outside of one lung)

FIRST LINE (as your first treatment):

- **Keytruda (pembrolizumab, a PD-1 inhibitor)** – Keytruda alone can be given if you have the right biomarker (see page 9). Usually, this is a test showing your cancer is PD-L1 “high” (more than half the tumor cells are positive).
- **Keytruda (pembrolizumab) plus chemotherapy** – Keytruda can be given with chemotherapy drugs, which are determined by the type of lung cancer you have. (No test result is needed.)
 - For non-squamous, Keytruda is given with the chemotherapy drugs Alimta (pemetrexed) and carboplatin
 - For squamous, Keytruda is given with carboplatin and either Taxol (paclitaxel) or Abraxane (nab-paclitaxel)
- **Tecentriq (atezolizumab)** can be given with Avastin (bevacizumab) and chemotherapy (paclitaxel and carboplatin) for advanced non-squamous lung cancer with no EGFR or ALK changes.

LATER LINES OF THERAPY (after another treatment):

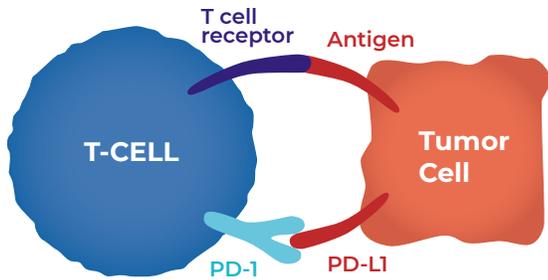
- **Keytruda (pembrolizumab, a PD-1 inhibitor)** – with a positive PD-L1 biomarker test (more than 1% of cancer cells are positive).
- **Opdivo (nivolumab, a PD-1 inhibitor)**
- **Tecentriq (atezolizumab, a PD-L1 inhibitor)**

▶ FDA Approved Drugs for Stage III Non-Small Cell Lung Cancer:

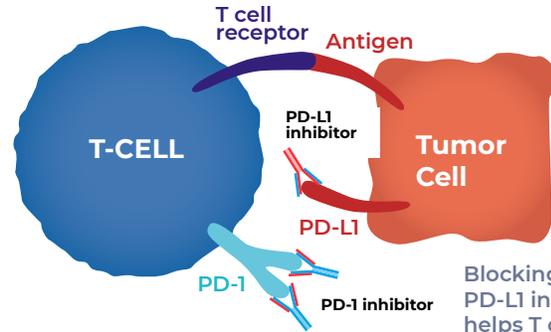
If you have Stage III lung cancer, your doctor will determine if it is treatable by surgery. If not, you will likely have both chemotherapy and radiation. This is sometimes called chemoradiation. Immunotherapy can also be given in the following cases:

- **Imfinzi (durvalumab, a PD-L1 inhibitor)** – given to help keep the cancer from coming back after chemoradiation.
- **Keytruda (pembrolizumab, a PD-1 inhibitor)** – can be given if you are not able to have either surgery or chemoradiation and you have a positive biomarker test for PD-L1 (more than 1% of cancer cells are positive).

The PD-1/PD-L1 Checkpoint



The PD-1/PD-L1 interaction helps protect the cancer cell from immune destruction



Blocking the PD-1/PD-L1 interaction helps T cells to destroy tumor cells

FDA Approved Drugs for Small Cell Lung Cancer

FIRST LINE (as your first treatment):

- **Tecentriq (atezolizumab, a PD-L1 inhibitor) plus chemotherapy** – Tecentriq may be given with platinum-based chemotherapy as a first treatment for extensive-stage SCLC.

LATER LINES OF THERAPY (after another treatment):

The following drugs can be given to patients with extensive-stage SCLC after two other treatments stop working:

- **Keytruda (pembrolizumab)**
- **Opdivo (nivolumab)**

FDA Approved Drugs for Extensive-Stage or Stage IV Small Cell Lung Cancer

- **Opdivo (nivolumab, a PD-1 inhibitor)** – Opdivo can be given to patients with extensive-stage, Stage 4, SCLC who have progressed on platinum-based chemotherapy and at least one other line of therapy.

Recent research has shown that immunotherapy in combination with chemotherapy as a first treatment can result in better overall survival than chemotherapy alone in patients with late stage SCLC. The FDA may approve this combination as a first treatment soon.

MORE INFORMATION ABOUT PD-1/PD-L1 INHIBITORS

These drugs work very well for some people and can keep working for a long time. However, in most situations, only about 1 in 5 people have their cancers respond when taking one of these drugs alone.

While many people have few side effects from these drugs, it is possible to have very serious immune side effects. Ask your treatment team if this is the right choice for you. Also, watch closely for side effects and talk with your treatment team about any that you experience.

We suggest biomarker testing to guide your treatment path (see page 9). If testing shows you are PD-L1 “high,” these drugs may be the right option for you. If your cancer tests positive for other biomarkers (such as EGFR, ALK and a few others), immunotherapy drugs may not work as well and you should likely consider targeted therapies (see our *Targeted Therapies* brochure).

PD-1/PD-L1 inhibitors are new and are being studied in many clinical trials for both NSCLC and SCLC. The drugs are being studied alone and in combination with other drugs. A clinical trial may be a good option for you to discuss with your treatment team.

IMPORTANT INFORMATION ABOUT IMMUNOTHERAPY

- Immunotherapy is typically given through a vein, like chemotherapy, but other methods may be used.
- Response to an immunotherapy is often different from that of chemotherapy or targeted therapies. With immunotherapy, the cancer may seem to grow initially even if the treatment is working. Scans can show what seem to be larger tumors, but really the tumor has a lot of immune cells in it which are working to fight the cancer. These spots can decrease on later scans.
- Some immunotherapies have been approved to treat lung cancer but many are only available through clinical trials.
- Side effects from immunotherapy are generally caused by the increased activity of the immune system. These may include fatigue, flu-like symptoms, rashes, diarrhea and inflammation within the lungs, liver, kidneys or hormone-producing glands such as thyroid or the pituitary.
- Often the side effects from immunotherapy can be milder than those from chemotherapy; however, there can be severe immune-related side effects. Close monitoring is necessary for early detection and successful management of these side effects. Be sure to tell your treatment team about any side effects you experience.

BIOMARKER TESTING

A biomarker is something in the body that can be measured to provide useful information. For cancer, biomarkers can be used to guide whether a certain therapy is a good choice for a particular individual.

Tests, called biomarker tests or molecular tests, can tell how much of the PD-L1 protein is in cancer (see page 6). In general, for NSCLC, if there is a lot of PD-L1, the cancer is more likely to respond to a PD-1 or PD-L1 inhibitor (such as Keytruda, Opdivo, or Tecentriq). PD-L1 is not a useful biomarker for SCLC.

Unlike biomarker testing for targeted therapies, testing for immunotherapies is not black and white. A cancer can be PD-L1 “high” and not respond to the drug. It can also be “low” and still respond. This is just less likely.

Biomarker testing can also show if there are a lot of gene changes (mutations) in the cancer. Some immunotherapies seem to work better if your cancer has a large number of changes. Gene changes may be caused by exposure to environmental agents like cigarette smoke. Gene changes can also happen when genes do not repair themselves properly. Some cancers have problems with

genes repairing themselves called microsatellite instability (MSI) or deficient mismatch repair (MMR). If you have these biomarkers, your cancer is also more likely to respond to PD-1/PD-L1 inhibitors.

Research is ongoing to find new and better biomarkers to guide your treatment decisions. For example, studies are currently looking at a measure of the number of gene changes in the cancer, called tumor mutational burden (TMB). Early research data shows that immunotherapies may work better in cancers with high TMB. This may guide treatment decisions soon.

Know your options

New ways to understand and treat lung cancer are being tested and approved more quickly than ever before. Knowing your treatment options is important so you can be an informed and empowered member of your team.

If you have not had biomarker testing, we can help you get it. Call our Treatment and Trial Navigators at 1-800-298-2436 or visit www.lungmatch.org.

LungMATCH



THE FUTURE OF IMMUNOTHERAPY

Excitingly, researchers are studying combinations of immunotherapies with other kinds of therapies, such as chemotherapy, radiation therapy and targeted therapies. In fact, immunotherapies are showing promise as both neoadjuvant and adjuvant therapies for earlier-stages of lung cancer.

OTHER CHECKPOINT INHIBITORS

PD-1/PD-L1 is not the only checkpoint on immune cells. Drugs targeting many other checkpoints are also being studied in clinical trials alone and in combination with the PD-1/PD-L1 inhibitors.

CTLA-4 Checkpoint

CTLA-4 (Cytotoxic T-Lymphocyte Associated protein 4) is one well-known immune checkpoint protein. Drugs such as Yervoy (ipilimumab), which is FDA approved in melanoma, target the CTLA-4 receptor. These drugs are currently being studied in clinical trials for lung cancer and may work particularly well when used with PD-L1 checkpoint inhibitors. These combinations are being studied in both SCLC and NSCLC.

Neoadjuvant Therapy:

Immunotherapy is now showing promise before surgery and to shrink the cancer - known as neoadjuvant therapy.

Adjuvant Therapy: After your initial treatment with chemotherapy and radiation you may receive more treatment with immunotherapy to reduce the chance of the cancer returning - known as adjuvant therapy.

A clinical trial is a research study to determine whether a new drug, combination of drugs, procedure or medical device is safe and effective.

To learn more and find clinical trials near you, call our clinical trial specialists at 1-800-298-2436 or visit www.lungmatch.org.

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VACCINES

There are two types of cancer vaccines that are being studied: therapeutic vaccines, which can treat cancer and preventive vaccines, which can keep cancer from developing. You may already be familiar with vaccines, such as the flu shot, chickenpox or measles vaccine. In vaccines, a small amount of foreign protein (an antigen) is injected into the body. The goal is to teach the immune system what to attack to fight the cancer.

Therapeutic vaccines are used when you already have cancer. For most therapeutic cancer vaccines, the antigen is something normally found in lung cancer or is from a sample of your cancer. The vaccination then boosts the immune system's ability to fight the cancer. There are many clinical trials testing these types of cancer vaccines.

In some cases, such as the CIMAvax therapeutic vaccine (see below), the antigen is a protein that the cancer needs to grow. The immune system attacks that protein, with the goal of "starving" the tumor.

Preventive vaccines are not currently available for lung cancer. The only preventive cancer vaccines approved in the U.S. are human papillomavirus (HPV) vaccines and hepatitis B vaccines.

There is a lot of interest in the CIMAvax-EGF vaccine from Cuba. It is important to note that we do not yet have the scientific data we need to show this drug works. CIMAvax is being studied in a clinical trial at Roswell Park Cancer Institute. Only if it is shown to be safe and effective will it be approved for use in the United States.



ADOPTIVE CELL THERAPY INCLUDING CAR T-CELL THERAPY

T-cells are a type of immune cell that moves through the body looking for foreign cells (such as bacteria, viruses and cancer) and attacking them. For this type of cancer therapy, T-cells from your blood are removed and in some cases changed to make them more effective against the cancer cells. The T-cells are then multiplied and put back into you to improve your immune system's anti-cancer response.

Two T-cell therapies are approved by the FDA in blood cancers: Kymriah (tisagenlecleucel) for acute lymphoblastic leukemia and Yescarta (axicabtagene ciloleucel) for non-Hodgkin lymphoma. Research is ongoing to see if adoptive cell therapy could be effective in lung cancer.

ONCOLYTIC VIRUSES

Another class of immunotherapy drugs is called oncolytic viruses. These are viruses made by scientists to infect cancer cells and grow inside of them. Once there is a large amount of the virus in a cancer cell, it causes that cancer cell to burst open and die. When the cells burst open, they also release proteins. These proteins get the immune system working in a similar way as a vaccine (which result in the body having an immune response similar to one caused by a vaccine). These drugs work in two ways: by killing cancer cells directly and by helping the body's immune system work better. There is an oncolytic virus therapy approved for treatment of melanoma called Imylgic (talimogene laherparepvec or TVEC). None have been approved yet to treat lung cancer.

ABOUT GO₂ FOUNDATION

Founded by patients and survivors, GO₂ Foundation for Lung Cancer transforms survivorship as the world's leading organization dedicated to saving, extending, and improving the lives of those vulnerable, at risk, and diagnosed with lung cancer.

GO₂ Foundation works to change the reality of living with lung cancer by ending stigma, increasing public and private research funding, and ensuring access to care.

For more information about lung cancer and current treatments, to discuss support options or for referral to other resources, please contact us:

HELPLINE | 1-800-298-2436 or support@go2foundation.org

**BIOMARKER TESTING &
CLINICAL TRIAL MATCHING** | lungmatch.org

WEBSITE | go2foundation.org



Empower Everyone. Ignore No One.



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