

# IMMUNOTHERAPY FOR LUNG CANCER

A GUIDE FOR THE PATIENT



LUNG CANCER ALLIANCE



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# LUNG CANCER

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## — THE BASICS —

Cancer that begins in the lungs – lung cancer – is one of the most commonly diagnosed cancers in the United States. But lung cancer is not one disease. There are two types of lung cancer:

- ▶ **NON-SMALL CELL LUNG CANCER (NSCLC)**, the most common type. The two subtypes diagnosed most frequently are:
  - Adenocarcinoma
  - Squamous Cell Carcinoma
  
- ▶ **SMALL CELL LUNG CANCER (SCLC)**

## — WHAT'S NEW? —

There have been many exciting advances in the field of lung cancer. Until the mid-2000's, treatment options were mostly limited to surgery, chemotherapy and radiation. Now, people diagnosed with lung cancer often have newer treatment options. The way lung cancer is found and watched during therapy is also changing.

The purpose of this brochure is to help you understand advances in the treatment of lung cancer using agents that boost your body's immune system and what this means for you.

Immunotherapies work in similar ways in all cancers but certain drugs are more effective in certain subtypes of lung cancer. Knowing the type and subtype of lung cancer is important as that guides treatment options.



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## IMMUNOTHERAPY

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

The body’s immune system normally fights off infection and other foreign invaders that can make us sick. Without help, the immune system does not work well against cancer for several reasons.

Cancer develops from normal cells in the body that have changed so the immune system may not see the cancer as a foreign invader. Cancer cells can fool the immune system so it cannot work against the cancer properly. Also, the immune system may not be strong enough to fight the cancer.

Immunotherapy is a way of increasing the body’s natural defenses to target and attack the cancer and to make the immune system work better against the cancer. Many types of immunotherapies are being tested to treat lung cancer, including checkpoint inhibitors, monoclonal antibodies, vaccines, adoptive T-cell transfer and oncolytic viruses.

## CHECKPOINT INHIBITORS

If the immune system went after all the normal cells in the body, we would all have auto-immune diseases, like lupus. The body's normal immune system has "checkpoints" that stop the immune cells from attacking everything. Instead, when the checkpoint is turned on, it prevents the immune system from attacking normal cells.

Cancer can trick the body's natural defenses so that the cancer cells continue to grow without being slowed down or stopped. It can often fool the body's immune system by producing proteins that activate these safety checkpoints. Then the immune system does not fight the cancer effectively.

Treatments called checkpoint inhibitors work to fix the problem at the checkpoint so the normal immune system can fight the tumors. Many of these checkpoint inhibitors are actually monoclonal antibodies (see page 9) that target a specific protein involved in the checkpoint.

## PD-1/PD-L1 Checkpoint

When a tumor produces a protein called PD-L1 (Programmed Death-Ligand 1), that protein can bind to a protein on one of your normal immune cells called PD-1 (Programmed Death 1). When these two proteins bind, it turns on the checkpoint, slowing the immune system.

A new category of drugs target either the PD-1 or PD-L1 protein to "take the brakes off" the immune system by turning off the checkpoint. This allows your immune system to stay active and keep working to fight the cancer. The drugs in this class that have received official approval from the Food and Drug Administration (FDA) for advanced NSCLC are:

### ► **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 12). Usually, this is a test showing your tumor is PD-L1 "high" (more than half the tumor cells are positive). Less common in lung cancer, if the tumor is MSI-H or (microsatellite instability-high) or dMMR (mismatch repair deficient).
- [Keytruda](#) (pembrolizumab) plus chemotherapy – Keytruda can be given at the same time as chemotherapy for advanced nonsquamous lung cancer.

### ► **LATER LINES OF THERAPY** (after another treatment):

- [Opdivo](#) (nivolumab, a PD-1 inhibitor)
- [Keytruda](#) (pembrolizumab, a PD-1 inhibitor) – with a positive PD-L1 biomarker test (more than 1% of tumor cells are positive)
- [Tecentriq](#) (atezolizumab, a PD-L1 inhibitor)

## ADDITIONAL INFORMATION

- ▶ It is important to remember that these drugs work very well for some people and can continue to work for a long time. However, in most situations, only about 1 in 5 people have their cancers respond to this category of drugs. There are also potential serious side effects. You should discuss with your treatment team if this is the right option for you.
- ▶ We recommend biomarker testing to guide your treatment path (see page 12). If you are PD-L1 “high”, these drugs may be the right option for you; however, if you are positive for other biomarkers (such as EGFR, ALK or others) there is emerging data that these drugs may not be as effective and you should likely consider targeted therapies.
- ▶ This type of drug is new and being studied in many clinical trials alone and in combination with other drugs -- both in NSCLC and SCLC. A clinical trial may be a good option for you to discuss with your treatment team.
- ▶ Many new PD-1/PD-L1 inhibitors are in development, so others may be approved in the future.

## CTLA-4 Checkpoint

CTLA-4 (Cytotoxic T-Lymphocyte Associated protein 4) is a well-known immune checkpoint protein. Drugs such as Yervoy (ipilimumab), which is approved in melanoma, and tremelimumab, are checkpoint inhibitors that target the CTLA-4 receptor. These drugs are currently being studied in clinical trials for lung cancer and may be particularly beneficial when used in combination with the PD-L1 checkpoint inhibitors (see page 7).

## MONOCLONAL ANTIBODIES

Antibodies are proteins produced 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 cells or to make the cancer cells more receptive to the body's immune system. They are commonly used as therapies to fight cancers with a specific gene change (to learn more, see our [Targeted Therapies brochure](#)). These proteins can also carry other drugs or substances directly to the cancer.

## VACCINES

There are two types of cancer vaccines: therapeutic vaccines, which can treat cancer and preventative vaccine which can keep cancer from developing. Cancer vaccines are based on the same concept as a normal, preventative vaccines like the flu shot. A small amount of foreign protein (an antigen) is injected into the body. The goal of the vaccine is to teach the immune system what to attack to efficiently fight the cancer.

For most therapeutic cancer vaccines, the antigen is something normally found in lung cancer or is from a sample of the individual patient's cancer. The vaccination then boosts the immune system's ability to fight the cancer. There are multiple ongoing clinical trials testing these types of cancer vaccines. In some cases, such as the Cimavax vaccine from Cuba that is being studied in the U.S., the antigen is a protein that the tumor needs to grow. An immune response eliminating that protein is intended to "starve" the tumor.

Preventative vaccines have yet to show they are effective in lung cancer. The only preventative cancer vaccines approved in the U.S. are human papillomavirus (HPV) vaccines and hepatitis B vaccines.

## ADOPTIVE CELL THERAPY

INCLUDING CAR T CELL THERAPY

T-cells are a type of immune cell that move 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 a patient's blood are removed and in some cases changed to make them more effective against the tumors. The T-cells are then multiplied and put back into the patient to improve the immune system's anti-cancer response. This type of therapy has recently been recommended for approval for childhood leukemia and clinical trials are underway for 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). So 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, but there are not yet any to treat lung cancer.

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# MOLECULAR TESTS & BIOMARKERS

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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 treatment option for a particular individual. Researchers are trying to determine if there are biomarkers that can predict whether the cancer will respond to immunotherapy.

Currently, there are tests, called molecular tests or biomarker tests, that can tell how much of the PD-L1 protein (see page 7) is in a tumor. In general, 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 Opdivo, Keytruda or Tecentriq).

Unlike molecular 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 or it can be “low” and still respond, it is just not as likely to respond.

Some immunotherapies seem to work better if you have a lot of gene changes (mutations) in your cancer. In some cases, there are a lot of gene changes because a tumor has microsatellite instability (MSI) or a problem in mismatch repair (MMR). These happen when the genes don't repair themselves properly and both can be identified by molecular testing. In other cases, gene changes may be caused by exposure to environmental agents like cigarette smoke. Scientists are studying if tumor mutational burden (TMB), which determines the amount of gene changes in your cancer, could be a good biomarker to guide immunotherapy treatment decisions.

Research is ongoing to find new and better biomarkers to guide your treatment decisions.

## — 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 molecular testing, we can help you get it. Call our treatment and trial navigators at 1-800-298-2436 or visit [www.lungmatch.org](http://www.lungmatch.org).

 **LungMATCH**  
Lung Cancer Alliance



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## IMPORTANT INFORMATION

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- ▶ 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 may be experiencing.

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# ABOUT

## LUNG CANCER ALLIANCE

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

### HELPLINE

1-800-298-2436

### MOLECULAR TESTING & CLINICAL TRIAL MATCHING

[lungmatch.org](http://lungmatch.org)

### EMAIL

[support@lungcanceralliance.org](mailto:support@lungcanceralliance.org)

### WEBSITE

[lungcanceralliance.org](http://lungcanceralliance.org)

### MAIL

1700 K Street NW, Suite 660  
Washington, DC 20006

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## OUR MISSION

Saving lives and advancing research by empowering those living with and at risk for lung cancer.

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## WHAT WE DO

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- ▶ Offer personalized support, information and referral services at no cost through a team of trained, dedicated staff members to help patients, their loved ones and those at risk.
- ▶ Advocate for increased lung cancer research funding and equitable access, coverage and reimbursement for screening, treatment, diagnostics and testing.
- ▶ Conduct nationwide education campaigns about the disease, risk and early detection.



## LUNG CANCER ALLIANCE

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