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GUIDELINES
FOR PATIENTS®

2023

Metastatic Non-Small Cell Lung Cancer



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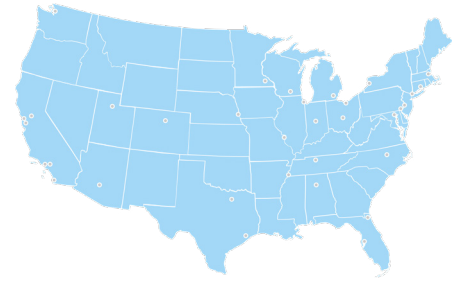
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Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).



Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer, Version 3.2023 — April 13, 2023.

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Lung cancer basics

- 5 What is NSCLC?
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Non-small cell lung cancer is the most common type of lung cancer. It is a challenging cancer to treat, but treatment is improving. Experts have identified some of the ways by which lung cancer grows and developed new treatments to control it.

What is NSCLC?

Non-small cell lung cancer (NSCLC) is a cancer of lung cells. The lungs are the main organs of the respiratory system. They deliver oxygen to the blood and remove carbon dioxide from the blood.

Cancers that have spread to the lungs are not lung cancers. For example, stomach cancer that has spread to the lungs is still stomach cancer.

Cancer is a disease that causes cells to grow out of control. The overgrowth of lung cancer cells becomes a mass called a tumor. Lung cancer cells also don't stay in place and may grow through the lung wall. They may break away from a tumor, spread outside the lung, and form more tumors.

Airways of the lungs

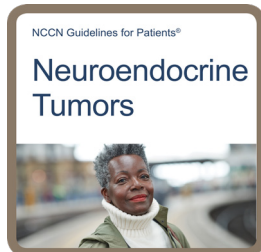
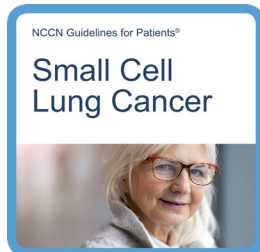
The air you breathe moves through a series of airways. It travels down your throat and through your windpipe (trachea). The windpipe splits into two airways called bronchi. Inside the lung, each bronchus branches off into the parts of the lung, called lobes. The right lung has three lobes, and the left lung has two lobes. The bronchi divide into smaller airways called the bronchioli. At the end of the bronchioli are sacs called alveoli. Oxygen is transferred from air into the blood in the alveoli.



NSCLC is the most common type of lung cancer

Almost all lung cancers are carcinomas. Lung carcinomas are cancers of cells that line the airways of the lungs. The airways of the lungs are the bronchus, bronchioli, and alveoli.

NSCLC is the most common lung carcinoma. Other lung carcinomas are neuroendocrine tumors, including small cell lung cancer. Information on lung neuroendocrine tumors is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



There are several types of NSCLC

Each type of NSCLC forms from a particular kind of cell. Below are the most common types of NSCLC:

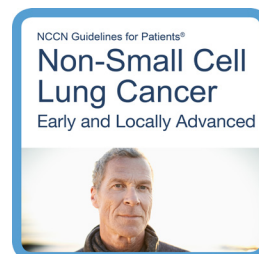
- **Adenocarcinoma** often forms from cells that line the alveoli and make mucus. It is the most common type of NSCLC.
- **Squamous cell carcinoma** forms from cells that line the bronchi.
- **Large cell carcinoma** forms from any of the large cells that are found throughout the airways.

What is metastatic NSCLC?

Metastatic NSCLC is cancer that has spread far from the lung in which it started. Stage 4 lung cancer is metastatic cancer, and some lung cancers diagnosed at earlier stages become metastatic cancer as well.

A cancer stage describes the growth and spread of lung cancer in the body. There are four main stages of lung cancer that are often written with Roman numerals—stages I, II, III, and IV.

Stage 1, stage 2, and stage 3 cancers have grown from the airway into lung tissue. Some have spread to nearby disease-fighting structures called lymph nodes, but none have spread far at the time of diagnosis. Information about these early and locally advanced cancers is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Stage 4 cancer has already spread far by the time of diagnosis. It is called metastatic cancer. NSCLC can affect any organ but tends to spread to the brain, liver, bone, and adrenal glands and from one lung to the other lung.

Some early and locally advanced cancers may have metastasized, but scans don't show the metastases until they are larger. If metastases are found after treatment, the cancer is not staged again. Instead, it is referred to as metastatic lung cancer.

What's the best treatment for metastatic NSCLC?

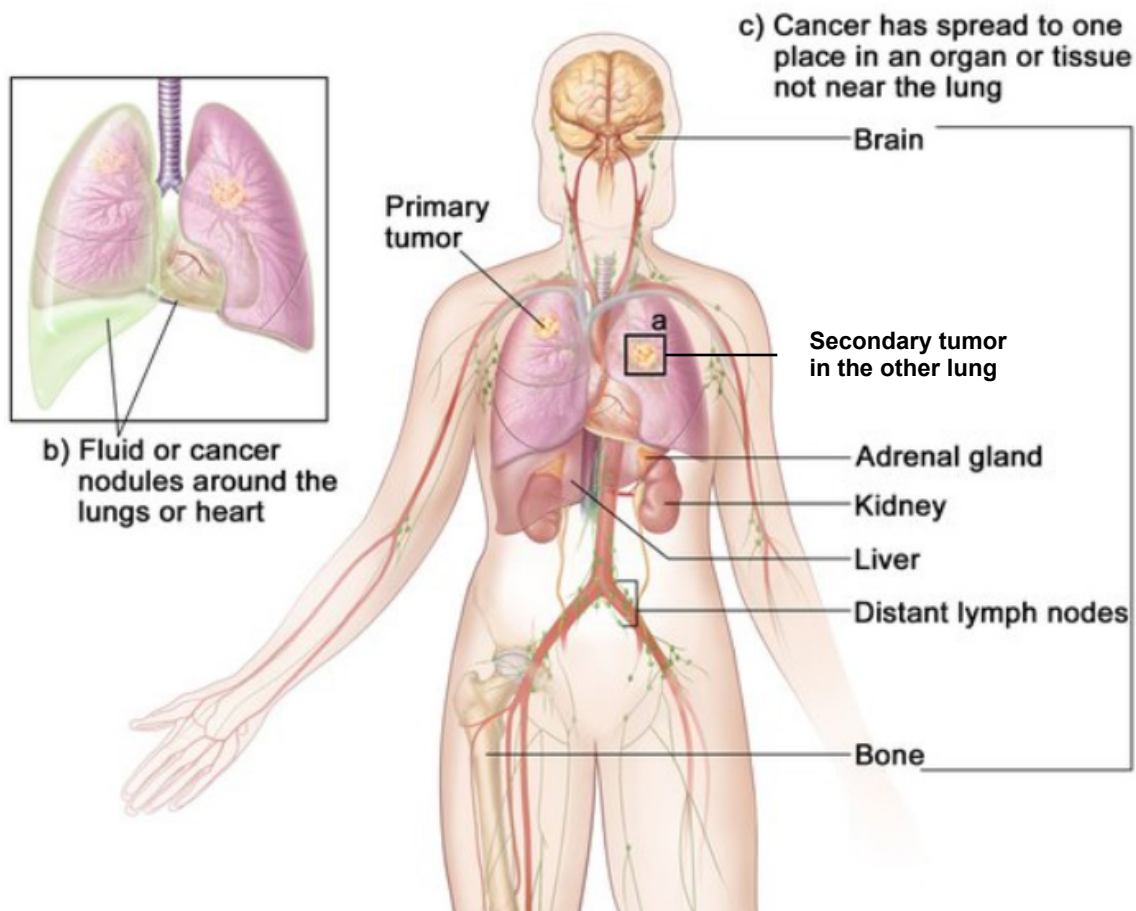
There's no treatment for NSCLC that's best for everyone. The best treatment is the treatment that's right for you. Your treatment plan should follow best practices—cancer care based on science and expert consensus. The following chapters explain the best practices of testing for and treating metastatic NSCLC.

Metastatic lung cancer is not often treated with local treatment. Local treatment includes surgery, radiation therapy, and chemoradiation. It may be an option if metastases are limited. An example is cancer that has spread to only the brain or adrenal gland. Local treatments may also be used to reduce (palliate) symptoms caused by a metastasis.

Metastatic lung cancer

Metastatic sounds like met·uh·stat·ik.

Lung cancer that has spread far from the main lung tumor is called metastatic lung cancer. It includes spread from one lung to the other lung (exhibit a in the image). It also includes spread to the tissue lining or fluid around the lung or heart (see b). Lung cancer that has spread outside the chest is also metastatic lung cancer (see c).



Most often, systemic therapy is used to treat metastatic lung cancer and is the focus of this book. Systemic therapy treats cancer wherever it is in the body. Most people with metastatic lung cancer will be on treatment for the rest of their lives. Newer therapies are better at controlling the cancer, improving quality of life, and prolonging life.

Clinical trials offer hope to all people with lung cancer. Clinical trials are a type of health research that tests new ways of fighting cancer. More information about clinical trials is in Chapter 5.

Enrolling in a trial may be an option at any point of your cancer care. Ask your care team if there is an open clinical trial that is a good fit for you.

- There are newer treatments for metastatic lung cancer that better control the cancer and improve quality of life.



DO NOT be afraid to ask your medical team ANY questions at any time!!! Your questions will help you and them. No question is stupid.”

Key points

- Non-small cell lung cancer (NSCLC) is a cancer of lung cells. Other cancers that spread to the lungs are not lung cancer.
- Lung cancer often starts in the cells that line the airways. These cancers are called carcinomas. NSCLC is a group of carcinomas.
- Common types of NSCLC are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.
- Metastatic NSCLC is cancer that has spread far from the lung in which it started.
- Most often, systemic therapy is used to treat metastatic lung cancer. Systemic therapy affects all cancer in the body.

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Tests for metastatic NSCLC

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Your care team will make a treatment plan just for you. To make the plan, they'll need to learn about your general health and the cancer. This chapter describes the tests that are needed for treatment planning and supportive services that you'll receive before treatment.

Goals of testing

Not all non-small cell lung cancers (NSCLC) are alike. Before you can be treated, several tests are needed to learn about the cancer and you. These tests are needed to:

- Assess your general health and well-being
- Stage the cancer by testing areas where it may have spread, which may be done at the same time as diagnosis
- Profile the cancer by testing for defining features called biomarkers

Tests for metastatic NSCLC are listed in **Guide 1**.

Guide 1

Initial tests and services for metastatic NSCLC

| | |
|--------------------------------|---|
| Health history and exam | <ul style="list-style-type: none"> • Medical history including weight loss and smoking history • Physical exam and performance status |
| Blood tests | <ul style="list-style-type: none"> • CBC • Chemistry profile |
| Imaging | <ul style="list-style-type: none"> • Diagnostic CT of the chest and upper abdomen using contrast • FDG-PET/CT scan • Brain MRI |
| Cancer cell tests | <ul style="list-style-type: none"> • Biopsy of metastasis • Molecular tests for driver mutations • PD-L1 test |
| Lung tests | <ul style="list-style-type: none"> • Pulmonary function tests |
| Initial services | <ul style="list-style-type: none"> • Supportive care • Smoking treatment |

It takes a team to plan treatment of NSCLC. You are part of the team. Tell your team about your goals and any challenges you are having. Your team may consist of many members, including a:

- A pulmonologist, thoracic radiologist, interventional radiologist, thoracic surgeon, and pathologist to diagnose and stage the cancer
- Medical oncologist, radiation oncologist, and thoracic surgical oncologist to treat NSCLC
- Palliative care provider, social worker, mental health provider, and registered dietitian to provide supportive services

Many of these experts are supported by nurses, technicians, or assistants who are often on the frontline of cancer care. Look for descriptions of team members throughout this book.

Health history

Expect your care team to review your health in detail. This is known as taking a medical history. Your team will want to know a lot about your past and current health. You will likely be asked about:

- Illnesses and injuries
- Symptoms like unexplained weight loss, trouble breathing, chest pain, and cough
- Prescribed and over-the-counter medicines and supplements, as well as surgeries
- Lifestyle choices, including your diet, how active you are, and whether you smoke or drink alcohol

Bring a list of your medications, herbals, and supplements to appointments.

Some cancers and other diseases run in families. Be prepared to discuss the health problems of your close blood relatives. Such family members include siblings, parents, and grandparents related to you by birth and not by adoption.

Physical exam

A team member will also perform a thorough physical exam of your body. This exam may include:

- Checking your vital signs—blood pressure, heart rate, breathing rate, and body temperature—and assessing your overall appearance
- Feeling and listening to organs, including your spleen and liver
- Feeling for enlarged lymph nodes, which are small disease-fighting structures throughout the body
- Assessing your level of pain, if any, when you are touched

Based on your health history and exam, your care team will rate your performance status. Performance status is your ability to do day-to-day activities. It is one of the most important factors that your team will use to plan treatment.

Blood tests

Blood tests are commonly used to screen for disease. They are also used to assess if cancer is affecting organs. Samples of your blood will be removed with a needle that is inserted into a vein. This is called a blood draw.

CBC

A complete blood count (CBC) is needed. A CBC measures parts of the blood including counts of white blood cells, red blood cells, and platelets.

Chemistry profile

Chemicals in your blood come from your liver, kidneys, bone, and other organs. A chemistry profile assesses if the chemicals in your blood are too low or high.

Imaging

Imaging takes pictures of the inside of your body. It is used to help stage the cancer by showing cancer in lung tissue and if the cancer has spread from the lung.

A radiologist is a doctor who's an expert in reading images. This doctor will convey the test results to your care team. Scans that were done more than 60 days ago should not be used to decide your treatment.

Diagnostic CT

Computed tomography (CT) is a more detailed kind of x-ray. It takes many pictures from different angles. A computer combines the images to make 3-D pictures.

A *diagnostic* CT shows body tissue more clearly. It is often the first scan done to stage lung cancer. Images of your chest and upper abdomen including the adrenal glands are needed.

A higher dose of radiation is used for diagnostic CT compared to regular CT. You'll receive an injection of contrast if it's safe for you. Contrast is a substance that makes images clearer. Contrast travels in the bloodstream and is flushed out in urine.

FDG-PET/CT

CT combined with positron emission tomography (PET) is referred as PET/CT. PET/CT is needed if you haven't had this scan. It may detect cancer that was not found by CT alone. Your whole body will be scanned, or the scan will extend from above your neck down to almost your knees.

PET highlights tissue in your body that may be cancerous. Before the scan, you will be injected with a sugar radiotracer called fluorodeoxyglucose (FDG). The tracer will pass out of your body in your urine in about 2 days.

Cancer cells take in more of the tracer than normal cells and show up as bright (or hot) spots on the scan. Multiple health problems can cause hot spots, so the cause of hot spots often needs to be confirmed by other testing.

Brain MRI

Lung cancer tends to spread to the brain. Magnetic resonance imaging (MRI) may show small brain tumors that aren't causing symptoms. If you have or may have metastatic lung cancer, brain MRI is very important.

MRI uses a magnetic field and radio waves to make pictures. Contrast should be used unless it would not be safe for you. If you can't have MRI, you may get a CT scan of your head with contrast.

Biopsy of metastasis

A biopsy is a procedure that removes body tissue or fluid for cancer testing. Often, tissue from the metastasis is removed rather than from the lung tumor. Your doctor will use imaging to select the biopsy site, which is often the adrenal gland, liver, or bone. The type of biopsy that will be done depends on the body part and the experience of your care team.

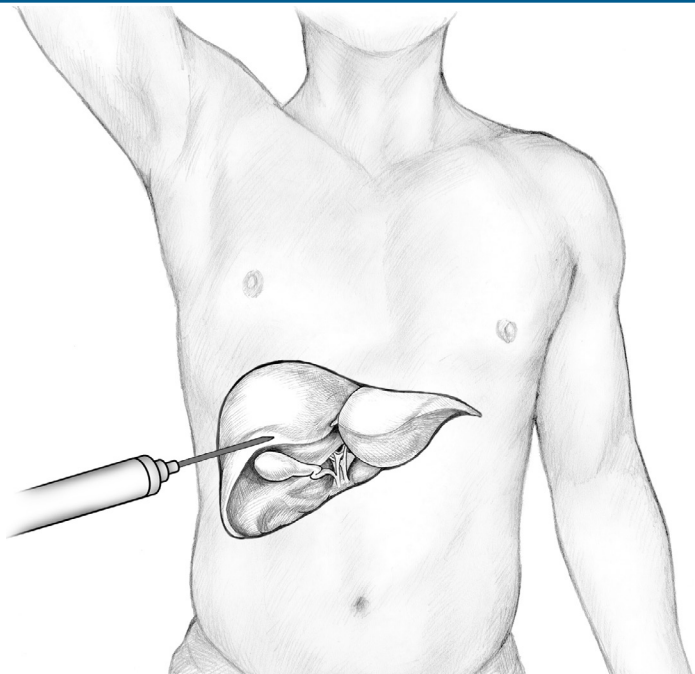
Common types of biopsies for metastatic lung cancer are:

- An external **needle biopsy** involves guiding a thin needle through your skin and into a tumor. These biopsies include transthoracic needle aspiration (TTNA), core needle biopsies, pericardiocentesis, and thoracentesis.
- **Down-the-throat biopsies** involve guiding tools down your throat into your windpipe (bronchus) or food pipe (esophagus). These procedures include many types of bronchoscopy.
- **Keyhole surgeries** involve making small openings into your chest. Small tools are inserted through the holes to remove tissue. Compared to open surgery, this method is minimally invasive. These surgeries include laparoscopy and thoracoscopy. Thoracoscopy is also called video-assisted thoracoscopic surgery (VATS).

Biopsy of metastasis

If your care team suspects metastatic lung cancer, you may have a biopsy of the metastasis instead of the lung tumor. A biopsy of the metastasis can diagnose and stage the cancer at the same time. A needle biopsy through the skin may reach some metastases, such as in the liver (shown). Imaging is often used to help guide the needle to the correct spot.

Credit: https://commons.wikimedia.org/wiki/File:Human_liver_biopsy.jpg



The removed tissue must be large enough for testing

A doctor called a pathologist will assess the tissue. Pathologists are experts in tissue and cells and diagnosing cancer.

The tissue must be large enough to run several special lab tests. At some cancer centers, the pathologist checks the tissue size right after removal. This method is called rapid on-site evaluation (ROSE). It helps to prevent having the same procedure a second time.

A pathologist will assess for cancer

Your pathologist will prepare the biopsy tissue. This may take a couple of days. Then, your pathologist will look at the tissue with a microscope and classify the disease. This is called histologic typing. If NSCLC is found, your pathologist will identify the type, which is very important for treatment of metastatic cancer:

- Adenocarcinoma
- Large-cell lung carcinoma
- Squamous cell carcinoma
- Mixed and rare types

The results of lab tests used for diagnosis are recorded in a pathology report. Ask your care team for a copy of the pathology report and to review the results with you. Take notes and ask questions.

Biomarker tests

Biomarker tests look for biological clues, or markers, of cancer that differ between people. Because of biomarkers, a treatment that helps one person might not help you. Biomarker tests are performed on tumor tissue removed with biopsy or during surgery, but a blood sample may be tested as well. **See Guide 2** for a list of biomarkers and which cancers should be tested for them.

Driver mutations are also called driver oncogenes. They cause normal cells to become cancer cells and support cancer growth. A driver mutation is found in at least 1 in 3 people with metastatic lung cancer. It is very rare for cancers to have more than one driver mutation.

Molecular tests are biomarker tests that assess for mutations. Very few squamous cell carcinomas have a driver mutation, so molecular testing is decided on a person-by-person basis.

NCCN experts strongly advise broad molecular profiling of all mutations listed in Guide 2. There are other known mutations linked with lung cancer that may be tested, too. This testing will help many people get the best treatment for their cancer. Since many genes are tested, it can take up to 3 weeks to get the results.

PD-L1 is a protein on the surface of cells. PD-L1 on cancer cells stops white blood cells called T cells from killing them. The cancer cells survive and make more cancer cells. All lung cancers should be tested for PD-L1. A lab method called immunohistochemistry (IHC) detects PD-L1.

What if there’s not enough tissue for testing? If not enough tissue was collected, a second biopsy may be scheduled. Sometimes, a blood sample may be drawn, and the plasma in the sample tested for biomarkers.

What if the cancer has no biomarkers? Some lung cancers do not have a known biomarker for which there is treatment. Treatment options for these cancers are based on the lung cell type as discussed in Chapter 5.

Guide 2 Biomarker tests for metastatic NSCLC

| | Adenocarcinoma, large cell carcinoma, and rare cell types | Squamous cell lung cancer |
|--|---|------------------------------|
| Driver mutation | | |
| <i>EGFR</i> exon 19 deletion or L858R mutation | ● | ● |
| <i>EGFR</i> S768I, L861Q, or G719X mutation | ● | ● |
| <i>EGFR</i> exon 20 insertion | ● | ● |
| <i>ALK</i> rearrangement | ● | ● |
| <i>ROS1</i> rearrangement | ● | ● |
| <i>BRAF</i> V600E mutation | ● | ● |
| <i>NTRK</i> gene fusion | ● | ● |
| <i>MET</i> exon 14 skipping | ● | ● |
| <i>RET</i> rearrangement | ● | ● |
| <i>KRAS</i> G12C mutation | ● | ● |
| <i>ERBB2</i> (<i>HER2</i>) mutation | ● | ● |
| Cell protein | | |
| PD-L1 | ● | ● |

● Testing is recommended for everyone

● Testing is a person-by-person decision

Pulmonary function tests

For some people, treatment of metastatic NSCLC includes radiation therapy or surgery. Treatment is based on how well the lungs work. There are three pulmonary function tests to assess how well you breathe:

- **Spirometry** involves blowing into a tube to measure how much air and how fast you breathe.
- A **gas diffusion test** involves breathing in a harmless gas and measuring how much you breathe out. It tells how much oxygen travels from your lungs into your blood.
- **Body plethysmography** involves sitting in a small room and breathing into a tube. This test measures how much air your lungs can hold and how much air is left in your lungs after you exhale.

Supportive services

This section explains some specialized services that you'll receive. It's important to start to receive these services right after a lung cancer diagnosis. They can improve your quality of life and may also help you live longer.

Start supportive care early

Supportive care is cancer care that improves your quality of life. It is not just for people at the end of life who need hospice. In fact, it has been shown to extend and enhance life for people with lung cancer.

Supportive care is sometimes called palliative care since symptom relief is a main goal. You

may undergo procedures that help you breathe and eat better and reduce coughing up blood.

Supportive care addresses many needs other than symptom relief. You can get help with making treatment decisions and coordination of care between health providers. You can get emotional or spiritual support, financial aid, or family counseling.

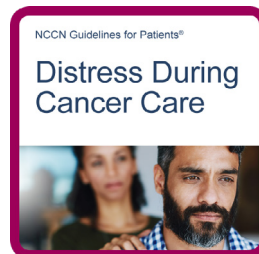
Your palliative care provider will work with your care team to provide you with the best care. Other specialists who may be involved in your care include:

- Respiratory therapists
- Rehabilitation specialists
- Registered dietitians
- Social workers

Supportive care guidelines

The library of NCCN Guidelines for Patients has books on supportive care. These books focus on common physical and emotional effects of many cancers and their treatment.

One of the NCCN books is about distress. Everyone with cancer feels distress at some point. It is normal to be worried, sad, helpless, or angry. Distress can become severe and affect the way you live. More information on managing distress is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](https://www.nccn.org/patientguidelines) app.



It's never too late to quit smoking

If you smoke, it is important to quit. Smoking can limit how well cancer treatment works.

Nicotine addiction is one of the hardest addictions to stop. The stress of having cancer may make it harder to quit.

There is help. Ask your care team about counseling and drugs to help you quit.

If you tried to quit before, try again. Most people slip or relapse before quitting for good.

- Biomarker tests look for small yet important features of cancer that differ between people. There are treatments for some markers.
- Your ability to breathe may be tested with pulmonary functioning tests.
- Supportive care aims to improve your quality of life. It is important for everyone, not just people at the end of life.
- Ask your care team for help to quit smoking. Quitting may improve treatment results.

Key points

- Tests are needed to learn about your overall health and the cancer. A team of experts will use the results to make a treatment plan for you.
- Be ready to tell your care team about any health problems and treatments you've had in your lifetime.
- A member of your team will examine your body for signs of disease. The exam will include touching parts of your body to see if anything feels abnormal.
- Your team will rate your ability to do day-to-day activities in order to decide your treatment options.
- Your care team will order blood tests. Blood tests are used to look for signs of cancer.
- Diagnostic CT can help show where the cancer has spread. PET/CT may detect cancer that CT did not. You may get a brain MRI.
- To help stage the cancer, a body part that appears to have cancer and is far from the lung tumor will likely be tested.



A common myth is that palliative care is only for terminally ill patients. It is so much more! It is worth reaching out to palliative care in your hospital or clinic. They treat the whole patient, not just cancer.”

3

Treatment of driver mutations

| | | | |
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Driver mutations promote the growth of cancer. They are most often found in adenocarcinomas and mixed cell types of lung cancer. Targeted therapy of lung cancer stops the effects of driver mutations.

What are driver mutations?

A driver mutation is an abnormal gene that supports the growth of cancer cells. It enables cancer cells to quickly duplicate, survive, and spread in the body.

Several driver mutations of lung cancer have been found

A gene is a small segment of DNA. There are tens of thousands of genes in a cell. Most of them contain instructions for making proteins that control how the cell works.

An abnormal change in a gene is called a mutation. All cancer cells have mutations, but not all mutations promote cancer. Only mutations that support cancer growth are called driver mutations.

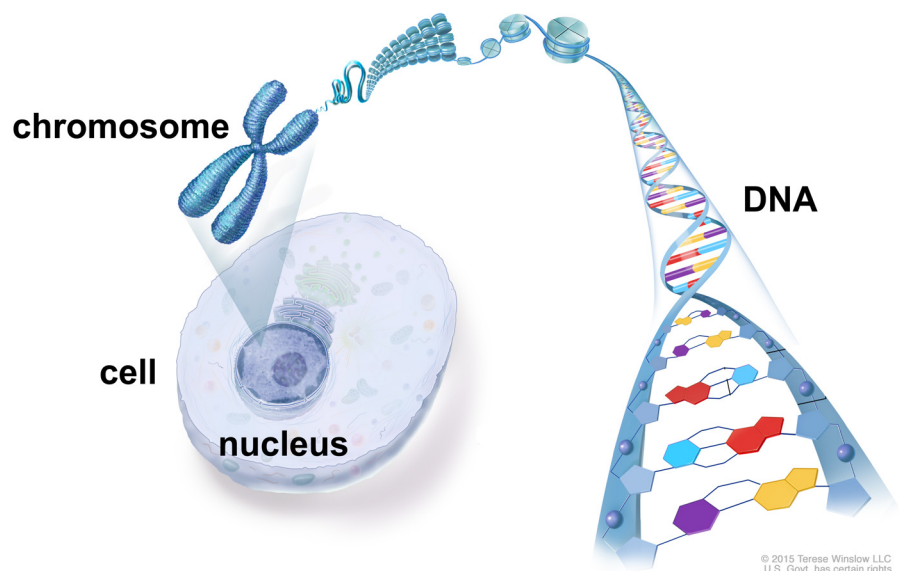
At this time, several driver mutations in lung cancer are known. They can be detected by molecular testing. Ongoing research is looking for more driver mutations.

Treating mutations is more precise

Chemotherapy destroys fast-growing cells whether or not they're cancer cells. It was once

Genetic information

The nucleus is the control center or “brain” of cells. Within the nucleus is genetic information that tells the cells what to do. The information is stored in DNA, which looks like a twisted ladder. Genes are parts of DNA that contain “instructions” for the cell. At times, strands of DNA tightly coil and form into chromosomes.



the only treatment for metastatic lung cancer. Newer treatments target the effects of driver mutations and harm fewer normal cells.

Targeted therapy

Driver mutations create abnormal cell proteins that help cancer cells grow. Targeted therapy works by stopping these proteins.

What if I already started a treatment other than targeted therapy? Some cancers with known driver mutations should be first treated based on cell type as explained in Chapter 5. When targeted therapy is recommended as the first treatment, you have two options:

- You may stop your current treatment early and start targeted therapy, or
- You may finish your current treatment (including the last phase called maintenance therapy), and then start targeted therapy.

Kinase inhibitors

Kinases are a type of cell protein. They are part of many chemical pathways, some of which start cell growth. Kinase inhibitors stop the activity of kinases and, in turn, lower the number of new cancer cells being made. They are pills that can be taken at home.

VEGF antibodies

Cancer cells need blood to grow, so they release a protein called VEGF. VEGF triggers endothelial cells to form new blood vessels on tumors. VEGF antibodies stop VEGF, and the cancer cells die from a lack of blood. You will need to go to a health care center to

receive VEGF antibodies through a slow drip (infusion).

EGFR antibodies

Lung cancer cells have a receptor on their surface called EGFR. Cell receptors receive and send signals like antennas. Antibodies stop receptors from sending growth signals to the cell. EGFR antibodies are given by infusion.

Antibody-drug conjugate

An antibody-drug conjugate combines two drugs in one medicine: One drug finds and binds to certain cancer cells, and the other drug attacks the cancer from within the cells. Antibody-drug conjugates are given by infusion.

New targeted therapy for lung cancer

Other types of targeted therapy are being studied in clinical trials. Clinical trials are a type of medical research. Ask your treatment team if there is an open clinical trial that's a good fit for you.

Side effects

Side effects are unwanted health problems caused by treatment. All cancer treatments cause side effects. But side effects differ between people based on the type and length of treatment as well as the person.

Ask your treatment team for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms you get. There may be ways to help you feel better. There are also ways to prevent some side effects.

EGFR mutations

Some lung cancers have certain mutations in the gene that makes EGFR. These mutations cause the receptor to be overactive. EGFR overactivity makes the cancer cells quickly grow.

Starting EGFR-targeted therapy

Targeted therapy of EGFR-mutated NSCLC is based on the type of mutation. **See Guide 3** for treatment options.

Among *EGFR* mutations, **EGFR exon 19 deletion and L858R mutations** are the most common. NCCN experts recommend a kinase inhibitor for the first treatment. The same inhibitors also treat the less common **EGFR S768I, L861Q, or G719X mutations**.

Among the EGFR inhibitors, erlotinib (Tarceva) and gefitinib (Iressa) were the first of their kind. The second group of EGFR inhibitors to be developed were afatinib (Gilotrif) and dacomitinib (Vizimpro). The newest EGFR

Guide 3

Options when starting EGFR-targeted therapy for metastatic NSCLC

EGFR exon 19 deletion or EGFR L858R mutation

Preferred option:

- Osimertinib

Other options:

- Erlotinib
- Afatinib
- Gefitinib
- Dacomitinib
- Erlotinib and ramucirumab
- Erlotinib and bevacizumab

EGFR S768I, L861Q, or G719X mutation

Preferred options:

- Afatinib
- Osimertinib

Other options:

- Erlotinib
- Gefitinib
- Dacomitinib

EGFR exon 20 insertion

Targeted therapy is started if the cancer worsens after chemotherapy:

- Amivantamab-vmjw
- Mobocertinib

inhibitor is osimertinib (Tagrisso). If your first treatment was immunotherapy, a short delay in starting osimertinib may be needed to prevent health problems.

Erlotinib is sometimes combined with a VEGF antibody. VEGF antibodies include bevacizumab (Avastin) and ramucirumab (Cyramza). It is not safe to receive bevacizumab if you are coughing up blood (hemoptysis).

Lung cancers with ***EGFR* exon 20 insertion** are first treated based on their cell type as explained in Chapter 5. If the cancer grows, you may receive an EGFR inhibitor called mobocertinib (Exkivity) or an EGFR antibody called amivantamab-vmjw (Rybrevant).

Options when cancer grows again

Within a few years of starting targeted therapy, lung cancer starts to grow again in most people. The next treatment options are listed in **Guide 4** based on the type of *EGFR* mutation.

For lung cancer with *EGFR* exon 19 deletion or *EGFR* L858R, S768I, L861Q, or G719X mutations, you may first get a biopsy to test for:

- ▶ Mutations that stop targeted therapy from working—a *T790M* mutation is common after taking erlotinib, afatinib, gefitinib, or dacomitinib
- ▶ A change in the type of cancer from an adenocarcinoma to small cell lung cancer

Guide 4

Options after metastatic NSCLC grows during EGFR-targeted therapy

Lung cancer with *EGFR* exon 19 deletion or L858R, S768I, L861Q, or G719X mutations

- Local treatment of limited tumors and targeted therapy
- Stay on the first targeted therapy if it has some benefit
 - Stay on osimertinib if the cancer didn't spread to many more places
 - Stay on erlotinib, afatinib, gefitinib, or dacomitinib regimens if there is no *T790M* mutation and no widespread cancer
- Switch to a different targeted therapy
 - Switch to osimertinib if there is a *T790M* mutation after erlotinib, afatinib, gefitinib, or dacomitinib
 - Switch to afatinib with cetuximab
- Start treatment for cell type as listed in Chapter 5

EGFR exon 20 insertion

- Switch to amivantamab-vmjw or mobocertinib
- Try another systemic therapy for cell type as listed in Chapter 5

If the cancer did not spread to many more places, your doctor may recommend local treatment and staying on targeted therapy. Local treatment is used to treat cancer in a specific area:

- Radiation therapy uses very precise, high-dose x-ray beams to treat limited areas of metastatic lung cancer, such as stereotactic ablative body radiation (SABR)
- Surgery removes tumors or organs with cancer
- Image-guided thermal ablation therapy uses extreme heat or cold to destroy cancer

The cancer may be growing again, but targeted therapy could be slowing down its growth. For this reason, you may stay on your current treatment. Otherwise, the cancer may grow faster if targeted therapy is stopped.

Switching to a different targeted therapy may help, especially if there are new mutations. Osimertinib after erlotinib, afatinib, gefitinib, or dacomitinib may be an option if there is a *T790M* mutation. Afatinib with an EGFR antibody called cetuximab (Erbix) may be another option.

If targeted therapy is not likely to help, your doctor may recommend other treatment. See Chapter 5 for options.

For lung cancer with *EGFR* exon 20 insertion, switching to a different targeted therapy may help. Since amivantamab-vmjw and mobocertinib work differently, you may switch to the one you weren't receiving. Another option is to try a second-line therapy for cell type listed in Chapter 5.

ALK rearrangement

For some lung cancers, the ALK surface receptor is overactive causing lung cells to quickly grow. The overactivity is caused by parts of two genes switching places called a gene rearrangement. Targeted therapy is recommended for the first treatment.

Starting ALK-targeted therapy

There are five ALK inhibitors used to treat lung cancer. Crizotinib (Xalkori) was the first ALK inhibitor to be used. The second group of ALK inhibitors to be developed were ceritinib (Zykadia), alectinib (Alecensa), and brigatinib (Alunbrig). The newest ALK inhibitor is lorlatinib (Lorbrena). Targeted therapy is listed in **Guide 5** with preferred regimens noted.

Options when cancer grows again

Within a few years of starting targeted therapy, lung cancer starts to grow again in most people. You may get a biopsy to test for new

Guide 5 Options when starting ALK-targeted therapy for metastatic NSCLC

| | |
|--------------------------|---|
| Preferred options | <ul style="list-style-type: none"> • Alectinib • Brigatinib • Lorlatinib |
| Other options | <ul style="list-style-type: none"> • Ceritinib |
| Sometimes useful | <ul style="list-style-type: none"> • Crizotinib |

mutations that limit how well targeted therapy works. **See Guide 6** for the next treatment options.

If the cancer did not spread to many more places, your doctor may recommend local treatment and staying on targeted therapy. Local treatment is used to treat cancer in a specific area:

- Radiation therapy uses very precise, high-dose x-ray beams to treat limited areas of metastatic lung cancer, such as stereotactic ablative body radiation (SABR)
- Surgery removes tumors or organs with cancer
- Image-guided thermal ablation therapy uses extreme heat or cold to destroy cancer

The cancer may be growing again, but targeted therapy could be slowing down its growth. For this reason, you may stay on your current treatment. Otherwise, the cancer may grow faster if targeted therapy is stopped.

Switching to a different targeted therapy may help, especially if there are new mutations. Lorlatinib after alectinib, brigatinib, or ceritinib may be an option if there is an *ALK* G1202R mutation. After taking crizotinib, you may switch to alectinib, brigatinib, ceritinib, or lorlatinib.

If targeted therapy is not likely to help, your doctor may recommend other treatment. See Chapter 5 for options.

Guide 6

Options after metastatic NSCLC grows during *ALK*-targeted therapy

Local treatment of limited tumors may be helpful for some people

Stay on first-line therapy if it has some benefit

- Stay on alectinib, brigatinib, ceritinib, or lorlatinib if the cancer didn't spread to many more places
- Stay on crizotinib if the cancer didn't spread to the brain or many more places

Switch to a newer *ALK* inhibitor

- Switch to lorlatinib if there's an *ALK* G1202R mutation after taking alectinib, brigatinib, or ceritinib
- Switch to alectinib, brigatinib, ceritinib, or lorlatinib if on crizotinib

Start treatment for cell type as listed in Chapter 5

ROS1 rearrangement

A cell surface receptor called ROS can be overactive causing lung cells to quickly grow. The overactivity is caused by parts of two genes switching places called a gene rearrangement..

Entrectinib (Rozlytrek) and crizotinib (Xalkori) are preferred options. Entrectinib may work better for treating and preventing the spread of lung cancer in the brain. The other option is ceritinib (Zykadia).

In time, the cancer will grow on targeted therapy. If the cancer didn't spread to many more places, your doctor may recommend local treatment, such as surgery or radiation therapy. You may also stay on your current treatment if there is some benefit.

A different targeted therapy may be used. If lung cancer spread to the brain, you may be switched to entrectinib or lorlatinib. Lorlatinib may also be used to treat lung cancer that has become more widespread.

If targeted therapy is not likely to help, your doctor may recommend other treatment. See Chapter 5 for options.

BRAF V600E mutation

A signaling protein inside of cells called BRAF can be overactive causing lung cells to quickly grow. Its overactivity is caused by a *BRAF* V600E mutation.

Preferred treatment is dabrafenib plus trametinib. Dabrafenib (Tafinlar) stops growth signals from BRAF. Trametinib (Mekinist) stops growth signals from MEK. MEK is a protein within the same signaling pathway as BRAF.

If dabrafenib plus trametinib makes you too sick, you may receive dabrafenib alone or vemurafenib (Zelboraf). Vemurafenib also stops growth signals from BRAF. Sometimes, treatment based on cancer cell type is used as the first treatment (see Chapter 5).

In time, the cancer will worsen on targeted therapy. After targeted therapy, treatment based on cell type may be received. If not used before, dabrafenib plus trametinib may be started if the cancer grows on another type of treatment.



When you are deciding on your treatment options, remember that even though some decisions need to be made fast, don't rush. Think through your options and get second, or even third opinions. Have people you can trust to talk through your options so you feel comfortable in your decisions."

NTRK gene fusion

Lung cells have a family of three cell surface receptors called TRK. *NTRK* genes contain instructions for making TRK. Some lung cancers have too much TRK, which causes fast cell growth. The cause of excess TRK is a joining (fusion) of *NTRK* with another gene.

Preferred treatment is TRK inhibitors. These treatments include larotrectinib (Vitrakvi) and entrectinib (Rozlytrek). Sometimes, treatment based on cancer cell type is useful as the first treatment (see Chapter 5).

In time, the cancer will worsen on targeted therapy. Your next treatment may be based on cell type. If not used before, a TRK inhibitor may be started if the cancer grows on another type of treatment.

MET exon 14 skipping

Some lung cancers have too much of a cell surface receptor called MET. Too much MET causes fast cell growth. The cause of excess MET is a deleted (skipped) part of the *MET* gene called exon 14.

Preferred treatment is MET inhibitors. These treatments include capmatinib (Tabrecta) and tepotinib (Tepmetko). Crizotinib (Xalkori) is useful for some people. It inhibits MET and other kinases. Sometimes, treatment based on the cancer cell type is useful as the first treatment (see Chapter 5).

In time, the cancer will worsen after targeted therapy. Your next treatment may be based on cell type. If not used before, a MET inhibitor may be started if the cancer grows on other types of treatment.

Ask your care team about clinical trials. Current treatments of lung cancer were once tested in clinical trials. You may also be able to help make a new way of fighting cancer become standard treatment.



RET rearrangement

A cell surface receptor called RET can be overactive causing lung cells to quickly grow. The overactivity is caused by parts of genes switching places called a gene rearrangement.

Preferred treatment is RET inhibitors. These treatments include selpercatinib (Retevmo) and pralsetinib (Gavreto). Cabozantinib (Cometriq, Cabometyx) is useful for some people. It inhibits RET and other kinases but doesn't work as well as preferred treatments. Sometimes, treatment used for cancer cell type is used as the first treatment (See Chapter 5).

In time, the cancer will worsen on targeted therapy. After targeted therapy, treatment used for cell type may be an option. If not used before, a RET inhibitor may be started if the cancer grows on other types of treatment.

KRAS G12C mutation

A signaling protein inside of lung cells called KRAS can be overactive causing the cells to quickly grow. Its overactivity is caused by a mutation in the *KRAS* G12C gene.

Lung cancers with *KRAS* G12C mutation are first treated by cancer cell type. See Chapter 5 for treatment options. If the cancer grows, a KRAS inhibitor is recommended for the next treatment. Sotorasib (Lumakras) and adagrasib (Krazati) are options. If the cancer grows during targeted therapy, treatment options are again based on cancer cell type.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

ERBB2 (HER2) mutation

Lung cancer cells have a receptor on their surface called HER2. Certain mutations in the gene that makes HER2 cause the receptor to be overactive. HER2 overactivity makes the cancer cells grow quickly.

Lung cancers with *HER2* mutations are first treated by cancer cell type. See Chapter 5 for treatment options. If the cancer grows, you may receive an antibody-drug conjugate. Fam-trastuzumab deruxtecan-nxk (Enhertu) is the preferred treatment. Another option is ado-trastuzumab emtansine (Kadcyla). Treatment options after a conjugate are again based on cancer cell type.

your treatment team about any new or worsening symptoms you get.

- For almost all known driver mutations, there is at least one preferred targeted therapy and often other regimens. When cancer grows during targeted therapy, treatment may be continued or switched to a different targeted therapy.
- When targeted therapy is not likely to help, you may receive treatment for cell type.

Key points

- A driver mutation causes normal cells to become cancer cells. It enables the cancer cells to quickly duplicate, survive, and spread in the body. Biomarker tests detect driver mutations.
- Targeted therapy is used to treat driver mutations of lung cancer.
- Enroll in a clinical trial to improve cancer care and potentially gain access to new ways of fighting cancer, including targeted therapies.
- Sometimes, targeted therapy is recommended based on biomarker tests, but another treatment has already been started. In this case, you could stay on your current treatment then take targeted therapy. A second option is to switch from your current treatment to targeted therapy.
- Ask your care team for a complete list of side effects of your treatments. Also, tell

4

Treatment based on low and high PD-L1

- 30 Immune checkpoints
- 30 Immunotherapy
- 31 PD-L1 levels
- 32 Treatment options
- 35 Key points

Some lung cancers evade death by immune T cells. Read this chapter to learn more about this survival skill of cancer cells. Immunotherapy restores the killing ability of T cells.

Immune checkpoints

The body's defense against disease is called the immune system. White blood cells called T cells are a key part of this system. T cells that kill cancer cells are called cytotoxic or killer T cells.

The immune system has “brakes” that prevent or slow down an immune response. The brakes are called immune checkpoints. They protect the body's healthy cells. CTLA-4 and PD-1 are two types of brake pedals on T cells.

In people with lung cancer, the brake pedals on T cells may be overused. CTLA-4 is activated when attached to B7 on immune cells called dendritic cells. PD-1 is activated when attached to PD-L1 on lung cancer cells. With the brakes on, T cells are not able to kill cancer cells.

Immunotherapy

Immunotherapy is a treatment that uses the immune system to kill cancer cells. Immune checkpoint inhibitors are a type of immunotherapy that releases the brake pedals on T cells.

There are seven checkpoint inhibitors discussed in this chapter. These checkpoint inhibitors block proteins to keep the immune checkpoint turned off.

- Pembrolizumab (Keytruda), nivolumab (Opdivo), and cemiplimab-rwlc (Libtayo) are PD-1 inhibitors. They attach to PD-1 on T cells to block PD-L1 on cancer cells from attaching.
- Atezolizumab (Tecentriq) and durvalumab (Imfinzi) are PD-L1 inhibitors. They attach to PD-L1 on cancer cells so PD-1 on T cells can't attach.
- Ipilimumab (Yervoy) and tremelimumab-actl (Imjudo) are CTLA-4 inhibitors. They attach to CTLA-4 on T cells and block attachment to B7.

Checkpoint inhibitors are slowly injected into a vein (infusion). It may take 30 or 60 minutes to get the full dose. Infusions are received every few weeks. The number of weeks between treatments depends on the inhibitor used. Often, people get infusions for up to 2 years or until they stop working.

When not to take immunotherapy

Not all lung cancers should be treated with immunotherapy:

- Cancers with known driver mutations should first be treated as explained in Chapter 3.
- Immunotherapy may not be safe if you have an autoimmune disease or you are taking medications that suppress your immune system.
- Immunotherapy may not be safe if you've had an organ transplant.

- Immunotherapy is not safe if your performance status is high. High scores of 3 or 4 reflect poorer health. NCCN experts advise receiving supportive care.

Side effects

Immune checkpoint inhibitors may cause your immune cells to attack your healthy cells. Immune-related side effects can occur during or after treatment. More information on immune-related side effects is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



PD-L1 levels

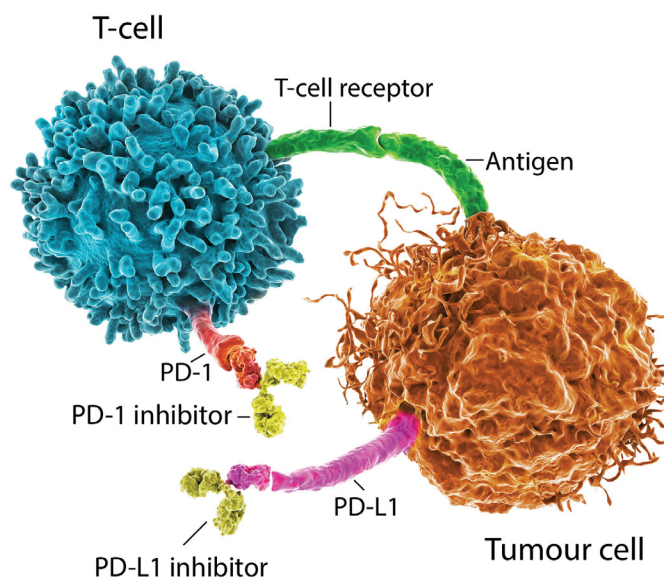
Immunotherapy options are partly based on PD-L1. A pathologist will assess the percentage of cancer cells with PD-L1. A sample of a lung tumor is needed for testing.

- High PD-L1 means that at least half of the cancer cells have PD-L1 (50% or more)
- Low PD-L1 means that less than half of cancer cells have PD-L1 (1% to 49%)
- No PD-L1 means that fewer than 1 out of 100 cells have PD-L1 (less than 1%)

Treatment of lung cancer with no PD-L1 is discussed in Chapter 5.

PD-1 and PD-L1 inhibitors

Some lung cancers consist of cells that have PD-L1 on their surface. PD-L1 can attach to PD-1 on T cells and stop T cells from killing cancer cells. There are two types of immunotherapy used to stop PD-L1 on cancer cells. PD-L1 inhibitors attach to cancer cells, and PD-1 inhibitors attach to T cells. When either inhibitor is attached, T cells are able to attack cancer cells.



Treatment options

In addition to low or high PD-L1 level, treatment is based on the type of NSCLC. A list of treatment options for adenocarcinoma, large cell carcinoma, and rare cell types is in **Guide 7** and for squamous cell carcinoma in **Guide 8**.

For first-line therapy, some lung cancers with high PD-L1 are treated only with an immune checkpoint inhibitor. Combining checkpoint inhibitors with chemotherapy is also an option when PD-L1 is low or high.

Guide 7

Treatment of metastatic NSCLC with low or high PD-L1: Adenocarcinoma, large cell carcinoma, and rare cell types

| Regimens | Low PD-L1 | High PD-L1 |
|--|-----------|------------|
| Atezolizumab | | ● |
| Cemiplimab-rwlc | | ● |
| Pembrolizumab | ● | ● |
| Pembrolizumab, carboplatin, pemetrexed | ● | ● |
| Pembrolizumab, cisplatin, pemetrexed | ● | ● |
| Nivolumab, ipilimumab, carboplatin, pemetrexed | ● | ● |
| Nivolumab, ipilimumab, cisplatin, pemetrexed | ● | ● |
| Atezolizumab, carboplatin, paclitaxel, bevacizumab | ● | ● |
| Atezolizumab, carboplatin, albumin-bound paclitaxel | ● | ● |
| Cemiplimab-rwlc, carboplatin, paclitaxel | ● | ● |
| Cemiplimab-rwlc, cisplatin, paclitaxel | ● | ● |
| Cemiplimab-rwlc, carboplatin, pemetrexed | ● | ● |
| Cemiplimab-rwlc, cisplatin, pemetrexed | ● | ● |
| Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel | ● | ● |
| Tremelimumab-actl, durvalumab, carboplatin, pemetrexed | ● | ● |
| Tremelimumab-actl, durvalumab, cisplatin, pemetrexed | ● | ● |
| Nivolumab, ipilimumab | ● | ● |

● preferred regimen ● other regimen

Platinum-doublet chemotherapy is used with checkpoint inhibitors. It consists of either cisplatin or carboplatin and another type of chemotherapy.

Bevacizumab is a part of one atezolizumab regimen. It is a targeted therapy called a VEGF

antibody. It stops the growth of blood vessels on tumors. Without blood, cancer cells die.

In addition to the recommended regimens, a clinical trial may be an option. Ask your team if there is an open clinical trial that's a good fit for you.

Guide 8

Treatment of metastatic NSCLC with low or high PD-L1: Squamous cell carcinoma

| Regimens | Low PD-L1 | High PD-L1 |
|--|-----------|------------|
| Atezolizumab | | ● |
| Cemiplimab-rwlc | | ● |
| Pembrolizumab | ● | ● |
| Pembrolizumab, carboplatin, paclitaxel | ● | ● |
| Pembrolizumab, carboplatin, albumin-bound paclitaxel | ● | ● |
| Nivolumab, ipilimumab, carboplatin, paclitaxel | ● | ● |
| Cemiplimab-rwlc, carboplatin, paclitaxel | ● | ● |
| Cemiplimab-rwlc, cisplatin, paclitaxel | ● | ● |
| Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel | ● | ● |
| Tremelimumab-actl, durvalumab, carboplatin, gemcitabine | ● | ● |
| Tremelimumab-actl, durvalumab, cisplatin, gemcitabine | ● | ● |
| Nivolumab, ipilimumab | ● | ● |

● preferred regimen ● other regimen

Maintenance therapy

If treatment results are good, you may shift to maintenance therapy, which includes some of your first-line therapy. This is called continuation maintenance. The goal of maintenance therapy is to prolong the time until the cancer worsens. Options for maintenance therapy are listed in **Guide 9**.

Within a few years on first-line therapy, lung cancer starts to grow again in most people. The next treatment is based on cell type as explained in Chapter 5.



The good news is that today the medical industry has made great advances in treating cancer. They create a custom designed treatment specifically for you.”

Guide 9

Maintenance therapy for metastatic NSCLC with low or high PD-L1

Adenocarcinoma, large cell carcinoma, and rare cell types

The maintenance regimen is based on your first-line therapy:

- Pembrolizumab
- Nivolumab, ipilimumab
- Atezolizumab
- Pembrolizumab, pemetrexed
- Atezolizumab, bevacizumab
- Cemiplimab-rwlc
- Cemiplimab-rwlc, pemetrexed
- Durvalumab
- Durvalumab, pemetrexed

Squamous cell lung cancer

The maintenance regimen is based on your first-line therapy:

- Pembrolizumab
- Nivolumab, ipilimumab
- Atezolizumab for NSCLC with high PD-L1
- Cemiplimab-rwlc
- Durvalumab

Key points

- The body's defense against disease is called the immune system. T cells are part of this system. They kill cancer cells.
- Immune checkpoints keep immune responses in check. PD-1 and CTLA-4 are two types of immune checkpoints on T cells.
- In people with NSCLC, PD-1 and CTLA-4 are often activated and stop T cells from killing cancer cells.
- Immune checkpoint inhibitors are a type of immunotherapy that stops PD-1 and CTLA-4 from being activated.
- There are many checkpoint inhibitor regimens. The one chosen for treatment is based on the level of PD-L1 and type of NSCLC.
- If cancer growth slows down, you may stay on some of them to increase the time until the cancer grows again. This is called maintenance therapy.

5

Treatment based on cell type

- 37 Planning cancer care
- 37 Types of systemic therapy
- 39 First-line therapy
- 42 Monitoring and maintenance
- 42 Second-line therapy
- 44 Clinical trials
- 45 Key points

When lung cancer does not have a biomarker for which there is treatment, it is treated mainly based on cell type. Read this chapter to learn about recommended treatments.

Treatments listed in this chapter may also be used for lung cancer with biomarkers as explained in Chapter 3 and Chapter 4.

Planning cancer care

Most non-small cell lung cancers (NSCLC) do not have a known biomarker for which there is treatment. When there is no such biomarker, cancer care is based on other factors.

One deciding factor is your ability to do day-to-day activities. This ability is called performance status. Cancer and other diseases can limit what you can do. If your ability is limited, some cancer treatments may cause serious health problems.

The Eastern Cooperative Oncology Group (ECOG) Performance Status is a common scoring system. It consists of five scores ranging from 0 to 4. Lower scores represent a better ability to do self-care.

A performance status of 0, 1, or 2 means that you are fairly healthy. NCCN experts advise receiving systemic therapy. Systemic therapy treats cancer anywhere it is in the body. It can treat cancer that is in many places and in hard-to-reach places.

A performance score of 3 or 4 suggests that cancer treatment will be harmful. NCCN experts advise receiving supportive care. Supportive care aims to improve your quality of life. It is sometimes called palliative care. One of its goals is to treat the symptoms caused by the cancer. It also helps with mental, social, and spiritual issues. Discuss supportive care with your care team to get the best plan for you.

Types of systemic therapy

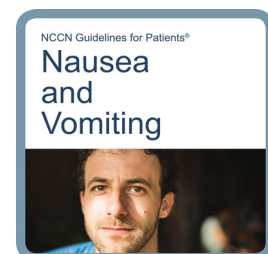
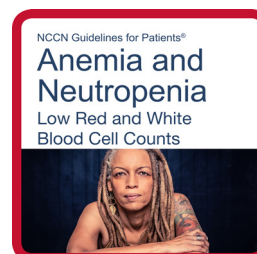
Medical oncologists are doctors trained to prescribe systemic therapy. Your oncologist will prescribe a regimen for you. A regimen consists of one or more drugs that are taken at a specific dose, schedule, and length of time.

Chemotherapy

The classic treatment of widespread metastatic lung cancer is chemotherapy. It kills fast-growing cells including cancer.

Chemotherapy for NSCLC is often a liquid that is injected into a vein. Some injections are done in the arm or hand while others are done through an implanted device called a port. An infusion is a slow drip controlled by a pump that may take hours.

Chemotherapy causes side effects because it kills fast-growing normal cells as well as cancer cells. It can cause nausea and vomiting, hair loss, and low blood cell counts. Each chemotherapy has its own set of side



effects, so ask your care team about what to expect. More information on common side effects of chemotherapy is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.

Immunotherapy

Immunotherapy is a treatment that uses the immune system to kill cancer cells. Immune checkpoint inhibitors are a type of immunotherapy. They restore the ability of immune T cells to kill lung cancer cells.

Checkpoint inhibitors are given by infusion. It may take 30 or 60 minutes to get the full dose.

Immune checkpoint inhibitors may cause your immune cells to attack your healthy cells. More information on management of immune-related side effects is available at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines) and on the [NCCN Patient Guides for Cancer](#) app.



Targeted therapy

Bevacizumab is a part of some regimens used to treat lung cancer. It is a targeted therapy called a VEGF antibody. It stops the growth of blood vessels on tumors. Without blood, cancer cells die.

Bevacizumab is given by infusion. The first dose takes about 90 minutes to receive. Later doses each take about 30 to 60 minutes.

Some of the common side effects of bevacizumab are high blood pressure, headache, changes in taste, dry or inflamed skin, watery eyes, and back pain.

Less common, but severe problems that may occur are tears in your digestive tract, wounds that don't heal, serious bleeding, and blood clots in deep veins.



People will ask how they can help. Be specific. For example, you could say, 'You can cook for me. Please pack meals in 4-ounce containers because that is all I can handle at any one time.'

First-line therapy

The first treatment given is referred to as first-line therapy. Your oncologist will choose a regimen for you based on:

- Your health conditions and medications
- A performance status of 0, 1, or 2
- The cell type—adenocarcinoma, large cell carcinoma, squamous cell carcinoma, or a rare type of NSCLC

Rare cell types of NSCLC are sometimes described as not otherwise specified (NOS).

Regimens with immunotherapy

If your performance status is either 0 or 1, immune checkpoint inhibitors may be part of treatment. Immune checkpoint inhibitors treat lung cancer with PD-L1 as explained in

Chapter 4. But they also extend life when lung cancer does not have PD-L1.

- Pembrolizumab (Keytruda), nivolumab (Opdivo), and cemiplimab-rwlc (Libtayo) are called PD-1 inhibitors. They attach to PD-1 on T cells and block PD-L1.
- Atezolizumab (Tecentriq) and durvalumab (Imfinzi) are PD-L1 inhibitors. They attach to PD-L1 on cancer cells so PD-L1 can't attach to T cells.
- Ipilimumab (Yervoy) and tremelimumab-actl (Imjudo) are CTLA-4 inhibitors. They attach to CTLA-4 on T cells and blocks attachment to B7.

Your oncologist will prescribe immune checkpoint inhibitors only if they are safe and work for you. They may not be safe if you have an autoimmune disease or you are taking medications that suppress your immune

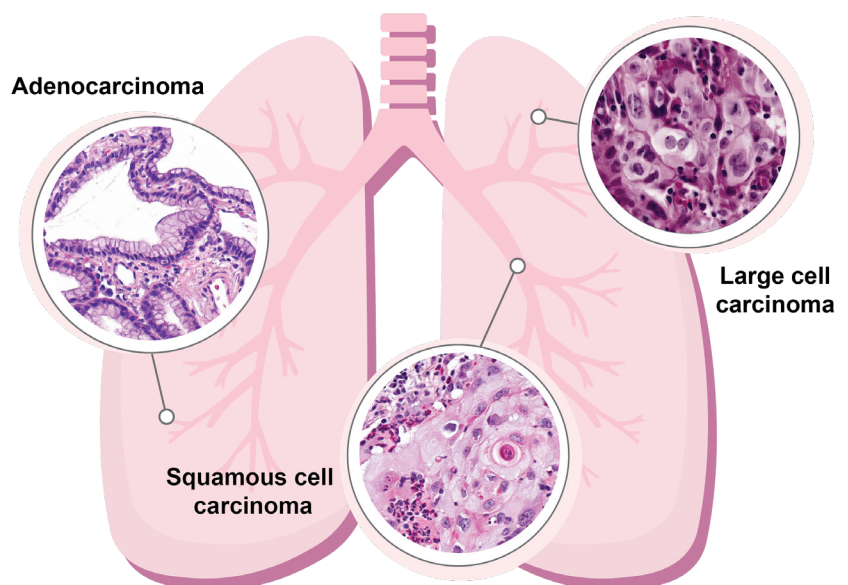
Types of non-small cell lung cancer

There are 3 main types of non-small cell lung cancer. **Adenocarcinoma is the most common type. It is a cancer of mucus-making cells. Large cell carcinoma starts in large cells of the lung. Squamous cell carcinoma starts in squamous cells.**

Credit: https://commons.wikimedia.org/wiki/File:Mucinous_lung_adenocarcinoma_-_high_mag.jpg

https://commons.wikimedia.org/wiki/File:Large_cell_carcinoma_of_the_lung.jpg

https://commons.wikimedia.org/wiki/File:Lung_squamous_carcinoma_-_high_mag.jpg



system. They may not work well if the cancer has EGFR or ALK biomarkers.

Immune checkpoint inhibitors are most often used with platinum-doublet chemotherapy. This combined treatment is called chemoimmunotherapy. See **Guide 10** and **Guide 11** for regimens.

Platinum-doublet chemotherapy consists of two types of chemotherapy. It consists of either cisplatin or carboplatin. The second chemotherapy is pemetrexed (Alimta, Pemfexy), paclitaxel, paclitaxel with human albumin (Abraxane), or gemcitabine (Gemzar, Infugem).

Guide 10

First-line therapy of metastatic NSCLC by performance status (PS): Adenocarcinoma, large cell carcinoma, and rare cell types

| Regimens with immunotherapy | PS 0 or 1 | PS 2 |
|--|-----------|------|
| Carboplatin or cisplatin, pemetrexed, pembrolizumab | ● | |
| Carboplatin, paclitaxel, bevacizumab, atezolizumab | ● | |
| Carboplatin, albumin-bound paclitaxel, atezolizumab | ● | |
| Nivolumab, ipilimumab | ● | |
| Carboplatin or cisplatin, pemetrexed, nivolumab, ipilimumab | ● | |
| Carboplatin or cisplatin, pemetrexed, cemiplimab-rwlc | ● | |
| Carboplatin or cisplatin, paclitaxel, cemiplimab-rwlc | ● | |
| Carboplatin or cisplatin, pemetrexed, tremelimumab-actl | ● | |
| Carboplatin, albumin-bound paclitaxel, durvalumab, tremelimumab-actl | ● | |
| Regimens without immunotherapy | | |
| Carboplatin, pemetrexed | ● | ● |
| Carboplatin or cisplatin, pemetrexed, bevacizumab | ● | |
| Carboplatin, paclitaxel, bevacizumab | ● | |
| Carboplatin and one other chemotherapy | ● | ● |
| Cisplatin and one other chemotherapy | ● | |
| Gemcitabine and either docetaxel or vinorelbine | ● | ● |
| Single-agent chemotherapy | | ● |

● preferred regimen ● other regimen

In addition to chemoimmunotherapy, immunotherapy by itself may be another option for you. You may receive nivolumab and ipilimumab if your performance status is either 0 or 1.

Regimens *without* immunotherapy

When immunotherapy is not an option, chemotherapy is used for treatment. Most of the options are platinum-doublet chemotherapy regimens. Bevacizumab is a part of some regimens.

Guide 11

First-line therapy of metastatic NSCLC by performance status (PS): Squamous cell carcinoma

| Regimens with immunotherapy | PS 0 or 1 | PS 2 |
|--|-----------|------|
| Carboplatin, paclitaxel, pembrolizumab | ● | |
| Carboplatin, albumin-bound paclitaxel, pembrolizumab | ● | |
| Nivolumab, ipilimumab | ● | |
| Carboplatin, paclitaxel, nivolumab, ipilimumab | ● | |
| Carboplatin or cisplatin, paclitaxel, cemiplimab-rwlc | ● | |
| Carboplatin, albumin-bound paclitaxel, durvalumab, tremelimumab-actl | ● | |
| Carboplatin or cisplatin, gemcitabine, durvalumab, tremelimumab-actl | ● | |
| Regimens without immunotherapy | | |
| Carboplatin, albumin-bound paclitaxel | ● | ● |
| Carboplatin, gemcitabine | ● | ● |
| Carboplatin, paclitaxel | ● | ● |
| Carboplatin, docetaxel | ● | ● |
| Carboplatin, etoposide | ● | ● |
| Cisplatin and one other chemotherapy | ● | |
| Gemcitabine and either docetaxel or vinorelbine | ● | ● |
| Single-agent chemotherapy | | ● |

● preferred regimen ● other regimen

In addition to platinum-doublet chemotherapy, options include gemcitabine with either docetaxel or vinorelbine. Plus, there are several options for single-agent chemotherapy, including:

- Albumin-bound paclitaxel
- Docetaxel
- Gemcitabine
- Paclitaxel
- Pemetrexed (only for non-squamous cell types)

Monitoring and maintenance

Systemic therapy is given in cycles of treatment days followed by days of rest. One cycle typically lasts for 3 to 4 weeks. In general, systemic therapy is given for 4 cycles. If treatment isn't making you too sick, a total of 6 cycles may be completed.

After 2 cycles, your doctor will assess the results. The extent of the cancer can be seen on computed tomography (CT) scans. Contrast may be used. CT will be repeated after another 2 to 4 cycles.

If a line of treatment works, you may receive maintenance therapy after the regimen is finished. The goal of maintenance therapy is to increase the time until the cancer grows.

If results are good at the end of treatment, you may stay on at least one of the medicines. This is called continuation maintenance. Another option is changing to a medicine that you didn't take as a first-line therapy. This is called switch maintenance. Options for maintenance therapy are listed in **Guide 12**.

You may stay on maintenance therapy for 2 years if your first-line therapy included immunotherapy. If immunotherapy was part of second-line therapy, stay on maintenance therapy until the cancer grows.

Second-line therapy

In time, lung cancer often starts to grow again after first-line therapy. Second-line therapy is the second treatment used for cancer care. If more lines of therapy are needed, the options mentioned in this section may be tried.

Your care team will suggest a different treatment than used for first-line therapy. A different type of treatment may control cancer growth. Options for second-line therapy are listed in **Guide 13**.

- Immune checkpoint inhibitors are preferred if not received before. If the cancer grew while taking a checkpoint inhibitor, switching to another checkpoint inhibitor is not advised.
- Other options include docetaxel with ramucirumab. Ramucirumab is a VEGF antibody.
- Single-agent chemotherapy is another option.

Your doctor will monitor treatment results. You will get a CT scan every 6 to 12 weeks. Contrast may be used.

Guide 12

Maintenance therapy for metastatic NSCLC by cell type

| | |
|---|--|
| <p>Adenocarcinoma, large cell carcinoma, and rare cell types</p> | <p>Continuation maintenance</p> <ul style="list-style-type: none"> • Bevacizumab • Pemetrexed • Bevacizumab, pemetrexed • Pembrolizumab, pemetrexed • Atezolizumab, bevacizumab • Atezolizumab • Nivolumab, ipilimumab • Gemcitabine • Cemiplimab-rwlc with or without pemetrexed • Durvalumab with or without pemetrexed <p>Switch maintenance</p> <ul style="list-style-type: none"> • Pemetrexed |
| <p>Squamous cell carcinoma</p> | <p>Continuation maintenance</p> <ul style="list-style-type: none"> • Nivolumab and ipilimumab • Gemcitabine • Pembrolizumab • Cemiplimab-rwlc • Durvalumab |

Guide 13

Second-line therapy for metastatic NSCLC

| | |
|---|---|
| <p>Preferred options when you haven't had immunotherapy before</p> | <ul style="list-style-type: none"> • Nivolumab • Pembrolizumab • Atezolizumab |
| <p>Other options whether you've had immunotherapy or not</p> | <ul style="list-style-type: none"> • Docetaxel • Gemcitabine • Ramucirumab, docetaxel • Albumin-bound paclitaxel • Pemetrexed (non-squamous lung cancers only) |

Clinical trials

Despite advances in treatment, more research is needed. Current treatment does not cure lung cancer or give people a long life. Improving treatment is made possible with clinical trials.

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I trials** study the dose, safety, and side effects of a drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II trials** study how well the drug or approach works against a type of cancer.
- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.



Finding a clinical trial

In the United States

NCCN Cancer Centers

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide

The U.S. National Library of Medicine (NLM)

clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

[cancer.gov/contact](https://www.cancer.gov/contact)

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside the clinical trial at any time.

Start the conversation

Don't wait for your care team to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study for which you may be eligible, ask your treatment team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Key points

- Treatment of lung cancer without treatable biomarkers is partly based on performance status. Performance status is your ability to do day-to-day activities.
- Whole-body treatment called systemic therapy is used to treat people with performance status of 0, 1, or 2. Support care is recommended if performance status is 3 or 4.
- Systemic therapy options differ by cancer cell type. Regimens for squamous cell carcinoma differ from those used to treat adenocarcinoma, large cell, and rare types of lung cancer.

- Chemotherapy with immunotherapy is recommended for fairly healthy people. Other options are chemotherapy by itself or chemotherapy with bevacizumab.
- Your doctor will monitor the results of treatment. You may receive between 4 and 6 cycles of treatment.
- Maintenance therapy slows down the growth of cancer. It consists of one or more drugs from your first treatment.
- The next treatment options for lung cancer are immunotherapy if not received before, chemotherapy with ramucirumab, and single-agent chemotherapy.
- Clinical trials are a type of research. New ways of fighting cancer are studied among people in clinical trials. A clinical trial may be an option in addition to standard treatment.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

6

Making treatment decisions

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It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor.

If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Resources

American Lung Association

lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer

Cancer Hope Network

cancerhopenetwork.org

Caring Ambassadors Program, Inc.

LungCancerCAP.org

Free Me from Lung Cancer

freemefromlungcancer.org

Go2 Foundation for Lung Cancer

go2foundation.org

LiveLung (Dusty Joy Foundation)

dustyjoy.org

Lung Cancer Action Network (LungCAN)

lungcan.org

Lung Cancer Research Foundation

lcrf.org

Triage Cancer

triagecancer.org



Words to know

ablation

A cancer treatment that uses extreme temperature to kill cancer cells..

adrenal gland

A small organ on top of each kidney that makes hormones.

alveoli

The tiny sacs in the lungs where gases are transferred in and out of the blood.

anaplastic lymphoma kinase (ALK)

A type of protein on the edge of a cell that sends signals for cell growth.

biomarker

Any molecule in your body that can be measured to assess your health.

biopsy

A procedure that removes fluid or tissue samples to be tested for a disease.

board certified

A status for doctors who finished training in a specialized field of medicine.

body plethysmograph

A test of how much air is in your lungs after inhaling or exhaling.

bronchioli

Small airways within the lungs.

bronchoscopy

A procedure to work inside the airways with a device that is guided down the throat.

bronchus

One of the two main airways that extends into the lungs.

cancer stage

A rating of the outlook of a cancer based on its growth and spread.

carcinoma

A cancer of cells that line the inner or outer surfaces of the body.

chemoradiation

A cancer treatment with both cell-killing drugs and high-energy rays.

chemistry profile

A lab test of the amount of 8 chemicals in a sample of blood. Also called metabolic panel.

chemoimmunotherapy

A combined treatment with both chemotherapy and immunotherapy.

chemotherapy

Treatment with cancer drugs that kill fast-growing cells.

clinical stage

The rating of the extent of cancer before treatment is started.

clinical trial

A type of research that assesses how well health tests or treatments work in people.

complete blood count (CBC)

A lab test that measures the parts of the blood.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the insides of the body.

continuation maintenance

A treatment phase using one or more first-line drugs to prolong good treatment results.

contrast

A substance put into your body to make clearer pictures during imaging.

core needle biopsy

A procedure that removes tissue samples with a hollow needle. Also called core biopsy.

diagnosis

An identification of an illness based on tests.

DNA

deoxyribonucleic acid

driver mutation

An abnormal gene that supports the growth of cancer cells.

ECOG

Eastern Cooperative Oncology Group

FDA

Food and Drug Administration

FDG

fluorodeoxyglucose

gas diffusion

A test that uses harmless gas to measure how much you can breathe out.

gene

Coded instructions in cells for making new cells and controlling how cells behave.

gene rearrangement

A coded instruction within a cell that is made from parts of other coded instructions.

immunohistochemistry (IHC)

A special lab test done on a tissue sample.

immunotherapy

A treatment with drugs that help the body find and destroy cancer cells.

large-cell lung carcinoma

A cancer of lung cells that lack features to classify as another type of lung cancer.

lobe

A clearly seen division in an organ.

lymph node

A small, bean-shaped, disease-fighting structure.

magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

maintenance therapy

A treatment phase that is given to prolong good treatment results.

medical history

A report of all your health events and medications.

metastasis

The spread of cancer from the first tumor to a new site.

mutation

Abnormal changes in coded instructions within cells (genes).

NCCN

National Comprehensive Cancer Network

non-small cell lung cancer (NSCLC)

A cancer that starts in lung cells that are not small.

NOS

Not otherwise specified

pathologic stage

A rating of the extent of cancer based on tests given after treatment.

pathologist

A doctor who's an expert in testing cells and tissue to find disease.

performance status

A rating of one's ability to do daily activities.

pericardiocentesis

A procedure that removes fluid from around the heart with a needle.

physical exam

A review of the body by a health expert for signs of disease.

platinum-doublet chemotherapy

A treatment with two cell-killing drugs, one of which contains the chemical platinum.

positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

positron emission tomography/computed tomography (PET/CT)

A test that uses two picture-making methods to show the shape and function of tissue.

pulmonary function tests

A set of breathing tests to test the strength of the lungs.

radiation oncologist

A doctor who's an expert in treating cancer with radiation.

radiation therapy

A treatment that uses intense energy to kill cancer cells.

rapid on-site evaluation (ROSE)

A size assessment of removed tissue during a medical procedure.

respiratory system

The group of organs that transfers gases in and out of the body.

side effect

An unhealthy or unpleasant physical or emotional response to treatment.

small cell lung cancer (SCLC)

A cancer of small, round lung cells.

spirometry

A test that uses a tube to measure how fast you breathe.

squamous cell carcinoma

A type of cancer of thin and flat cells that line the surface of organs.

stereotactic ablative radiotherapy (SABR)

Treatment with high-dose radiation within one or a few sessions. Also called stereotactic body radiation therapy (SBRT).

supportive care

Health care that includes symptom relief but not cancer treatment. Also sometimes called palliative care.

surgery

An operation to remove or repair a part of the body.

switch maintenance

A treatment phase with a new drug that is given to prolong good treatment results.

targeted therapy

A drug treatment that impedes the growth process specific to cancer cells.

thoracic radiologist

A doctor who's an expert in reading imaging tests of the chest.

thoracoscopy

A procedure to do work in the chest with a device passed through a small cut in the skin. Also called video-assisted thoracoscopic surgery (VATS).

trachea

The airway between the throat and airway into the lungs. Also called the windpipe.

transthoracic needle aspiration (TTNA)

A procedure that removes tissue samples with a thin needle guided through the ribs.

VATS

video-assisted thoracoscopic surgery



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and help make the
NCCN Guidelines for Patients
better for everyone!

[NCCN.org/patients/comments](https://www.nccn.org/patients/comments)

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This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer, Version 3.2023. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • penmedicine.org/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmancancer.org

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Robert H. Lurie Comprehensive Cancer Center
of Northwestern University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmeltcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

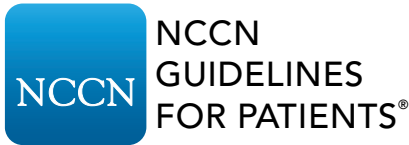
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

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