NCCN GUIDELINES FOR PATIENTS®

2025

# Metastatic Non-Small Cell Lung Cancer

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NATIONAL COMPREHENSIVE CANCER NETWORK®
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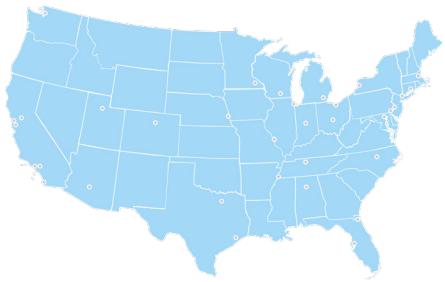
# About the NCCN Guidelines for Patients®

National Comprehensive Cancer Network®



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 3.2025 – January 14, 2025.**

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# 1
# About metastatic NSCLC

**Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. Treatment combined with supportive care have improved the lives of people with NSCLC. But NSCLC that has spread is challenging to treat.**

# What is metastatic NSCLC?

Metastatic non-small cell lung cancer (NSCLC) is an abnormal spreading of certain types of lung cells to the lining of the lung or to another organ.

This description is important because treatment differs between lung cancer types and where lung cancer is in the body.

## Types of NSCLC

NSCLC is a group of cancers. Each cancer in this group affects a different type of lung cell.

You have NSCLC if you have one of these cancers:

- Lung adenocarcinoma (A-deh-noh-KAR-sih-NOH-muh) affects lung cells that make mucus.
- Large cell carcinoma (kar-sin-OH-ma) of the lung forms from large cells in the airways.
- Squamous (squay-mous) cell carcinoma of the lung affects protective cells that line the airways.

There are more types of NSCLC, but they are much less common. And some lung cancers are a mix of cell types.

## Metastatic sites of NSCLC

Lung cancer cells grow out of control. They can also break away from a lung tumor, spread outside the lung, and form more tumors. Cancer that has spread from where it started is described as metastatic.

NSCLC can spread to many different places. It often spreads to the brain, liver, bone, and adrenal glands. NSCLC also spreads into the tissue lining around the lung and from one lung to the other lung.

# How is metastatic NSCLC treated?

Treatment of metastatic NSCLC is based on features of the cancer, your overall health, and your goals for treatment. There's no single treatment plan that's best for everyone.

## Testing is needed to plan treatment

Your care team will need to know the type of lung cancer and where the cancer is. They will also test for important cancer features called biomarkers. A list of tests needed to plan treatment is in *Chapter 2: Testing for metastatic NSCLC.*

## Supportive care addresses the challenges of cancer

Supportive care involves multiple types of aid that improve quality of life. Receiving supportive care early has been shown to extend and enhance life for people with lung cancer. More information is in *Chapter 3: Improving life with supportive care.*

## Systemic therapy is the most common treatment

Systemic therapy consists of prescribed drugs that treats cancer throughout the entire body. It is the focus of this book.

Less often, local treatment is used to try to cure limited metastases. For example, surgery may be done to remove lung cancer that has spread to only an adrenal gland.

Most people with metastatic lung cancer will be on systemic therapy for the rest of their lives. Typically, a person takes one treatment then switches to another when the cancer grows again.

Systemic therapy is based on the biomarkers, if any, the cancer has. This book has 3 chapters that explain the types and order of systemic therapy:

- *Chapter 4: Treatment for driver mutations*
- *Chapter 5: Treatment based on PD-L1*
- *Chapter 6: Treatment by cell type*

To learn which of these chapters explains treatment for the cancer you have, read *Chapter 2: Testing for metastatic NSCLC.*

## Confused about lung cancer?

People use the term lung cancer to describe many cancers. Sometimes, they misuse the term, so here's an explanation of what lung cancer is and what it isn't.

### What lung cancer is

Simply, lung cancer causes uncontrolled growth of lung cells. There are many types of cells in the lungs, so there are many types of lung cancer.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer. So when people talk about lung cancer, they're likely talking about NSCLC.

This book is part of a 2-book series on NSCLC. There are NCCN Guidelines for Patients on other types of lung cancers.

### What is not lung cancer

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. Treatment for cancers that have spread to the lungs is discussed in the guidelines for that cancer type.

The library of NCCN Guidelines for Patients can be found at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

### Clinical trials offer hope

Clinical trials are a type of health research that tests new ways of fighting cancer. Ask your care team if there is a clinical trial that is a good fit for you. Learn more about clinical trials in *Chapter 6: Treatment by cell type.*

## What can you do to get the best care?

Advocate for yourself. You have an important role to play in your care. In fact, you're more likely to get the care you want by asking questions and making shared decisions with your care team.

The NCCN Guidelines for Patients will help you understand cancer care. With better understanding, you'll be more prepared to discuss your care with your team and share your concerns. Many people feel more satisfied when they play an active role in their care.

You may not know what to ask your care team. That's common. Each chapter in this book ends with an important section called *Questions to ask.* These suggested questions will help you get more information on all aspects of your care.

Take the next step and keep reading to learn what is the best care for you!

### Why you should read this book

Making decisions about cancer care can be stressful. You may need to make tough decisions under pressure about complex choices.

The NCCN Guidelines for Patients are trusted by patients and providers. They clearly explain current care recommendations made by respected experts in the field. Recommendations are based on the latest research and practices at leading cancer centers.

Cancer care is not the same for everyone. By following expert recommendations for your situation, you are more likely to improve your care and have better outcomes as a result. Use this book as your guide to find the information you need to make important decisions.

# 2
# Testing for metastatic NSCLC

**This chapter explains the tests used to confirm lung cancer and plan treatment. Your care team will collect information on your overall health. They will also test for the type of lung cancer, extent of the cancer, and for cancer markers.**

# Confirming cancer

Lung cancer is confirmed, or diagnosed, by testing samples of body tissue or fluid for cancer cells. How tissue is removed for testing differs between people. It partly depends on where the cancer might be in your body.

## It takes a team

A team of experts will decide what is the best way to confirm if you have lung cancer. Your diagnostic team may include these experts:

- A pulmonologist is an expert in lung diseases.
- A thoracic radiologist is an expert in reading pictures (images) of the inside of the chest.
- A thoracic surgeon is an expert in performing operations within the chest.
- An interventional radiologist is an expert in performing image-guided biopsies.
- A pathologist is an expert in tissue and cells and confirming cancer.

You are an important part of the team. Your input is just as important as tests for planning treatment.

## Imaging detects possible cancer

Imaging creates pictures (images) of the insides of the body and can detect cancer. Using the images, your team will decide where to remove tissue samples for cancer testing.

Your team will also use imaging for cancer staging. A cancer stage describes the extent of lung cancer. For many people, diagnosis and cancer staging are done at the same time.

### Diagnostic CT scan

Diagnostic computed tomography (CT) is often the first scan done to stage lung cancer. Your team will look for tumors in images of your chest and upper abdomen, including the adrenal glands.

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

A diagnostic CT shows body tissue more clearly than low-dose CT. A higher dose of radiation is used. You'll receive an injection of contrast if it's safe for you. Contrast is a substance that makes images clearer.

### FDG-PET/CT scan

Positron emission tomography (PET) combined with a CT scan is necessary if not done before. PET highlights tissue in your body that may be cancerous. A PET/CT scan may detect cancer that was not found by CT alone and show signs of cancer spreading.

Your whole body will be scanned, or the scan will extend from your neck to the middle of your thighs.

Before the scan, you will be injected with a radiotracer called fluorodeoxyglucose (FDG). The tracer makes cancer cells show up as bright (or hot) spots on the scan. Multiple health problems can cause hot spots, so hot spots that suggest cancer often need to be confirmed by other tests.

### Brain MRI

Lung cancer tends to spread to the brain, so it's very important to test if it has. Magnetic resonance imaging (MRI) may show small brain tumors that aren't causing symptoms.

MRI uses a safe magnetic field and radio waves to make pictures, so you don't need to worry about radiation. Contrast will also be used unless it is not safe for you. If you can't have an MRI, you may get a CT scan of your head with contrast.

## Cancer stages and metastatic cancer

There are 4 main stages of lung cancer. You may see them written with Roman numerals—stages I (1), II (2), III (3), and IV (4).

Stage 4 is metastatic cancer at diagnosis. The cancer has spread to the lining of the lung or to other organs. In some people, earlier stages can become metastatic cancer.

## Imaging

**Imaging is used to make pictures of the insides of your body. You will lie on a table that will move into the tunnel of the machine during the scan. A radiologist will view the pictures on a computer and look for signs of cancer.**

## Biopsy type depends on where the cancer will be sampled

A biopsy is a procedure that removes samples of body tissue or fluid for cancer testing. Often, tissue from the organ with the metastasis is taken rather than from the lungs. Your team will use imaging to select the biopsy site, which is often the adrenal gland, liver, or bone.

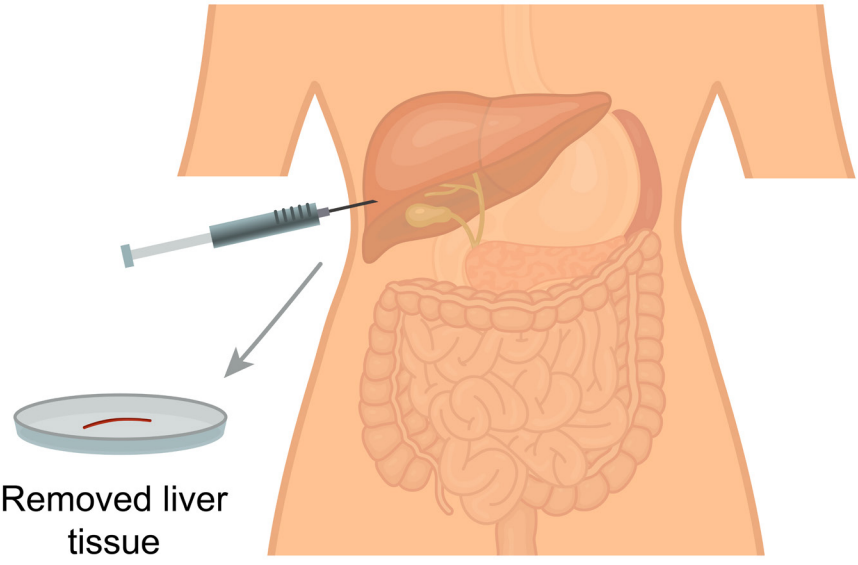
The type of biopsy that will be done depends on the body part and the experience of your team. Common types of biopsies for metastatic lung cancer are:

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

At some cancer centers, the pathologist checks the tissue size right away because it must be large enough to run several tests. This method is called rapid on-site evaluation. It helps to prevent having the same procedure a second time.

### 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.**



Removed liver tissue

### Pathology review of biopsy samples

A pathologist will prepare and then look at the tissue with a microscope. This takes a few days. The remaining tissue will be saved for possible future testing.

If non-small cell lung cancer (NSCLC) is found, the pathologist will identify the type:

- **Adenocarcinoma** is a cancer of cells that often line the air sacs in the lungs and make mucus. This is the most common type of NSCLC.
- **Large cell carcinoma** is a cancer of cells that are large in size compared to other cells in the airways.
- **Squamous cell carcinoma** is a cancer of thin, flat cells that protect the airways.
- There are also **rare and mixed types** of NSCLC.

The results of lab tests used for diagnosis are recorded in a pathology report.

## Planning treatment

Your care team will plan treatment using diagnostic tests and the tests described in this section. A complete list of tests for metastatic NSCLC is in **Guide 1.**

You might need to get new scans. Scans that were done more than 60 days ago should not be used to decide your treatment.

### Treatment team

Treating members of your team may include:

- A medical oncologist is an expert in treating cancer with drugs.
- A radiation oncologist is an expert in treating cancer with radiation.
- A thoracic surgical oncologist is an expert in removing cancer from the chest.

Many people also have team members who provide supportive care, which is discussed in *Chapter 3: Improving life with supportive care.*

### Health history

Expect your 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:

- Illnesses and injuries
- Symptoms like unexplained weight loss, trouble breathing, chest pain, and cough
- Prescribed and over-the-counter medicines and supplements
- Previous surgeries

- Lifestyle choices, including your diet, how active you are, and whether you smoke or drink alcohol

Some cancers and other diseases run in families. Be prepared to discuss the health of your close blood relatives. Such family members include siblings, parents, and grandparents related to you by birth.

## 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
- Feeling or listening to organs, including your lungs, spleen, and liver
- Feeling for enlarged lymph nodes, which are small disease-fighting structures throughout your body
- Assessing your level of pain, if any, when you are touched

## Performance status

Performance status is your ability to do day-to-day activities. It is based on your health history and exam. Your team will use your performance status to decide if your body can endure intense treatment.

**Guide 1**
**Tests for metastatic non-small cell lung cancer**

| | |
|---|---|
| **Imaging** | • Diagnostic CT scan of the chest and upper abdomen with contrast<br>• FDG-PET/CT scan<br>• Brain MRI |
| **Cancer cell tests** | • Biopsy of metastasis<br>• Pathology review |
| **History and exam** | • Medical history including weight loss and smoking history<br>• Physical exam and performance status |
| **Lung tests** | • Pulmonary function tests |
| **Blood tests** | • Complete blood count<br>• Chemistry profile |
| **Biomarker tests** | • Molecular tests for driver mutations<br>• Immunohistochemistry for PD-L1 levels<br>• Immunohistochemistry or HER2 overexpression |

## Pulmonary function tests

Pulmonary function tests are breathing activities used to assess how well your lungs work. Your team will use the results to decide if certain treatments are safe.

## 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 needed for these 2 blood tests:

- A **complete blood count** measures parts of the blood including counts of white blood cells, red blood cells, and platelets.
- A **chemistry profile** assesses sugar and natural salts in your body and how well your liver and kidneys are working.

## Biomarker tests

Biomarker tests look for biological clues, or markers, that care providers use to make care decisions. Biomarkers differ between cancers and people.

Many biomarkers of lung cancer help the cancer grow. There are treatments for some biomarkers. To plan treatment for you, your team needs to know which biomarkers your cancer has.

Biomarker tests are performed on tumor tissue removed during a biopsy or surgery. A blood sample also may be tested.

Metastatic NSCLC has 2 main types of biomarkers: driver mutations and protein expression. A list of biomarkers is in **Guide 2.**

### Driver mutations

Driver mutations are abnormal genes that boost cancer growth.

Biomarker testing for driver mutations is recommended for adenocarcinoma, large cell carcinoma, and rare cell types. The decision

**Guide 2**
**Biomarker tests for metastatic NSCLC**

**Driver mutations**

- *EGFR* exon 19 deletion or L858R mutation
- *EGFR* S768I, L861Q, or G719X mutation
- *EGFR* exon 20 insertion
- *ALK* rearrangement
- *ROS1* rearrangement
- *BRAF* V600E mutation
- *NTRK* gene fusion
- *MET* exon 14 skipping
- *RET* rearrangement
- *KRAS* G12C mutation
- *ERBB2* (*HER2*) mutation
- *NRG1* gene fusion

**Protein expression**

- PD-L1 levels
- HER2 overexpression

to test squamous cell lung cancer for driver mutations is decided on a person-by-person basis.

NCCN experts strongly advise use of broad molecular profiling when testing for driver mutations. This testing looks for many genes at the same time, so it can take up to 3 weeks to get the results.

### Protein expression

Cells make proteins, some of which are on the surface of the cancer cells. The level of these proteins, called expression, is detected with a lab test called immunohistochemistry. High levels are referred to as overexpression.

*PD-L1*

PD-L1 is a surface protein. Expression of PD-L1 on lung cancer cells helps them grow and spread. All lung cancers should be tested for PD-L1 levels.

*HER2*

High HER2 levels cause the lung cells to grow and divide. NCCN experts recommend testing for HER2 overexpression when lung adenocarcinoma, large cell carcinoma, and rare cell types grow after starting treatment. Testing for overexpression in squamous cell lung cancer is decided on a person-by-person basis.

## What's next?

Your team will explain the test results to you and what they recommend for cancer care.

A care plan usually includes treatment for cancer and support for you. It's important to start supportive care early because it has been shown to extend and enhance life. To learn more, read *Chapter 3: Improving life with supportive care*.

To learn what NCCN experts recommend for cancer treatment, read the chapter that pertains to the type of biomarker, if any, the cancer has:

- If the cancer has a driver mutation or HER2 overexpression, we advise you to read *Chapter 4: Treatment of driver mutations.*
- Cancers with PD-L1 and without driver mutations are covered in *Chapter 5: Treatment based on PD-L1*.
- Some lung cancers do not have a known biomarker for which there is treatment. Treatments for these cancers are explained in *Chapter 6: Treatment by cell type.*

## Key points

- Imaging is used to show where lung cancer may be in your body.
- To diagnose and stage metastatic lung cancer, a body part that appears to have cancer and is far from the lung tumor will likely be sampled and tested.
- To plan treatment, your care team will ask about your health, examine your body, and test blood samples.
- Biomarker tests look for small yet important features of lung cancer that differ between people. There are treatments for some markers.

## Questions to ask

- Could the tests be wrong or cause health problems?
- Will I need to pay any costs for the tests?
- What are the procedures for removing and storing tissue samples for future testing?
- How can I get a copy of the test results in case I want a second opinion?
- What do I need to do to prepare for testing?

# 3

# Improving life with supportive care

**Metastatic lung cancer often has a major impact on the body. Supportive care, especially when started early, can improve your quality of life. A key part of care is reducing symptoms.**

# What is supportive care?

Supportive care helps improve your quality of life during and after cancer treatment. The goal is to prevent or manage side effects and symptoms, like pain and cancer-related fatigue. It also addresses the mental, social, and spiritual concerns faced by those with cancer.

Supportive care is available to everyone with cancer and their families, not just those at the end of life. Palliative care is another name for supportive care.

Supportive care can also help with:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

# Start supportive care early

NCCN experts recommend combining supportive care with cancer care shortly after diagnosis of non-small cell lung cancer (NSCLC). Many studies have shown that receiving specialized supportive care early in your diagnosis can be more helpful than starting supportive care later. Early supportive care can extend and enhance life for people with NSCLC.

## Palliative care team

A palliative care specialist may be a member of your care team. This specialist has received specific training to provide maximal supportive care to you. They have a holistic approach to managing lung cancer symptoms and work with the other specialists on your team.

Other specialists who may be involved in your care include a:

- Radiation oncologist
- Respiratory therapist
- Rehabilitation specialist
- Registered dietitian
- Social worker

More information on the palliative care team can be found in NCCN Guidelines for Patients: Palliative Care.

# Help to quit smoking

Smoking can limit how well cancer treatment works.

- If you don’t smoke, it’s important that you don’t start now.
- If you smoke, it is important to quit. It’s never too late.

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

The NCCN Guidelines for Patients: Quitting Smoking provides critical support and guidance for people with cancer. This book explains how to best use the tools that exist to help you quit for good.

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

## Lung cancer complications

People with metastatic NSCLC often have health issues, called complications, that are caused by the cancer. Your care team will create a management plan based on your needs.

Local treatment is commonly used to reduce complications caused by metastasis. It's called local treatment because it focuses on a specific area of cancer.

There are 3 types of local treatment. Surgery may be used to remove some lung cancer. Radiation therapy kills an area of cancer with very precise, high-dose x-ray beams. Chemoradiation combines chemotherapy and radiation therapy.

Local treatment is used to:

- Improve breathing if lung cancer is blocking the airways
- Improve eating if lung cancer is blocking the digestive tract
- Reduce coughing up blood caused by lung cancer
- Prevent and relieve pain caused by lung cancer pressing against tissue and nerves
- Relieve symptoms caused by lung cancer that has spread to the brain

**"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."**

# Common cancer effects

People with different types of cancer experience common health issues. Cancers share some common symptoms because they disrupt the body in similar ways. Treatment is similar for different cancers and causes common side effects.

Information on managing common effects can be found in the library of NCCN Guidelines for Patients. Books from the supportive care series are briefly described next so that you can find the information you need.

## Palliative care

The NCCN Guidelines for Patients: Palliative Care describe care for physical and emotional symptoms:

- Diarrhea, constipation, and sleep issues
- Stress and grief

They also provide guidance on talking with your team about cancer treatment and advance care planning.

## Distress

Everyone with cancer feels distressed at some point. It is normal to feel worried, sad, helpless, or angry. NCCN Guidelines for Patients: Distress During Cancer Care empowers people to get help for distress.

## Fatigue

Cancer-related fatigue is not the typical tiredness that follows an active or long day. It's a lack of energy that is distressing, does not improve with normal rest or sleep, and disrupts life. Read NCCN Guidelines for Patients: Fatigue and Cancer to learn about physical activity and other methods that reduce cancer-related fatigue.

## Nausea and vomiting

Both chemotherapy and radiation therapy can cause nausea and vomiting. Nausea is the feeling that you are going to throw up. Vomiting is forcefully throwing up what's in your stomach. Treatments that prevent and manage both conditions are discussed in NCCN Guidelines for Patients: Nausea and Vomiting.

## Anemia and neutropenia

Chemotherapy often causes a drop in red and white blood cells. A low number of red blood cells, called anemia, may cause fatigue. A low white blood cell count, called neutropenia, raises your risk of infections. Treatment for low blood cells is described in NCCN Guidelines for Patients: Anemia and Neutropenia.

## Immunotherapy side effects

Immune checkpoint inhibitors are used to treat many types of NSCLC. This treatment may cause your immune cells to attack your healthy cells. NCCN Guidelines for Patients: Immunotherapy Side Effects: Immune Checkpoint Inhibitors explains treatment for:

- Skin and mouth symptoms
- Bowel and liver symptoms
- Thyroid, pituitary, and pancreas symptoms
- Lung symptoms

### Blood clots

Some drug treatments for NSCLC increase the risk for blood clots. A thrombus is a type of blood clot that can dangerously block blood flow. The NCCN book on blood clots explains ways to prevent and treat thrombi.

## Key points

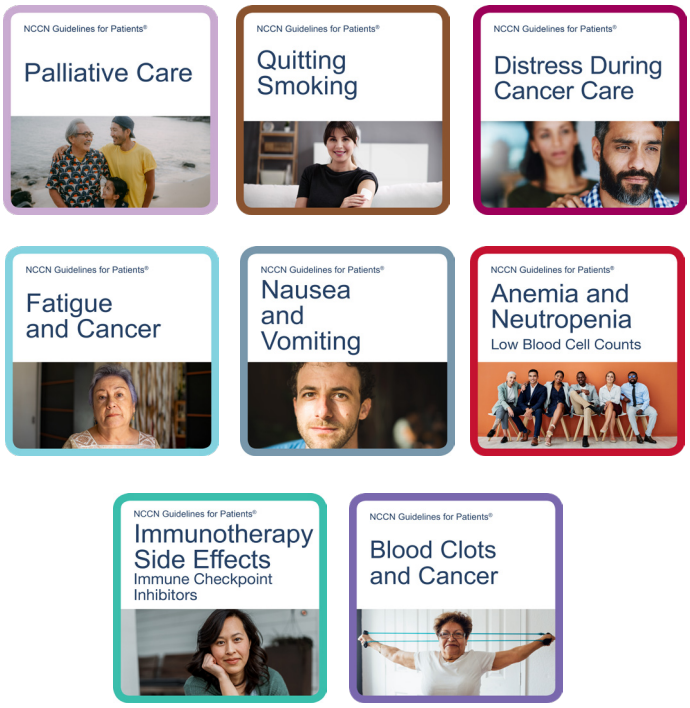
- Supportive care aims to improve your quality of life, including preventing and relieving symptoms.
- A supportive care specialist is called a palliative care doctor.
- Starting supportive care early has more benefits than starting later.
- Quitting smoking may improve treatment results.

## Questions to ask

- When will we discuss a supportive care plan for me?
- Should I tell health care providers I'm getting supportive care? They may incorrectly think I'm getting hospice care.
- What are the best methods to help me quit smoking?
- How will you prevent symptoms or relieve the symptoms I have?
- Who should I contact if my symptoms get worse?

## Supportive care resources

**More information on supportive care is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.**



# 4

# Treatment of driver mutations

**Driver mutations promote the growth of many lung cancers. Medicine that targets these mutations can help slow cancer growth. Read this chapter to learn more.**

## What are driver mutations?

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

At this time, several driver mutations in non-small cell lung cancer (NSCLC) have been found. And researchers are looking for more. Recommendations for driver mutation testing are in *Chapter 2: Testing for metastatic NSCLC.*

### Treating mutations is more precise

Chemotherapy destroys any fast-growing cells even if they're not cancer cells. It was once the only treatment for metastatic lung cancer.

Today, newer treatments target the effects of driver mutations and harm fewer normal cells. These newer treatments are called targeted therapy.

### Targeted therapy

**Targeted therapy is an important treatment for lung cancer with a driver mutation.**

**Driver mutations help cancers grow. Several types of driver mutations have been found in lung cancer.**

**Your care team will plan your treatment based on what type of driver mutation is found.**

# Types of targeted therapy

Driver mutations create cell proteins that help cancer cells grow. Targeted therapy is a drug treatment that stops these proteins.

## Kinase inhibitors

Kinases are a type of cell protein. They are part of many chemical pathways, and some of them 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.

## Antibody therapy

Cells have receptors on their surface. Cell receptors receive and send signals like antennas. Antibody therapy stops receptor signals:

- Some antibody therapies attach to receptors on cancer cells, such as EGFR and MET, and stop signals that tell the cancer cells to grow.
- VEGF antibodies stop the growth of blood vessels on tumors. Without blood, cancer cells die.

You will need to go to a health care center to receive antibody therapy through a slow drip (infusion) from a needle into a vein.

## Antibody-drug conjugate

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

# NCCN levels of preference

The next sections in this chapter list treatments for specific driver mutations.

NCCN experts recommend these treatments based on science and safety. When helpful, they assign a level of preference to their recommendations:

- **Preferred therapies** have the most evidence they work better and may be safer than other therapies.
- **Other recommended therapies** may not work quite as well as preferred therapies, but they can still help treat cancer.
- **Therapies used in certain cases** work best for people with specific cancer features or health circumstances.

These levels of preference are noted on the next pages.

### Side effects of targeted therapy

Side effects are unwanted health problems caused by treatment. All cancer treatments cause side effects. Side effects vary between people based on the type and length of treatment as well as differences among people. Management of side effects is discussed in *Chapter 3: Improving life with supportive care*.

# *EGFR* deletions and mutations

Some lung cancers have a deletion or mutation in the gene that makes EGFR proteins. These changes cause the receptor to be overactive. EGFR overactivity makes the cancer cells grow quickly.

## Targeted therapy

NCCN experts recommend targeted therapy to treat NSCLC with *EGFR* deletions and mutations. If you are taking a different type of treatment, you may stop your current treatment early and start targeted therapy. Options for targeted therapy are listed in **Guide 3.**

Kinase inhibitors have been a standard treatment for years. The therapies in Guide 3 that end in -nib are EGFR kinase inhibitors.

**Guide 3**
**Targeted therapy for metastatic NSCLC with *EGFR* deletions and mutations**

| | |
|---|---|
| ***EGFR* exon 19 deletion or *EGFR* exon 21 L858R mutation** | **Preferred therapy**<br>• Osimertinib (Tagrisso)<br>**Other recommended therapies**<br>• Amivantamab-vmjw (Rybrevant) and lazertinib (Lazcluze)<br>• Osimertinib with pemetrexed (Alimta, Axtle, Pemfexy) and either cisplatin or carboplatin for adenocarcinoma, large cell carcinoma, and rare cell types<br>**Therapies used in certain cases**<br>• Afatinib (Gilotrif)<br>• Dacomitinib (Vizimpro)<br>• Erlotinib (Tarceva)<br>• Erlotinib and bevacizumab (Avastin)<br>• Erlotinib and ramucirumab (Cyramza)<br>• Gefitinib (Iressa) |
| ***EGFR* S768I, L861Q, or G719X mutation** | **Preferred therapies**<br>• Afatinib (Gilotrif)<br>• Osimertinib (Tagrisso)<br>**Other recommended therapies**<br>• Erlotinib (Tarceva)<br>• Gefitinib (Iressa)<br>• Dacomitinib (Vizimpro) |

Some treatments combine kinase inhibitors and other medicines:

- Osimertinib is sometimes used with chemotherapy for lung adenocarcinoma, large cell carcinoma, and rare cell types.
- Lazertinib is used with an antibody called amivantamab-vmjw.
- Erlotinib with a VEGF antibody (bevacizumab or ramucirumab) is an option for some people.

## Options when NSCLC grows again

Within a few years of starting targeted therapy, lung cancer starts to grow again in most people.

To plan the next treatment, you may need to get a biopsy to check 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 adenocarcinoma to small cell lung cancer

The next treatment options are listed in **Guide 4**.

### Guide 4
### Options after metastatic NSCLC grows during EGFR-targeted therapy

Local treatment of limited tumors and targeted therapy

Stay on the first targeted therapy if it has some benefit

- Stay on osimertinib or amivantamab-vmjw with lazertinib 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 taking erlotinib, afatinib, gefitinib, or dacomitinib
- Switch from osimertinib to afatinib with cetuximab (Erbitux)
- Switch from osimertinib to amivantamab-vmjw, carboplatin, and pemetrexed for adenocarcinoma, large cell carcinoma, and rare cell types with *EGFR* exon 19 deletion or L858R mutation

Start treatment for cell type as described in Chapter 6

### Adding local treatment

If the cancer did not spread to many more places, your team may recommend local treatment and keep you on targeted therapy.

Local treatment is used to treat cancer in a specific area or organ:

- Radiation therapy uses very precise, high-dose x-ray beams to damage cancer cells.
- Surgery removes tumors or organs with cancer.
- Image-guided thermal ablation therapy uses extreme heat or cold to destroy cancer.

### Staying on current targeted therapy

Although the cancer may be growing again, targeted therapy could be slowing its growth. You'll likely stay on your current treatment. It depends on how slowly the cancer is growing or if it's only growing in 1 or 2 places in the body. Otherwise, the cancer may grow faster if targeted therapy is completely stopped.

### Switching targeted therapy

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 may be an option after osimertinib.

For multiple new tumors causing symptoms, switching from osimertinib to amivantamab-vmjw with chemotherapy is the preferred option for cancer with *EGFR* exon 19 deletion or L858R mutation.

### Treatment by cell type

If targeted therapy is not likely to help, your team may recommend treatment described in *Chapter 6: Treatment by cell type.*

## *EGFR* insertion

An *EGFR* exon 20 insertion makes EGFR overactive, which causes cancer cells to grow quickly. Treatment is based on the cell type.

- The preferred first-line therapy for lung adenocarcinoma, large cell carcinoma, and rare cell types is chemotherapy with an EGFR-MET antibody called amivantamab-vmjw (Rybrevant).
- Otherwise, lung cancers with *EGFR* exon 20 insertion are treated as explained in Chapter 6, and if the cancer grows, then amivantamab-vmjw is started.

**"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."**

# *KRAS* G12C mutation

A signaling protein inside of lung cells called KRAS can be overactive causing the cells to quickly grow. A mutation in the *KRAS* G12C gene causes this overactivity.

Lung cancers with *KRAS* G12C mutation are first treated based on PD-L1 level:

- For treatment of lung cancer with PD-L1, see *Chapter 5: Treatment based on PD-L1.*
- For treatment of lung cancer without PD-L1, see *Chapter 6: Treatment by cell type.*

If the cancer grows again, your treatment may be switched to one of the following KRAS inhibitors:

- Sotorasib (Lumakras)
- Adagrasib (Krazati)

If the cancer grows during targeted therapy, the next treatment options are based on cell type.

# *ALK* rearrangement

For some lung cancers, the ALK surface receptor is overactive, causing tumor cells to grow quickly. The overactivity is caused when parts of two genes switch places, called a gene rearrangement.

## Targeted therapy

NCCN experts recommend targeted therapy to treat NSCLC with an ALK rearrangement. If you are taking a different type of treatment, you may stop your current treatment early and start targeted therapy.

ALK inhibitors are used to treat cancer with an ALK rearrangement. Preferred therapies are alectinib, brigatinib, ensartinib, and lorlatinib. Ceritinib and crizotinib are options for some people. These options are listed with their brand names in **Guide 5.**

## Options when NSCLC grows again

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

**Guide 5**
**Targeted therapy for metastatic NSCLC with an *ALK* rearrangement**

| | |
|---|---|
| **Preferred therapies** | • Alectinib (Alecensa)<br>• Brigatinib (Alunbrig)<br>• Ensartinib (Ensacove)<br>• Lorlatinib (Lorbrena) |
| **Therapies used in certain cases** | • Ceritinib (Zykadia)<br>• Crizotinib (Xalkori) |

for new mutations, which might change your treatment options. Treatment options are listed in **Guide 6.**

### Adding local treatment

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

- Radiation therapy uses very precise, high-dose x-ray beams to damage cancer cells.
- Surgery removes tumors or organs with cancer.
- Image-guided thermal ablation therapy uses extreme heat or cold to destroy cancer.

### Staying on current targeted therapy

Although the cancer may be growing again, 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 completely stopped.

### Switching targeted therapy

Switching to a different targeted therapy may help, especially if there are new mutations. Lorlatinib after alectinib, brigatinib, ceritinib, or ensartinib may be an option if there is a mutation, such as an *ALK* G1202R or L1196M mutation. After taking crizotinib, you may switch to alectinib, brigatinib, ceritinib, ensartinib, or lorlatinib.

### Treatment by cell type

If targeted therapy is not likely to help, your team may recommend treatments listed in *Chapter 6: Treatment by cell type.*

**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<br>• Stay on alectinib, brigatinib, ensartinib, ceritinib, or lorlatinib if the cancer didn't spread to many more places<br>• Stay on crizotinib if the cancer didn't spread to the brain or many more places |
| Switch to a newer ALK inhibitor<br>• Switch to lorlatinib if there's a mutation that stops alectinib, brigatinib, or ceritinib from working<br>• Switch to alectinib, brigatinib, ensartinib, ceritinib, or lorlatinib if on crizotinib |
| Start treatment for cell type as listed in Chapter 5 |

# *ROS1* rearrangement

A cell surface receptor called ROS1 can be overactive, causing lung cells to quickly grow. The overactivity is caused by parts of two genes switching places called a gene rearrangement.

## Targeted therapy

NCCN experts recommend targeted therapy to treat NSCLC with a *ROS1* rearrangement. If you are taking a different type of treatment, you may stop your current treatment early and start targeted therapy.

Kinase inhibitors that target ROS1 are used for treatment. The preferred therapies are:

- Crizotinib (Xalkori)
- Entrectinib (Rozlytrek)
- Repotrectinib (Augtyro)

Entrectinib or repotrectinib may work better for treating and preventing the spread of lung cancer in the brain.

## Options when NSCLC grows again

In time, the cancer will grow despite ongoing targeted therapy. If the cancer didn't spread to many more places, your team 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 started in place of your current treatment. Repotrectinib or lorlatinib (Lorbrena) may be options. For cancer spread to the brain that's causing symptoms, lorlatinib is the preferred therapy while entrectinib after taking crizotinib is sometimes useful. Repotrectinib is an option for resistant mutations, such as *ROS1* G2032R.

If targeted therapy is not likely to help, your team may recommend treatments listed in *Chapter 6: Treatment by cell type.*

# *BRAF* V600E mutation

BRAF, a signaling protein, can be overactive, causing tumor cells to grow quickly. A *BRAF* V600E mutation causes its overactivity.

The 2 preferred therapies are combinations of kinase inhibitors:

- Dabrafenib (Tafinlar) with trametinib (Mekinist)
- Encorafenib (Braftovi) with binimetinib (Mektovi).

Dabrafenib and encorafenib stop growth signals from BRAF. MEK is a protein within the same signaling pathway as BRAF. Trametinib and binimetinib stop growth signals from MEK.

If you are not already taking kinase inhibitors, you may stop your current treatment early and start targeted therapy. The other option is to finish your current treatment (including the last phase called maintenance therapy) and then start targeted therapy.

If dabrafenib plus trametinib makes you too sick, you may receive dabrafenib alone or vemurafenib (Zelboraf). Vemurafenib also stops growth signals from BRAF.

Other recommended therapies are those described in *Chapter 6: Treatment by cell type*.

In time, the cancer will worsen. After targeted therapy, treatment based on cell type may be received. If not received before, dabrafenib with trametinib or encorafenib with binimetinib may be started.

## *NTRK* gene fusion

Lung cells have a family of 3 cell surface receptors called TRK. *NTRK* genes contain instructions for making TRK. Some lung cancers have too much TRK, which causes fast cell growth. Excess TRK occurs when *NTRK* joins (fuses) with another gene.

Preferred therapies are TRK inhibitors:

- Larotrectinib (Vitrakvi)
- Entrectinib (Rozlytrek)
- Repotrectinib (Augtyro)

If you are not taking a TRK inhibitor, you may stop your current treatment early and start targeted therapy.

For some people, it is useful to start with treatment described in *Chapter 6: Treatment by cell type.*

In time, the cancer will worsen. After targeted therapy, your next treatment may be based on cell type. If not used before, a TRK inhibitor may be started.

## *MET* exon 14 skipping

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

Preferred therapies are MET inhibitors:

- Capmatinib (Tabrecta)
- Tepotinib (Tepmetko)

Crizotinib (Xalkori) is useful in certain cases. It inhibits MET and other kinases.

If you are not already taking a MET inhibitor, you may stop your current treatment early and start targeted therapy. But some people start and continue with treatment described in *Chapter 6: Treatment by cell type*.

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.

## *RET* rearrangement

A cell surface receptor kinase called RET can be overactive and cause lung cells to multiply. The overactivity is caused by parts of genes switching places. This is called a gene rearrangement.

Preferred therapies are RET inhibitors:

- Selpercatinib (Retevmo)
- Pralsetinib (Gavreto)

If you are not already taking a RET inhibitor, you may stop your current treatment early and start targeted therapy.

In time, the cancer will worsen on targeted therapy. A different RET inhibitor called cabozantinib (Cometriq, Cabometyx) may be started. The other option is to start treatment described in *Chapter 6: Treatment by cell type*.

## *ERBB2 (HER2)* mutation and HER2 overexpression

Lung cancer cells have a receptor on their surface called HER2. Certain mutations in the *HER2* gene (also called the *ERBB2* gene) cause the receptor to be overactive. HER2 overactivity makes the cancer cells grow quickly.

Lung cancers with *ERBB2* mutations are first treated by cancer cell type. Treatment options are listed in *Chapter 6: Treatment by cell type*.

If the cancer grows, you may receive an antibody-drug conjugate:

- The preferred therapy is fam-trastuzumab deruxtecan-nxki (Enhertu)
- The other recommended therapy is ado-trastuzumab emtansine (Kadcyla)

Treatment options after a conjugate are again based on cancer cell type.

### HER2 overexpression

Lung cancer cells may be tested for high levels, or overexpression, of HER2 proteins. Immunohistochemistry (IHC) is the name of the lab test for HER2 overexpression. If the IHC score is 3+, the cancer is called HER2-positive IHC3+. Fam-trastuzumab deruxtecan-nxki (Enhertu) is recommended for treatment.

## *NRG1* gene fusion

*NRG1* gene fusion is a rare driver mutation of NSCLC but is more common in lung adenocarcinomas. The abnormal *NRG1* gene fusion makes a protein that increases cell growth signals from the HER3-HER2 pathway.

Lung cancers with *NRG1* gene fusions are first treated by cancer cell type. Treatment options are listed in *Chapter 6: Treatment by cell type*.

If the cancer grows, you may receive a HER2-HER3 antibody therapy called zenocutuzumab-zbco (Bizengri). Treatment options after zenocutuzumab-zbco are again based on cancer cell type.

## What's next?

It's common to have many concerns about cancer. Your care team will support you. More sources of support are listed in *Chapter 7: Other resources*.

## Key points

- A driver mutation causes normal cells to become cancer cells.
- Targeted therapy is a newer option for treating lung cancers with driver mutations.
- Targeted therapy is specific to the type of driver mutation. 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 based on the cell type affected by the cancer.

## Questions to ask

- How did you decide what treatment is best for me?
- What are the common and serious side effects of my treatment?
- Is there a clinical trial that's a good fit for me?

# 5
# Treatment based on PD-L1

**Some lung cancers avoid death by stopping cancer-fighting T cells. Immunotherapy restores the killing ability of these T cells. Read this chapter to learn about this survival skill of cancer cells and how it can be stopped.**

# What is PD-L1?

In short, PD-L1 is a protein on the surface of lung cancer cells. It stops the body from killing cancer cells. Let's look in more detail at how PD-L1 works to understand treatment for non-small cell lung cancer (NSCLC).

### T cells kill cancer cells

The immune system is the body's natural defense against disease, including cancer. 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.

### PD-1 limits T cell activity

The immune system has brakes that control an immune response. These brakes are called immune checkpoints. They ensure that the immune response doesn't damage the body. PD-1 is a brake pedal on T cells.

### PD-L1 turns on PD-1

In some people with NSCLC, the immune brakes are overused. The PD-1 brake is activated when PD-L1 on cancer cells attaches to it.

### Cancer treatment stops PD-L1

Immune checkpoint inhibitors are a treatment that keeps the immune brakes turned off. In other words, they enable T cells to kill cancer cells.

# PD-L1 expression levels

NCCN experts recommend treatment options based on PD-L1 expression level:

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

High and low PD-L1 are above-normal levels (also called overexpression). The rest of this chapter will explain the treatment recommendations for NSCLC with high and low PD-L1.

Treatment of lung cancer with a driver mutation and no PD-L1 is discussed in *Chapter 4: Treatment of driver mutations*.

If there are no driver mutations and no PD-L1, read *Chapter 6: Treatment by cell type.*

# Planning treatment

The type of treatment used for NSCLC with PD-L1 is called immune checkpoint inhibitors. Immune checkpoint inhibitors keep the immune brakes turned off. In other words, they enable T cells to kill cancer cells.

Not everyone should have immune checkpoint inhibitors. Your team will consider the following factors.

**Immune checkpoint inhibitors may not be safe if:**

- You have an autoimmune disease, are taking medications that suppress your immune system, or have had an organ transplant. Safer treatments are discussed in *Chapter 6: Treatment by cell type.*
- Your performance status is either 3 or 4 on the Eastern Cooperative Oncology Group scoring system. These high scores reflect poorer health. Your team may recommend receiving supportive care alone. Learn more by reading *Chapter 3: Improving life with supportive care*. If your performance score is 3, an immune checkpoint inhibitor called atezolizumab (Tecentriq) is an option.

**Immune checkpoint inhibitors have less benefit for lung cancers with:**

- An *EGFR* exon 19 deletion or L858R mutation
- An *ALK*, *RET*, or *ROS1* rearrangement

Treatment of these cancers is discussed in *Chapter 4: Treatment of driver mutations.*


## Side effects of immune checkpoint inhibitors

Immune checkpoint inhibitors sometimes cause immune cells to attack your healthy cells. Immune-related side effects can occur during or after treatment.

Read about immune-related side effects at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app

Management of side effects from other treatments is discussed in *Chapter 3: Improving life with supportive care*.

**Keep seeking out information and read information again as the diagnosis and treatment process continues."**

# Types of immune checkpoint inhibitors

There are 3 types of checkpoint inhibitors used to treat NSCLC.

Two types stop PD-L1 and are named after the protein they attach to:

- PD-1 inhibitors attach to PD-1 on T cells, which blocks PD-L1 from activating the PD-1 brake. PD-1 inhibitors are pembrolizumab (Keytruda), nivolumab (Opdivo), and cemiplimab-rwlc (Libtayo).
- PD-L1 inhibitors attach to PD-L1 on cancer cells so PD-L1 can't activate the PD-1 brake. PD-L1 inhibitors are atezolizumab (Tecentriq) and durvalumab (Imfinzi).

NSCLC also causes a second type of immune brake, called CTLA-4, to be overused. This brake is overused because lung cancer causes high CTLA-4 levels.

CTLA-4 on T cells is activated when attached to B7 on immune cells called dendritic cells.

- CTLA-4 inhibitors attach to CTLA-4 so that CTLA-4 isn't activated by B7. CTLA-4 inhibitors are ipilimumab (Yervoy) and tremelimumab-actl (Imjudo).

Most checkpoint inhibitors are slowly injected into a vein. This slow injection is called an infusion.

Atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) is given by an injection into the fat under the skin. It may be given instead of atezolizumab infused into a vein.

# First-line therapy

The first treatment that you will receive is called first-line therapy. First-line therapy is safe if your performance status is 0, 1, or 2.

## NCCN levels of preference

This section explains what NCCN recommends for first-line therapy of NSCLC with PD-L1. These recommendations are based on science and safety. When helpful, NCCN experts assign a level of preference to their recommendations:

- **Preferred therapies** have the most evidence they work better and may be safer than other therapies.
- **Other recommended therapies** may not work quite as well as preferred therapies, but they can still help treat cancer.
- **Therapies used in certain cases** work best for people with specific cancer features or health circumstances.

## NCCN recommended regimens

A regimen consists of one or more drugs that are taken at a specific dose, schedule, and length of time.

The regimen you will receive will be based on PD-L1 level.

The type of NSCLC is also very important since some drug treatments help specific lung cancers.

First-line therapy for metastatic lung adenocarcinoma, large cell carcinoma, and

rare cell types are listed in **Guide 7 and Guide 8**.

NCCN recommendations for metastatic squamous cell carcinoma are listed in **Guide 9 and Guide 10**.

| Guide 7<br>High PD-L1 treatment: Adenocarcinoma, large cell carcinoma, rare cell types | |
|---|---|
| **Preferred therapies** | • Pembrolizumab<br>• Carboplatin or cisplatin, pemetrexed, pembrolizumab<br>• Atezolizumab<br>• Cemiplimab-rwlc<br>• Cemiplimab-rwlc, pemetrexed, carboplatin or cisplatin |
| **Other recommended therapies** | • Carboplatin, paclitaxel, bevacizumab, atezolizumab<br>• Carboplatin, albumin-bound paclitaxel, atezolizumab<br>• Nivolumab, ipilimumab, pemetrexed, carboplatin or cisplatin<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, pemetrexed |
| **Therapy used in certain cases** | • Nivolumab, ipilimumab |

| Guide 8<br>Low PD-L1 treatment: Adenocarcinoma, large cell carcinoma, rare cell types | |
|---|---|
| **Preferred therapies** | • Carboplatin or cisplatin, pemetrexed, pembrolizumab<br>• Cemiplimab-rwlc, pemetrexed, carboplatin or cisplatin |
| **Other recommended therapies** | • Carboplatin, paclitaxel, bevacizumab, atezolizumab<br>• Carboplatin, albumin-bound paclitaxel, atezolizumab<br>• Nivolumab, ipilimumab, pemetrexed, carboplatin or cisplatin<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, pemetrexed<br>• Nivolumab, ipilimumab |
| **Therapy used in certain cases** | • Pembrolizumab |

## Single immunotherapy

Some lung cancers with PD-L1 are treated with only 1 drug—an immune checkpoint inhibitor.

Pembrolizumab, atezolizumab, and cemiplimab-rwlc are preferred options for all types of NSCLC with high PD-L1. Pembrolizumab by itself is useful for some people with low PD-L1.

## Chemoimmunotherapy

An option for many people is a checkpoint inhibitor paired with platinum-doublet

**Guide 9**
**High PD-L1 treatment: Squamous cell carcinoma**

| | |
|---|---|
| **Preferred therapies** | • Pembrolizumab<br>• Carboplatin, paclitaxel or albumin-bound paclitaxel, pembrolizumab<br>• Atezolizumab<br>• Cemiplimab-rwlc<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin |
| **Other recommended therapies** | • Nivolumab, ipilimumab, paclitaxel, carboplatin<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, gemcitabine |
| **Therapy used in certain cases** | • Nivolumab, ipilimumab |

**Guide 10**
**Low PD-L1 treatment: Squamous cell carcinoma**

| | |
|---|---|
| **Preferred therapies** | • Carboplatin, paclitaxel or albumin-bound paclitaxel, pembrolizumab<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin |
| **Other recommended therapies** | • Nivolumab, ipilimumab, paclitaxel, carboplatin<br>• Nivolumab, ipilimumab<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, gemcitabine |
| **Therapy used in certain cases** | • Pembrolizumab |

chemotherapy. This combined treatment is called chemoimmunotherapy.

Chemotherapy kills fast-growing cells including cancer cells. Platinum-doublet chemotherapy consists of two types of chemotherapy.

- The platinum-based chemotherapy is either cisplatin or carboplatin.
- The second chemotherapy is one of the following: pemetrexed (Alimta, Pemfexy), paclitaxel, paclitaxel with human albumin (Abraxane), or gemcitabine (Gemzar, Infugem).

Platinum-doublet chemotherapy can cause serious side effects, so you must be healthy enough to get this treatment.

### Chemoimmunotherapy and bevacizumab

Bevacizumab (Avastin) is used in one of the atezolizumab regimens for lung adenocarcinoma, large cell carcinoma, and rare cell types with high PD-L1.

Bevacizumab is a targeted therapy called a VEGF antibody. It stops the growth of blood vessels on tumors. Without blood, cancer cells die.

An FDA-approved biosimilar can be taken instead of bevacizumab. A biosimilar is almost an identical drug made by another company.

### Double immunotherapy

If you can't have platinum-doublet chemotherapy, nivolumab with ipilimumab may be an option.

## Monitoring results

First-line therapies are given in cycles of treatment days, followed by rest days. One cycle typically lasts for several weeks.

NCCN experts recommend checking treatment results after 2 cycles. A computed tomography (CT) scan will be done to assess results. Contrast may be used. If the cancer has not worsened, NCCN experts recommend getting more CT scans every 2 to 4 cycles.

Often, people get infusions for up to 2 years or until the treatment stops working.

**"It is important to understand what you are going through. If your doctor says something you do not understand, don't just nod like you do. Let your doctor know. You can say, 'I don't fully understand what you just said. Can you please explain it in simpler terms?'"**

## Maintenance therapy

If first-line therapy controls cancer growth, you may shift to maintenance therapy, which includes 1 or 2 drugs from your first-line therapy. This is called continuation maintenance.

The goal of maintenance therapy is to stop cancer growth for as long as possible. Options for maintenance therapy are listed in **Guide 11**.

NCCN experts recommend checking treatment results with a CT scan every 6 to 12 weeks during maintenance therapy.

## What's next?

Within a few years on first-line therapy, lung cancer starts to grow again in most people. The next treatment is explained in *Chapter 6: Treatment by cell type.*

- If you didn't receive chemoimmunotherapy, read the section in Chapter 6 called *First-line therapy.*
- If you had chemoimmunotherapy, read the section in Chapter 6 called *Second-line therapy.*

**Guide 11**
**Maintenance therapy for metastatic NSCLC with PD-L1**

| | |
|---|---|
| **Adenocarcinoma, large cell carcinoma, and rare cell types** | The maintenance regimen is based on your first-line therapy:<br>• Pembrolizumab<br>• Pembrolizumab, pemetrexed<br>• Atezolizumab, bevacizumab<br>• Atezolizumab<br>• Nivolumab, ipilimumab<br>• Cemiplimab-rwlc<br>• Cemiplimab-rwlc, pemetrexed<br>• Durvalumab<br>• Durvalumab, pemetrexed |
| **Squamous cell carcinoma** | The maintenance regimen is based on your first-line therapy:<br>• Pembrolizumab<br>• Atezolizumab for NSCLC with high PD-L1<br>• Nivolumab, ipilimumab<br>• Cemiplimab-rwlc<br>• Durvalumab |

## Key points

- Some lung cancers have above-normal levels of PD-L1, which stops immune cells from destroying cancer cells.
- Immune checkpoint inhibitors allow immune cells to attack cancer cells, but not everyone should take them.
- There are many checkpoint inhibitor regimens. The one chosen for your treatment will be based on the level of PD-L1 and the type of lung cancer.
- If cancer growth slows down, you may stay on some drug treatments to increase the time until the cancer grows again. This is called maintenance therapy.

## Questions to ask

- How did you decide what treatment is best for me?
- What are the common and serious side effects of my treatment?
- What is the schedule, or cycles, of my treatment?
- When will the results of my treatment be assessed?
- Is there a clinical trial that's a good fit for me?

**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**

# 6
# Treatment by cell type

**Lung cancer differs among people by the type of lung cell affected. Your treatment will be specific to the type of lung cancer you have. Read this chapter to learn which treatment is best for you.**

## What are cell types?

A cell type is a group of cells named after the features or function of the cells.

Non-small cell lung cancer (NSCLC) is a group of cancers. Each cancer in the group affects a different cell type:

- **Adenocarcinoma** is a cancer of mucus-making cells.
- **Large cell carcinoma** is a cancer of cells that are large compared to other cells.
- **Squamous cell carcinoma** is a cancer of thin, flat cells that protect body tissue.

Adenocarcinoma, large cell carcinoma, and squamous cell carcinomas are the most common cell types of NSCLC. There are also rare cell types that experts sometimes refer to as “not otherwise specified” or for short, “NOS.”

### Which lung cancers are treated by cell type?

NSCLC that doesn't have a known biomarker is treated based on the cell type and other factors explained in this chapter.

NSCLC with driver mutations or PD-L1 is also treated by cell type as explained in Chapter 4 and Chapter 5, but the order of treatments or the drugs in the regimens may differ.

## Planning safe treatment

In addition to cell type, another deciding factor of treatment 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 Performance Status is a common scoring system. It consists of five scores ranging from 0 to 4. The lower the score, the better your ability to care for yourself.

**A performance status of 0, 1, or 2** means that you are fairly healthy. NCCN experts advise treating the cancer with systemic therapy. The next sections explain what systemic therapy is and what the options for systemic therapy are.

**A performance score of 3 or 4** suggests that systemic therapy will be harmful to you. NCCN experts advise receiving supportive

care alone. Learn more by reading *Chapter 3: Improving life with supportive care.*

However, if your performance score is 3, an immune checkpoint inhibitor called atezolizumab (Tecentriq) may be an option.

# Types of systemic therapy

Systemic therapy consists of cancer drugs that can treat cancer wherever it is in the body. It can treat cancer in many places as well as hard-to-reach places.

## Chemotherapy

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

Chemotherapy that contains platinum is commonly used for NSCLC. The 2 platinum-based drugs used for NSCLC are cisplatin and carboplatin. They kill cancer cells by damaging their DNA.

Other types of chemotherapy may be used with platinum-based drugs or on their own to treat NSCLC.

Chemotherapy for NSCLC 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.

## Immune checkpoint inhibitors

Immune checkpoint inhibitors restore immune cells' ability to kill cancer cells. They treat lung cancer with PD-L1 as explained in

### Systemic therapy

**Systemic therapy treats widespread lung cancer with drugs that kill cancer cells.**

**Treatment is based on cell type and often combines chemotherapy with newer treatments.**

**Treatment is given by injection into a vein. An infusion is a slow drip controlled by a pump that may take hours.**

Chapter 5. But they may also extend life when lung cancer does not have PD-L1.

There are 3 types of checkpoint inhibitors each named after the protein it attaches to:

- **PD-1 inhibitors** – pembrolizumab (Keytruda), nivolumab (Opdivo), and cemiplimab-rwlc (Libtayo)
- **PD-L1 inhibitors** – atezolizumab (Tecentriq) and durvalumab (Imfinzi)
- **CTLA-4 inhibitors** – ipilimumab (Yervoy) and tremelimumab-actl (Imjudo)

Most checkpoint inhibitors are given by infusion. Atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) is given by an injection into the fat under the skin. It may be given instead of atezolizumab infused into a vein.

## Targeted therapy

Targeted therapy works by stopping the specific ways cancer cells grow. It's not as commonly used for NSCLC without driver mutations compared to other therapies.

### VEGF antibodies

Bevacizumab (Avastin) and ramucirumab (Cyramza) are a type of targeted therapy called VEGF antibodies. They stop the growth of blood vessels on tumors. Without blood, cancer cells die.

VEGF antibodies are given by infusion.

An FDA-approved biosimilar can be taken instead of bevacizumab. A biosimilar is almost an identical drug made by another company.

### Antibody-drug conjugate

Fam-trastuzumab deruxtecan-nxki (Enhertu) is an antibody-drug conjugate. It combines two drugs in one medicine. One drug finds and binds to certain cancer cells, and then the other drug attacks the cancer. Antibody-drug conjugates are given by infusion.

### Side effects of systemic therapy

All treatments of cancer can cause unwanted health issues called side effects.

Chemotherapy causes side effects because it kills fast-growing normal cells as well as cancer cells.

Immune checkpoint inhibitors sometimes cause immune cells to attack your healthy cells.

VEGF antibodies cause side effects because they stop new blood vessels from forming.

Management of side effects is discussed in *Chapter 3: Improving life with supportive care.*

# NCCN levels of preference

NCCN experts recommend options for systemic therapy based on science and safety. When helpful, they assign a level of preference to their recommendations:

- **Preferred therapies** have the most evidence they work better and may be safer than other therapies.
- **Other recommended therapies** may not work quite as well as preferred therapies, but they can still help treat cancer.
- **Therapies used in certain cases** work best for people with specific cancer features or health circumstances.

These levels of preference are noted in the next sections.

# First-line therapy

The first treatment that you will receive is called first-line therapy.

Your team will prescribe a regimen of systemic therapy that's best for you. A regimen consists of one or more drugs that are taken at a specific dose, schedule, and length of time.

## Preferred and other recommended therapies for first-line therapy

Preferred and other recommended therapies include immune checkpoint inhibitors.

Immune checkpoint inhibitors are not for everyone. You should not take these therapies if you have an autoimmune disease, are taking medications that suppress your immune system, or have had an organ transplant.

Immune checkpoint inhibitors are not recommended for first-line therapy of cancers with *EGFR* exon 19 deletion, L858R mutation, or an *ALK*, *RET*, or *ROS1* rearrangement.

### Chemoimmunotherapy

Chemoimmunotherapy combines immune checkpoint inhibitors with platinum-doublet chemotherapy.

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

Some regimens for lung adenocarcinoma, large cell carcinoma, and rare cell types include bevacizumab.

### Double immunotherapy

If you can't have platinum-doublet chemotherapy, you may receive only immune checkpoint inhibitors. Nnivolumab with ipilimumab may be an option.

## Therapies used in certain cases for first-line therapy

When immune checkpoint inhibitors are not an option, chemotherapy is used for treatment.

Platinum-doublet chemotherapy is most often used. Bevacizumab is a part of some regimens.

Additional options include gemcitabine with either docetaxel or vinorelbine.

And there are several options for single-agent chemotherapy, including:

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

A complete list of first-line therapies for metastatic lung adenocarcinoma, large cell carcinoma, and rare cell types is in **Guide 12**, and for metastatic squamous cell carcinoma, see **Guide 13**.

**Guide 12**
**First-line therapy of metastatic lung adenocarcinoma, large cell carcinoma, and rare cell types**

| | |
|---|---|
| **Preferred therapies** | • Pembrolizumab, carboplatin or cisplatin, pemetrexed<br>• Cemiplimab-rwlc, pemetrexed, carboplatin or cisplatin |
| **Other recommended therapies** | • Atezolizumab, carboplatin, paclitaxel, bevacizumab<br>• Atezolizumab, carboplatin, albumin-bound paclitaxel<br>• Nivolumab, ipilimumab<br>• Nivolumab, ipilimumab, pemetrexed, carboplatin or cisplatin<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, pemetrexed |
| **Therapies used in certain cases** | • Bevacizumab, carboplatin, paclitaxel<br>• Bevacizumab, carboplatin or cisplatin, pemetrexed<br>• Carboplatin and either albumin-bound paclitaxel, docetaxel, etoposide, gemcitabine, paclitaxel, or pemetrexed<br>• Cisplatin and either docetaxel, etoposide, gemcitabine, paclitaxel, or pemetrexed<br>• Gemcitabine and either docetaxel or vinorelbine<br>• One of these: albumin-bound paclitaxel, docetaxel, gemcitabine, paclitaxel, or pemetrexed |

# Monitoring results

Systemic therapy is given in cycles of treatment days, followed by rest days. One cycle typically lasts for 3 to 4 weeks.

In general, first-line 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 team will assess the results. The extent of the cancer can be seen on computed tomography (CT) scans. Contrast may be used. The CT scan will be repeated after another 2 to 4 cycles.

**"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."**

**Guide 13**
**First-line therapy of metastatic squamous cell carcinoma of the lung**

| | |
|---|---|
| **Preferred therapies** | • Pembrolizumab, carboplatin, paclitaxel or albumin-bound paclitaxel<br>• Cemiplimab-rwlc, paclitaxel, carboplatin or cisplatin |
| **Other recommended therapies** | • Nivolumab, ipilimumab<br>• Nivolumab, ipilimumab, paclitaxel, carboplatin<br>• Tremelimumab-actl, durvalumab, carboplatin, albumin-bound paclitaxel<br>• Tremelimumab-actl, durvalumab, carboplatin or cisplatin, gemcitabine |
| **Therapies used in certain cases** | • Carboplatin and either albumin-bound paclitaxel, docetaxel, gemcitabine, paclitaxel, or etoposide<br>• Cisplatin and either docetaxel, etoposide, gemcitabine, or paclitaxel<br>• Gemcitabine and either docetaxel or vinorelbine<br>• One of these: albumin-bound paclitaxel, docetaxel, gemcitabine, paclitaxel |

# Maintenance therapy

If first-line therapy controls cancer growth, you may receive maintenance therapy after the regimen is finished. The goal of maintenance therapy is stop the growth of cancer for as long as possible.

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 14.**

You may stay on maintenance therapy for 2 years if your first-line therapy includes immune checkpoint inhibitors.

**Guide 14**
**Maintenance therapy for metastatic NSCLC by cell type**

| | |
|---|---|
| **Adenocarcinoma, large cell carcinoma, and rare cell types** | Continuation maintenance<br>• Bevacizumab<br>• Pemetrexed<br>• Bevacizumab, pemetrexed<br>• Pembrolizumab, pemetrexed<br>• Atezolizumab, bevacizumab<br>• Nivolumab, ipilimumab<br>• Atezolizumab<br>• Gemcitabine<br>• Cemiplimab-rwlc with or without pemetrexed<br>• Durvalumab with or without pemetrexed<br>Switch maintenance<br>• Pemetrexed |
| **Squamous cell lung cancer** | Continuation maintenance<br>• Pembrolizumab<br>• Nivolumab, ipilimumab<br>• Gemcitabine<br>• Cemiplimab-rwlc<br>• Durvalumab |

# Second-line therapy

In time, lung cancer often starts to grow again after first-line therapy. Options for second-line therapy are based on your performance status:

- **Performance status 0, 1, or 2** – NCCN experts recommend systemic therapy. Options are listed in **Guide 15.**
- **Performance status 3 or 4** – Supportive care is recommended. Learn more by reading *Chapter 3: Improving life with supportive care.*

## Recommended therapies

Immune checkpoint inhibitors are preferred if you've not received one before. If the cancer grew while you were taking a checkpoint inhibitor, switching to another checkpoint inhibitor is not advised.

Other recommended therapies include ramucirumab with docetaxel and single-agent chemotherapy. For cancers with HER2 overexpression, fam-trastuzumab deruxtecan-nxki is an option.

Another way to obtain treatment is through a clinical trial. Clinical trials are described in the next section.

## Monitoring and maintenance

Your team will monitor your treatment results. NCCN experts recommend a CT scan every 6 to 12 weeks. Contrast may be used.

If an immune checkpoint inhibitor is part of second-line therapy, you can stay on maintenance therapy until the cancer grows again.

**Guide 15**
**Second-line therapy for metastatic NSCLC**

| | |
|---|---|
| **Preferred therapies when you haven't had an immune checkpoint inhibitor before** | • Nivolumab<br>• Pembrolizumab<br>• Atezolizumab |
| **Other recommended therapies whether you've had an immune checkpoint inhibitor or not** | • Docetaxel<br>• Gemcitabine<br>• Ramucirumab, docetaxel<br>• Albumin-bound paclitaxel<br>• Pemetrexed for lung adenocarcinoma, large cell carcinoma, and rare cell types<br>• Fam-trastuzumab deruxtecan-nxki for HER2 overexpression |

# Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a lab, 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 and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- Phase 3 trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

## Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They 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 research team. This group of experts will review the study with you in detail, including its purpose

### Finding a clinical trial

#### In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
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

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 people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

### 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. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

## What's next?

It's common to have many concerns about cancer. Your care team will support you. More sources of support are listed in *Chapter 7: Other resources.*

## Key points

- Treatment of lung cancer without treatable biomarkers is based on cell type.
- Whole-body treatment, called systemic therapy, is used to treat people who are fairly healthy. If systemic therapy may be harmful, supportive care is generally recommended.
- If safe and effective, chemoimmunotherapy or immunotherapy is recommended for the first treatment of lung cancer based on cell type. Another option is a chemotherapy regimen.
- You may receive between 4 and 6 cycles of treatment. Your team will monitor the results of your 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 an immune checkpoint inhibitor or a chemotherapy regimen. Cancers with HER2 overexpression may be treated with fam-trastuzumab deruxtecan-nxki.
- New ways of fighting cancer are studied among people in clinical trials. A clinical trial may be an option in addition to standard treatment.

# Questions to ask

- How did you decide what treatment is best for me?
- What are the common and serious side effects of my treatment?
- What is the schedule, or cycles, of my treatment?
- When will the results of my treatment be assessed?
- Is there a clinical trial that's a good fit for me?

**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**

# 7
# Other resources

**Want to learn more? Here's how you can get additional help.**

## What else to know

This book can help you improve your cancer care. It plainly explains expert recommendations and suggests questions to ask your care team. But it's not the only resource that you have.

You're welcome to receive as much information and help as you need. Many people are interested in learning more about:

- Support groups in the community and online
- Second opinions
- Making an advance care plan
- Clinical trials
- Getting financial help

## What else to do

Your health care center can help you with next steps. They often have on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself. Look through the list and visit the provided websites to learn more about these organizations.

## Where to get help

**American Lung Association**
lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer

**Cancer*Care***
Cancercare.org

**Cancer Hope Network**
cancerhopenetwork.org

**Cancer Survivor Care**
Cancersurvivorcare.org

**Caring Ambassadors Program, Inc.**
LungCancerCAP.org

**Free Me from Lung Cancer**
freemefromlungcancer.org

**Go2 Foundation for Lung Cancer**
go2foundation.org

**Imerman Angels**
Imermanangels.org

**LiveLung (Dusty Joy Foundation)**
dustyjoy.org

**LUNGevity**
lungevity.org

**Lung Cancer Action Network (LungCAN)**
lungcan.org

**Lung Cancer Research Foundation**
lungcancerresearchfoundation.org

**National Coalition for Cancer Survivorship**
canceradvocacy.org

**Triage Cancer**
triagecancer.org

# Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What assistance is available for transportation, childcare, and home care?
- Who can tell me what my options for health insurance are and assist me with applying for insurance coverage?
- How much will I have to pay for my treatment and what help is available for these costs?
- How can I connect with others and build a support system?

# Words to know

**adenocarcinoma**
A cancer of cells that line organs and make fluids or hormones.

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

**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.

**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.

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

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

**chemotherapy**
Treatment with cancer drugs that kill fast-growing cells.

**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.

**ECOG**
Eastern Cooperative Oncology Group

**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.

**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

**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.

**prognosis**
The likely course and outcome of a disease.

**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.

**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).

**transthoracic needle aspiration (TTNA)**
A procedure that removes tissue samples with a thin needle guided through the ribs.

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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 3.2025. 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 • pennmedicine.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*
*877.442.3324 • 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 • healthcare.utah.edu/huntsmancancerinstitute*

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

Johns Hopkins Kimmel Cancer Center
*Baltimore, Maryland*
*410.955.8964*
*www.hopkinskimmelcancercenter.org*

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 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 • uclahealth.org/cancer*

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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