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Treating Non-Small Cell Lung Cancer

If you've been diagnosed with non-small cell lung cancer (NSCLC), your cancer care team will discuss your treatment options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

How is non-small cell lung cancer treated?

Treatments for NSCLC can include:

- [Surgery for Non-Small Cell Lung Cancer](#)
- [Radiofrequency Ablation \(RFA\) for Non-Small Cell Lung Cancer](#)
- [Radiation Therapy for Non-Small Cell Lung Cancer](#)
- [Chemotherapy for Non-Small Cell Lung Cancer](#)
- [Targeted Drug Therapy for Non-Small Cell Lung Cancer](#)
- [Immunotherapy for Non-Small Cell Lung Cancer](#)
- [Palliative Procedures for Non-Small Cell Lung Cancer](#)

Common treatment approaches

The treatment options for non-small cell lung cancer (NSCLC) are based mainly on the stage (extent) of the cancer, but other factors, such as a person's overall health and lung function, as well as certain traits of the cancer itself, are also important. In many cases, more than one of type of treatment is used.

- [Treatment Choices for Non-Small Cell Lung Cancer, by Stage](#)

Who treats non-small cell lung cancer?

You may have different types of doctors on your treatment team, depending on the

stage of your cancer and your treatment options. These doctors could include:

- A **thoracic surgeon**: a doctor who treats diseases of the lungs and chest with surgery
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy
- A **medical oncologist**: a doctor who treats cancer with medicines such as chemotherapy, targeted therapy, and immunotherapy
- A **pulmonologist**: a doctor who specializes in medical treatment of diseases of the lungs

- [Clinical Trials](#)

Choosing to stop treatment or choosing no treatment at all

Surgery for Non-Small Cell Lung Cancer

Tests before lung surgery

If your doctor thinks the cancer can be treated with surgery, you might need certain tests:

- Pulmonary function tests (PFTs) to see if you would still have enough healthy lung tissue left after surgery
- An EKG (recording of your heart's electrical activity) and an echocardiogram (ultrasound of your heart) to check the function of your heart
- Lab work to check other organs to be sure you're healthy enough for surgery

Your doctor will also want to check if the cancer has already spread to the lymph nodes around the lungs. This is often done before surgery with **mediastinoscopy** or another technique.

To learn more about these tests, see [Tests for Lung Cancer](#)¹.

Types of lung surgery

Surgery for lung cancer usually involves removing all or part of a lung. This is called **lung resection**. There are different types of lung resection:

- **Pneumonectomy:** This surgery removes an entire lung. This might be needed if the tumor is close to the center of the chest.
- **Lobectomy:** The lungs are made up of 5 lobes (3 on the right lung and 2 on the left lung). In this surgery, the entire lobe containing the tumor(s) is removed. If it can be done, this is often the preferred type of operation for NSCLC.
- **Segmentectomy or wedge resection:** In these surgeries, only part of a lobe is removed. This approach might be used if a person doesn't have enough normal lung function to withstand removing the whole lobe.
- **Sleeve resection:** This operation may be used to treat some cancers in large airways in the lungs. If you think of the large airway with a tumor as similar to the sleeve of a shirt with a stain a few inches above the wrist, the sleeve resection would be like cutting across the sleeve (airway) above and below the stain (tumor) and then sewing the cuff back onto the shortened sleeve. A surgeon may be able to do this operation instead of a pneumonectomy to preserve more lung function.

The type of operation you have depends on the size and location of the tumor and on how well your lungs are functioning. Doctors often prefer to do a more extensive operation (for example, a lobectomy instead of a segmentectomy) if a person's lungs are healthy enough, as it may provide a better chance to cure the cancer.

For the surgeon, the robotic system may provide more maneuverability and more precision when moving the instruments than standard VATS. Still, the most important factor in the success of either type of thoracoscopic surgery is the surgeon's experience and skill.

Intraoperative imaging

Along with the results of [imaging tests](#)² (such as CT scans) done before surgery, surgeons also rely on what they can see and feel during the operation to help determine which parts of the lung need to be removed. However, some lung tumors might not be easily seen or felt, so in some situations it's possible that a tumor (or parts of tumor) might be missed.

Your surgeon might use a special **intraoperative imaging** system during the surgery to help find tumors that aren't easily seen or felt. For this approach, a fluorescent drug called **pafolacianine (Cytalux)** is injected into your blood within 24 hours before your surgery. The drug travels through your body and attaches to a specific protein found on lung cancer cells. Once in the operating room, the imaging system gives off near-infrared light that causes the drug to light up, which can help the surgeon see which areas of the lung need to be removed.

The most common side effects after getting pafolacianine are nausea, vomiting, belly pain, heartburn, chest pain, itching, and flushing. Your doctor will probably ask you to avoid any supplements that have folic acid in them for a few days before the procedure because they might affect how well this drug works.

Possible risks and side effects of lung surgery

Surgery for lung cancer is a major operation and can have serious side effects, which is why it isn't a good idea for everyone. All surgery carries some risks that depend to some degree on the extent of the surgery and the person's overall health.

Possible complications during and soon after surgery can include reactions to anesthesia, excess bleeding, blood clots in the legs or lungs, wound infections, and pneumonia. Rarely, some people may not survive the surgery.

Recovering from lung cancer surgery typically takes weeks to months. If the surgery is done through a thoracotomy (a long incision in the chest), the surgeon must spread ribs to get to the lung, so the area near the incision will hurt for some time after surgery. Your activity might be limited for at least a month or two. People who have VATS instead of thoracotomy tend to have less pain after surgery and to recover more quickly.

If your lungs are in good condition (other than the presence of the cancer), you can usually return to normal activities after some time if a lobe or even an entire lung has been removed. If you also have another lung disease, such as emphysema or chronic bronchitis (which are common among people who have smoked for a long time), you might become short of breath with certain levels of activity after surgery.

After surgery

When you wake up from surgery, you may have a tube (or tubes) coming out of your chest and attached to a special container to allow excess fluid and air to drain out. The tube(s) will be removed once the fluid drainage and air leak slow down enough. Generally, you will need to spend 1 to 7 days in the hospital depending on the type of surgery.

More information about Surgery

For more general information about surgery as a treatment for cancer, see [Cancer Surgery](#)³.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)⁴.

Hyperlinks

1. www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html
2. www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html
3. www.cancer.org/cancer/managing-cancer/treatment-types/surgery.html
4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Radiofrequency Ablation (RFA) for Non-Small Cell Lung Cancer

Many people with non-small-cell lung cancer (NSCLC) are not healthy enough to undergo surgery. Some people might have a lung tumor in a place that makes surgery very difficult. Others might have advanced lung cancer and lung surgery may not be helpful. In these cases, ablative treatments (ablation) may be a treatment option. Ablative treatment is the use of temperature (hot and cold) to kill cancer cells and their surrounding tissue.

- [Types of ablation for lung cancer](#)
- [Ways to do ablation for lung cancer](#)

Types of ablation for lung cancer

- **Radiofrequency ablation (RFA)** uses high-energy radio waves to heat and destroy the tumor cells.
- **Cryoablation** uses liquid nitrogen or argon gas to freeze and destroy the tumor cells.
- **Microwave ablation** uses electromagnetic energy to heat and destroy the tumor cells.

Ways to do ablation for lung cancer

- **Ablation using percutaneous approach:** A thin, needle-like probe is put through the skin and moved in until the tip is in the tumor. Placement of the probe is guided by CT scans. This is usually done as an outpatient procedure, using local anesthesia (numbing medicine) where the probe is inserted. You may be given medicine to help you relax.
- **Ablation using bronchoscopy:** You will be given anesthesia for the bronchoscopy. Ablation will be done through the bronchoscopy tube and your airway, rather than from the outside through the skin. This is still quite a new way to give ablative treatment.

Major complications are uncommon, but they can include the partial collapse of a lung (which often goes away on its own) or bleeding into the lung.

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Radiation Therapy for Non-Small Cell Lung Cancer

cancers when surgery isn't an option due to a person's health or in people who don't want surgery. It might also be considered for tumors that have limited spread to other parts of the body, such as the brain or adrenal gland.

Instead of giving a small dose of radiation each day for several weeks, SBRT uses very focused beams of high-dose radiation given in fewer (usually 1 to 5) treatments. Several beams are aimed at the tumor from different angles. To target the radiation precisely, you are put in a specially designed body frame for each treatment. This reduces the movement of the lung tumor during breathing.

- **Three-dimensional conformal radiation therapy (3D-CRT)** uses special computers to precisely map the tumor's location. Radiation beams are then shaped and aimed at the tumor(s) from several directions, which makes it less likely to damage normal tissues. **Intensity modulated radiation therapy (IMRT)** is a form of 3D therapy. Along with shaping the beams and aiming them at the tumor from several angles, the strength of the beams can be adjusted to limit the dose reaching nearby normal tissues. This technique is used most often if tumors are near important structures such as the spinal cord.

A variation of IMRT is called **volumetric modulated arc therapy (VMAT)**. It uses a machine that delivers radiation quickly as it rotates once around the body. This allows each treatment to be given over just a few minutes.

- **Four-dimensional conformal radiation therapy (4DCT)** shows where the tumor is in relation to other structures during each part of the breathing cycle, as opposed to just giving a "snapshot" of a point in time, like a standard CT does. This technique might also be used to help show if a tumor is attached to or invading important structures in the chest, which could help doctors determine if a patient might be eligible for surgery.
- **Stereotactic radiosurgery (SRS)** isn't really surgery, but a type of stereotactic radiation therapy that is given in only one session. It can sometimes be used instead of or along with surgery for single tumors that have spread to the brain. In one version of this treatment, a machine focuses about 200 beams of radiation on the tumor from different angles over a few minutes to hours. Your head is kept in the same position with a rigid frame. In another version, a linear accelerator (a machine that creates radiation) that is controlled by a computer moves around your head to deliver radiation to the tumor from many different angles. These treatments can be repeated if needed.

For more detailed descriptions of these procedures, see [External Beam Radiation Therapy](#)¹.

Brachytherapy (internal radiation therapy)

In people with NSCLC, [brachytherapy](#)² is sometimes used to shrink tumors in the airway to relieve symptoms.

The doctor places a small source of radioactive material (often in the form of small pellets) directly into the cancer or into the airway next to the cancer. This is usually done through a [bronchoscope](#)³, but it may also be done during surgery. The radiation travels only a short distance from the source, limiting the effects on surrounding healthy tissues. The radiation source is usually removed after a short time. Less often, small radioactive “seeds” are left in place permanently, and the radiation gets weaker over several weeks.

Proton therapy

In people with NSCLC, especially Stage III, proton therapy may be an option. Proton therapy is a type of radiation that uses protons rather than x-rays. A proton is a positively charged particle, which can be targeted specifically to the tumor. Compared to x-rays, proton therapy beams are less likely to damage surrounding organs, such as the heart and esophagus (tube we use to swallow). This form of radiation therapy continues to be studied, and is offered in most specialized lung cancer treatment centers.

Possible side effects of radiation therapy for NSCLC

If you are going to get radiation therapy, it's important to ask your doctor about the possible side effects so you know what to expect. Common side effects depend on where the radiation is aimed and can include:

- Fatigue
- Nausea and vomiting
- Loss of appetite and weight loss
- Skin changes in the area being treated, which can range from mild redness to blistering and peeling
- Hair loss where the radiation enters the body

Often these go away after treatment. When radiation is given with chemotherapy, the side effects may be worse.

Radiation therapy to the chest may damage your lungs and cause a cough, problems breathing, and shortness of breath. These usually improve after treatment is over, although sometimes they may not go away completely.

Your esophagus, which is in the middle of your chest, may be exposed to radiation, which could cause a sore throat and trouble swallowing during treatment. This might make it hard to eat anything other than soft foods or liquids for a while. This also often improves after treatment is finished.

Radiation therapy to large areas of the brain can sometimes cause memory loss, headaches, or trouble thinking. Usually these symptoms are minor compared with those

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Chemotherapy for Non-Small Cell Lung Cancer

Chemotherapy (chemo) is treatment with anti-cancer drugs that may be injected into a vein or taken by mouth.

- [When is chemotherapy used?](#)
- [Chemotherapy drugs used to treat NSCLC](#)
- [How is chemotherapy given?](#)
- [Possible side effects of chemo for NSCLC](#)
- [More information about chemotherapy](#)

When is chemotherapy used?

Chemotherapy travels through the bloodstream and reaches most parts of the body. Not

all people with non-small cell lung cancer (NSCLC) will need chemo, but depending on the cancer's [stage](#)¹ and other factors, chemo may be recommended in different situations:

- **Before surgery (neoadjuvant chemotherapy):** Neoadjuvant chemo may be used (sometimes with [radiation therapy](#)) to try to shrink a tumor to make it easier to remove it with less extensive surgery.
- **After surgery (adjuvant chemotherapy):** Adjuvant chemo may be used (sometimes with radiation therapy) to try to kill any cancer cells that might have been left behind or have spread but can't be seen on [imaging tests](#)².
- **For locally advanced NSCLC:** Sometimes, chemo along with radiation therapy is given as the main treatment for more advanced cancers that have grown into nearby structures if surgery is not an option or for people who aren't healthy enough for surgery.
- **For metastatic (stage IV) NSCLC:** Chemo may be given for lung cancer that has spread to areas outside the lung, such as the bones, liver, or adrenal gland.

Chemo is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemo.

Chemotherapy drugs used to treat NSCLC

The chemo drugs most often used for NSCLC include:

- Cisplatin
- Carboplatin
- Paclitaxel (Taxol)
- Albumin-bound paclitaxel (nab-paclitaxel, Abraxane)
- Docetaxel (Taxotere)
- Gemcitabine (Gemzar)
- Vinorelbine (Navelbine)
- Etoposide (VP-16)
- Pemetrexed (Alimta)

Combinations of 2 chemo drugs are often used to treat early-stage lung cancer. If a combination is used, it often includes cisplatin or carboplatin plus one other drug.

Advanced lung cancer though may be treated with a single chemo drug especially in

people who might not tolerate combination chemotherapy well, such as those in poor overall health or who are elderly.

For some people, a [targeted therapy](#) drug or an [immunotherapy](#) drug may be given alone or with chemotherapy. For more on this, see [Treatment Choices for Non-Small Cell Lung Cancer, by Stage](#).

How is chemotherapy given?

Chemo drugs for lung cancer are typically given into a vein (IV), either as an injection over a few minutes or as an infusion over a longer period of time. This can be done in a doctor's office, chemotherapy clinic, or in a hospital setting.

Often, a slightly larger and sturdier IV is required in the vein system to administer chemo. They are known as [central venous catheters](#)³ (CVCs), central venous access devices (CVADs), or central lines. They are used to put medicines, blood products, nutrients, or fluids right into your blood. They can also be used to take out blood for testing.

Many different kinds of CVCs are available. The most common types are the port and the PICC (peripherally inserted central catheter) line.

A port is a small quarter-sized device that is placed under the skin in your upper chest. A small tube connects the port to a large vein that goes into the heart, called the superior vena cava.

A PICC line is a small tube that is placed in the upper arm; that tube threads through the vein until reaches the superior vena cava.

Chemo is given in cycles. Each cycle includes the period of treatment followed by a rest period to give you time to recover from the effects of the drugs. Cycles are most often 3 or 4 weeks long. The schedule varies depending on the drugs used. For example, with some drugs, the chemo is given only on the first day of the cycle. With others, it is given for a few days in a row, or once a week. Then, at the end of the cycle, the chemo schedule repeats to start the next cycle.

Adjuvant and neoadjuvant chemo is often given for 3 to 4 months, depending on the drugs used. The length of treatment for advanced lung cancer is based on how well it is working and what side effects you have.

For advanced cancers, the initial chemo combination is often given for 4 to 6 cycles.

Some doctors now recommend giving treatment beyond this with a single chemo or targeted drug, in people who have responded well to their initial chemotherapy or have had no worsening of their cancer. Continuing this treatment, known as **maintenance**

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see [Chemotherapy](#)⁴.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)⁵.

Hyperlinks

1. www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/staging-nslc.html
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Targeted Drug Therapy for Non-Small Cell Lung Cancer

As researchers have learned more about the changes in non-small cell lung cancer (NSCLC) cells that help them grow, they have developed drugs to specifically target these changes.

- [When is targeted therapy used?](#)
- [Angiogenesis inhibitors](#)
- [KRAS inhibitors](#)
- [EGFR inhibitors](#)
- [ALK inhibitors](#)
- [ROS1 inhibitors](#)
- [BRAF inhibitors](#)
- [RET inhibitors](#)
- [MET inhibitors](#)
- [HER2-directed drugs](#)
- [TRK inhibitors](#)
- [More information about targeted therapy](#)

When is targeted therapy used?

Targeted drugs work differently from standard [chemotherapy](#) (chemo) drugs. They sometimes work when chemo drugs don't, and they often have different side effects. At this time, targeted drugs are most often used for advanced lung cancers, either along

with chemo or by themselves.

Angiogenesis inhibitors

How they work (mechanism of action): For tumors to grow, they need to form new blood vessels to keep them nourished. This process is called **angiogenesis**.

Angiogenesis inhibitors help stop the formation of new blood vessels. These inhibitors are generally **monoclonal antibodies** (lab-made versions of a specific immune system protein) that target vascular the endothelial growth factor (VEGF), a protein that helps new blood vessels to form, called **VEGF inhibitors**.

Examples of VEGF inhibitors:

- **Bevacizumab (Avastin)** is used in combination with chemotherapy, immunotherapy, or the targeted drug erlotinib for management of advanced or metastatic NSCLC.
- **Ramucirumab (Cyramza)** is used in combination with the targeted drug erlotinib or chemotherapy for management of advanced or metastatic NSCLC.

Side effects of angiogenesis inhibitors:

- **Common side effects:** Nosebleed, headache, high blood pressure, protein in urine, change in taste, dry skin, back pain, dry skin, excessive tearing
- **Rare, but serious side effects:** Severe bleeding, formation of holes (perforations) in the intestine, issues with wound healing, clots in the heart and/or brain, brain damage called reversible posterior leukoencephalopathy syndrome (RPLS), very high blood pressure, kidney damage, allergic reaction to the drug (infusion reaction), thyroid damage, ovarian failure, fetal harm

Because of the risks of bleeding, these drugs often aren't used in people who are coughing up blood or who are taking drugs called blood thinners. The risk of serious bleeding in the lungs is higher in patients with the squamous cell type of NSCLC, which is why current guidelines do not recommend using bevacizumab in people with this type of lung cancer.

KRAS inhibitors

How they work (mechanism of action): In some NSCLCs, the cancer cells have changes in the *KRAS* gene that cause them to make an abnormal form of the KRAS

protein. This abnormal protein helps the cancer cells grow and spread. About 1 in 8 people with NSCLC have a specific type of *KRAS* gene change called a ***KRAS G12C mutation***. KRAS inhibitors attach to the KRAS G12C protein, which helps keep cancer cells from growing.

These drugs are taken as pills, typically once or twice a day.

NSCLCs with this mutation are often resistant to other targeted drugs, such as EGFR inhibitors.

with these mutation(s). **Afatinib (Gilotrif)**, **erlotinib (Tarceva)**, **dacomitinib (Vizimpro)**, **gefitinib (Iressa)**, or erlotinib in combination with a VEGF inhibitor (see above) are also options.

- **EGFR inhibitors that target cells with S768I, L861Q and/or G719X mutations:** **Afatinib (Gilotrif)** or **osimertinib (Tagrisso)** is often the preferred first treatment for advanced NSCLC with these mutation(s). **Erlotinib (Tarceva)**, **dacomitinib (Vizimpro)**, and **gefitinib (Iressa)** are options as well.
- **EGFR inhibitors that target cells with an exon 20 mutation:** **Amivantamab (Rybrevant)** is a monoclonal antibody (a lab-made version of a specific immune system protein) that targets two proteins that help cancer cells grow: EGFR and MET. Because it binds to two proteins, it's called a *bispecific antibody*. It can be

brain better than crizotinib, a first-generation ALK inhibitor.

- **Alectinib (Alecensa)** can be given to patients with early stage ALK-positive NSCLC in the adjuvant setting (after the lung tumor has been removed).
- **First-generation ALK inhibitor: Crizotinib (Xalkori)** was the first ALK inhibitor approved for advanced NSCLC with an *ALK* rearrangement. It is still given in certain situations.

Side effects of ALK inhibitors:

- **Common side effects:** Vision changes, nausea, vomiting, diarrhea, swelling in hands and/or feet, tiredness, muscle soreness, nerve damage (peripheral neuropathy), changes in lab values
- **Rare, but serious side effects:** Liver damage; a lung condition called interstitial lung disease (ILD)/pneumonitis; changes in heart rhythm; harm to a fetus

ROS1 inhibitors

How they work (mechanism of action)Tj 0 g 1 0 0 1 95.35 492.75 Tm 0 OTs (I)Tj 0 Ts 0 g ET Q BT

- **Common side effects:** Vision changes, muscle soreness, swelling in hands and/or feet, nerve damage (called peripheral neuropathy), diarrhea, fatigue, changes in lab tests
- **Rare, but serious side effects:** Liver damage; changes in heart rhythm and heart function; lung condition called interstitial lung disease (ILD)/pneumonitis; high blood pressure; changes in mood or mental status; harm to a fetus

BRAF inhibitors

How they work (mechanism of action): In some NSCLCs, the cells have changes in the *BRAF* gene. Cells with these changes make an altered BRAF protein that helps them grow. Some drugs target this and related proteins.

These drugs are taken as pills or capsules each day.

Examples of BRAF inhibitors:

- **Combination treatment:** A combination of BRAF inhibitor and a MEK inhibitor is often given together as the first or later treatment for advanced NSCLC with the *BRAF* V600E mutation. Examples include:
 - **Dabrafenib (Tafinlar)**, a BRAF inhibitor, with **trametinib (Mekinist)**, a MEK inhibitor
 - **Encorafenib (Braftovi)**, a BRAF inhibitor, with **binimetinib (Mektovi)**, a MEK inhibitor
- **Single drug treatment:** **Vemurafenib (Zelboraf)**, another BRAF inhibitor, or **dabrafenib** can be taken alone if the patient can't take the combination treatment.

Side effects of BRAF inhibitors:

- **Common side effects:** Skin thickening, rash, itching, sensitivity to the sun, headache, fever, joint pain, tiredness, hair loss, nausea, diarrhea
- **Rare, but serious side effects:** Bleeding, heart rhythm problems, liver or kidney problems, lung problems, severe allergic reactions, severe skin or eye problems, increased blood sugar levels, squamous cell skin cancer

RET inhibitors

How they work (mechanism of action): In a small percentage of NSCLCs, the tumor cells have rearrangement in the *RET* gene that cause them to make an abnormal form of the RET protein. This abnormal protein helps the tumor cells grow. Drugs known as **RET inhibitors** can be used to treat advanced NSCLC with the RET rearrangement.

These drugs are taken by mouth as capsules, typically once or twice a day.

Examples of RET inhibitors:

- **Selpercatinib (Retevmo)** or **pralsetinib (Gayreto)** is often the preferred first treatment for metastatic NSCLC with the *RET* rearrangement.
- **Cabozantinib (Cometriq, Cabometyx)** has activity against RET, ROS1, MET, and VEGF. It can be used to treat *RET*-mutated NSCLC in certain situations.

Side effects of RET inhibitors:

- **Common side effects:** Dry mouth, diarrhea or constipation, high blood pressure, tiredness, swelling in hands and/or feet, skin rash, muscle and joint pain, low blood cell counts or changes in other blood tests
- **Rare, but serious side effects:** Liver damage, lung damage, allergic reactions, changes in heart rhythm, bleeding easily, and problems with wound healing

MET inhibitors

How they work (mechanism of action): In some NSCLCs, cancer cells have changes in the *MET* gene, called a MET exon 14 skipping mutation, that cause them to make an abnormal form of the MET protein. This abnormal protein helps the cancer cells grow and spread. Drugs called **MET inhibitors** can be used to treat metastatic NSCLC if the cancer cells have certain types of *MET* gene changes, by attacking the MET protein. They are taken as a pill once or twice a day.

Examples of MET inhibitors:

- **Capmatinib (Tabrecta)** or **tepotinib (Tepmetko)** is often the preferred first treatment for metastatic NSCLC with the *MET* exon 14 skipping mutation.
- **Crizotinib (Xalkori)** has activity against MET, ALK, and ROS1. It can be used to

treat *MET*-mutated NSCLC in certain situations.

Side effects of MET inhibitors:

- **Common side effects:** Nausea, vomiting, diarrhea, tiredness, swelling in hands and/or feet, muscle and joint pain, low blood cell counts, or changes in other blood tests
- **Rare, but serious side effects:** A lung condition called interstitial lung disease (ILD)/pneumonitis; liver damage; harm to a fetus; increased sensitivity to sunlight (photosensitivity)

HER2-directed drugs

How they work (mechanism of action): In a small percentage of NSCLCs, the cancer cells have certain changes in the *HER2 (ERBB2)* gene that help them grow. **HER2-directed drugs** can be used to treat metastatic NSCLC if the cancer cells have certain types of *HER2* gene changes. These drugs are infused into a vein (IV). They are typically given once every few weeks.

Examples of HER2 inhibitors:

- **Fam-trastuzumab deruxtecan-nxki (Enhertu)** is an *antibody-drug conjugate (ADC)*. It's made up of a lab-made antibody that targets the HER2 protein, which is linked to a chemotherapy drug. The antibody acts like a homing signal by attaching to the HER2 protein on cancer cells, bringing the chemo directly to them. It can be used to treat NSCLC with HER2 mutations if you've already had at least one other type of drug treatment.
- **Ado-trastuzumab emtansine (Kadcyla)** is also a HER2-targeted ADC. It can be used to treat HER2-mutated NSCLC in certain situations.

Side effects of HER2 inhibitors:

- **Common side effects:** Low white blood cell, red blood cell, and platelet counts; tiredness; hair loss; nausea and vomiting; muscle and joint pain; changes in other blood tests
- **Rare, but serious side effects, specific to fam-trastuzumab deruxtecan:**

Changes in heart function; severely low white blood cell count, which increases your risk of infection

TRK inhibitors

How they work (mechanism of action): A very small number of NSCLCs have changes in one of the *NTRK* genes, called *NTRK* gene fusions. Cells with these gene changes make abnormal TRK proteins, which can lead to abnormal cell growth and cancer. **TRK inhibitors** target and disable the proteins made by the *NTRK* genes.

These drugs are taken as pills, once or twice daily.

Examples of TRK inhibitors:

- **Larotrectinib (Vitrakvi)** or **entrectinib (Rozlytrek)** is often the preferred first treatment for metastatic NSCLC with an *NTRK* gene fusion mutation.

Side effects of *NTRK* inhibitors:

- **Common side effects:** Abnormal liver tests; decreased white blood cell and red blood cells; muscle and joint pain; tiredness; diarrhea or constipation; nausea and vomiting; stomach pain
- **Rare, but serious side effects:** Mental changes, such as confusion, changes in mood, changes in sleep; liver damage; changes in heart rhythm and/or function; vision changes; harm to a fetus

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see [Targeted Cancer Therapy](#)¹.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)².

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
2. www.cancer.org/cancer/managing-cancer/side-effects.html

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Immunotherapy for Non-Small Cell Lung Cancer

Immunotherapy is the use of medicines to help a person's own immune system to recognize and destroy cancer cells more effectively.

- [Immune checkpoint inhibitors](#)
- [More information about immunotherapy](#)

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses “checkpoint” proteins on immune cells, which act like switches that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system.

Drugs that target these checkpoints (called **checkpoint inhibitors**) can be used to treat some people with non-small cell lung cancer (NSCLC).

PD-1/PD-L1 inhibitors

Nivolumab (Opdivo), **Pembrolizumab (Keytruda)**, and **Cemiplimab (Libtayo)** target PD-1, a protein on certain immune cells (called **T cells**) that normally helps keep these cells from attacking other cells in the body. By blocking PD-1, these drugs boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

Atezolizumab (Tecentriq) and **Durvalumab (Imfinzi)** target PD-L1, a protein related to PD-1 that is found on some tumor cells and immune cells. Blocking this protein can help boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

These drugs can be used in different situations to treat NSCLC. In some cases, before one of these drugs can be used, [lab tests](#)¹ might need to be done on the cancer cells to show they have at least a certain amount of the PD-L1 protein (which would mean these drugs are more likely to work) and if the cancer cells have “driver mutations.” Depending on the results of those lab tests and the stage of lung cancer, the PD-1/PD-L1 inhibitors can be used in different ways. They can be given with or without chemotherapy, with or without a CTLA-4 inhibitor (see below), before or after surgery for early-stage lung

cancer, or for a long period of time for advanced-stage lung cancers.

All of these drugs are given as intravenous (IV) infusions. Depending on the drug, they might be given every 2, 3, 4, or 6 weeks.

Possible side effects

Side effects of these drugs can include fatigue, cough, nausea, itching, skin rash, loss of appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often.

Infusion reactions: Some people might have an infusion reaction while getting these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your cancer care team right away if you have any of these symptoms while getting these drugs.

Autoimmune reactions: These drugs work by removing one of the safeguards on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your cancer care team as soon as possible. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

CTLA-4 inhibitors

Ipilimumab (Yervoy) and **tremelimumab (Imjudo)** are also drugs that boost the immune response, but they block CTLA-4, another protein on T cells that normally helps keep them in check.

These drugs are used along with a PD-1 inhibitor (ipilimumab with nivolumab, and tremelimumab with durvalumab); they are not used alone. They might be an option as part of the first treatment for certain types of advanced NSCLC, most often along with

The most common side effects of these drugs include fatigue, diarrhea, skin rash, itching, muscle or bone pain, and belly pain.

Serious side effects seem to happen more often with CTLA-4 inhibitors than with the PD-1 and PD-L1 inhibitors.

Infusion reactions: Some people might have an infusion reaction while getting one of these drugs. This is like an allergic reaction, and can include fever, chills, flushing of the face, rash, itchy skin, feeling dizzy, wheezing, and trouble breathing. It's important to tell your doctor or nurse right away if you have any of these symptoms while getting an infusion.

It's very important to report any new side effects during or after treatment with any of these drugs to your cancer care team promptly. If serious side effects do occur, you may need to stop treatment and take high doses of corticosteroids to suppress your immune system.

Autoimmune reactions: These drugs can sometimes cause the immune system to attack other parts of the body, which can lead to serious problems in the intestines, liver, hormone-making glands, nerves, skin, eyes, or other organs. In some people, these side effects can be life-threatening.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see [Cancer Immunotherapy](#)².

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)³.

Hyperlinks

1. www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html
2. www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html
3. www.cancer.org/cancer/managing-cancer/side-effects.html

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Palliative Procedures for Non-Small Cell Lung Cancer

Palliative care (or supportive care) is meant to relieve symptoms and improve a person's quality of life.

- [Options for palliative support](#)
- [Treating fluid buildup in the area around the lung](#)
- [Treating fluid buildup around the heart](#)
- [Treating an airway blocked by a tumor](#)
- [More information about palliative care](#)

Options for palliative support

People with lung cancer often benefit from procedures to help with problems caused by the cancer. For example, people with advanced lung cancer can have shortness of breath. This can be caused by a number of things, including fluid around the lung or an airway that is blocked by a tumor. Although treating the cancer with [chemotherapy](#) or other drugs may help with this over time, other treatments may be needed as well.

Treating fluid buildup in the area around the lung

Sometimes fluid can build up in the chest outside of the lungs. This is called a **pleural effusion**. It can press on the lungs and cause trouble breathing.

Thoracentesis

2 main types are:

Chemical pleurodesis: A small cut is made in the skin of the chest wall, and a hollow tube (called a chest tube) is placed into the chest to remove the fluid. Then a substance is put into the chest through the tube that causes the linings of the lung (visceral pleura) and chest wall (parietal pleura) to stick together, sealing the space and limiting further fluid buildup. A number of substances can be used for this, such as talc, the antibiotic doxycycline, or a chemotherapy drug like bleomycin.

Surgical pleurodesis: Talc is blown into the space around the lungs during an operation. This is done using thoracoscopy through a small incision.

Catheter placement

One end of a catheter (a thin, flexible tube) is placed in the chest through a small cut in the skin, and the other end is left outside the body. Once in place, the catheter outside the body can be attached to a special bottle to allow the fluid to drain out on a regular basis.

Treating fluid buildup around the heart

Lung cancer can sometimes spread to the area around the heart. This can lead to fluid buildup inside the sac around the heart (called a **pericardial effusion**). The fluid can press on the heart and affect how well it works.

Pericardiocentesis

A pericardiocentesis is a procedure that drains the fluid with a needle placed into the space around the heart. This is usually done using an ultrasound of the heart (echocardiogram) to guide the needle.

Creating a pericardial window

During surgery, a piece of the sac around the heart (the pericardium) is removed to allow the fluid to drain into the chest or belly. This opening is called a **pericardial window** and helps to keep the fluid from building up again.

Treating an airway blocked by a tumor

Cancer can sometimes grow into an airway in the lung, blocking it and causing

problems like pneumonia or shortness of breath. Sometimes, this is treated with [radiation therapy](#), but other techniques can also be used.

Photodynamic therapy (PDT)

This type of treatment can be used to treat very early-stage lung cancers that are only in the outer layers of the lung airways, when other treatments aren't appropriate. It can also be used to help open up airways blocked by tumors to help people breathe better.

For this technique, a light-activated drug called porfimer sodium (Photofrin) is injected into a vein. This drug collects more in cancer cells than in normal cells. After a couple of days (to give the drug time to build up in the cancer cells), a bronchoscope is passed down the throat and into the lung. This can be done with either local anesthesia (numbing the throat) and sedation, or with general anesthesia (where you are in a deep sleep). A special laser light on the end of the bronchoscope is aimed at the tumor, which activates the drug and causes the cells to die. The dead cells are then removed a few days later during a bronchoscopy. This process can be repeated if needed.

PDT can cause swelling in the airway for a few days, which may lead to some shortness of breath, as well as coughing up blood or thick mucus. Some of this drug also collects in normal cells in the body, such as skin and eye cells. This can make you very sensitive to sunlight or strong indoor lights. Too much exposure can cause serious skin reactions (like a severe sunburn), so doctors recommend staying out of any strong light for several weeks after the injection.

For more information on PDT, see [Photodynamic Therapy](#)¹.

Laser therapy

Lasers can sometimes be used to treat very small tumors in the linings of airways. They can also be used to help open up airways blocked by larger tumors to help people breathe better.

The laser is on the end of a bronchoscope, which is passed down the throat and next to the tumor. The doctor then aims the laser beam at the tumor to burn it away. This treatment can usually be repeated, if needed. You are usually asleep (under general anesthesia) for this type of treatment.

Stent placement

If a lung tumor has grown into an airway and is causing problems, sometimes a

bronchoscope is used to put a hard silicone or metal tube called a stent in the airway to help keep it open. This is often done after other treatments such as PDT or laser therapy.

More information about palliative care

To learn more about how palliative care can be used to help control or reduce symptoms caused by cancer, see [Palliative Care](#)².

To learn about some of the side effects of cancer or treatment and how to manage them, see [Managing Cancer-related Side Effects](#)³.

Hyperlinks

1. www.cancer.org/cancer/managing-cancer/treatment-types/radiation/photodynamic-therapy.html
2. www.cancer.org/cancer/managing-cancer/palliative-care.html
3. www.cancer.org/cancer/managing-cancer/side-effects.html

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Treatment Choices for Non-Small Cell Lung Cancer, by Stage

The treatment options for non-small cell lung cancer (NSCLC) are based mainly on the stage (extent) of the cancer, but other factors, such as a person's overall health and lung function, as well as certain traits of the cancer itself, are also important.

- [Treating occult cancer](#)
- [Treating stage 0 NSCLC](#)
- [Treating stage I NSCLC](#)
- [Treating stage II NSCLC](#)
- [Treating stage IIIA NSCLC](#)
- [Treating stage IIIB NSCLC](#)
- [Treating stage IVA and IVB NSCLC](#)
- [NSCLC that progresses or recurs after treatment](#)

If you smoke: one of the most important things you can do to be ready for treatment is to [try to quit](#)¹. Studies have shown that people who stop smoking after a diagnosis of lung cancer tend to have better outcomes than those who don't.

Treating occult cancer

For these cancers, malignant cells are seen on sputum cytology, but no obvious tumor can be found with bronchoscopy or imaging tests. They are usually early-stage cancers. [Bronchoscopy](#)² and possibly other tests are usually repeated every few months to look for a tumor. If a tumor is found, treatment will depend on the stage.

Treating stage 0 NSCLC

Treating stage II NSCLC

Neoadjuvant (pre-operative) chemotherapy with or without immunotherapy is usually offered to patients with stage II NSCLC. After neoadjuvant therapy, people who have stage II NSCLC and are healthy enough for [surgery](#) usually have the cancer removed by lobectomy or sleeve resection. Sometimes removing the whole lung (pneumonectomy) is needed.

Any lymph nodes likely to have cancer in them are also removed. The extent of lymph node involvement and whether or not cancer cells are found at the edges of the removed tissues are important factors when planning the next step of treatment.

After surgery, the removed tissue is checked to see if there are cancer cells at the edges of the surgery specimen. This might mean that some cancer has been left behind, so a second surgery might be done to try to remove any remaining cancer. This may be followed by additional treatment with either chemotherapy, targeted therapy (ie. alectinib, osimertinib), or immunotherapy (ie. atezolizumab, pembrolizumab).

Treating stage IIIA NSCLC

The initial treatment for stage IIIA NSCLC may include some combination of [radiation therapy](#), [chemotherapy](#) (chemo), immunotherapy, and/or [surgery](#). For this reason, planning treatment for stage IIIA NSCLC often requires input from a medical oncologist,

Treating stage IIIB NSCLC

Stage IIIB NSCLC has spread to lymph nodes that are near the other lung or in the neck, and may also have grown into important structures in the chest. These cancers can't be removed completely by [surgery](#).

As with other stages of lung cancer, treatment depends on the patient's overall health. If you are in fairly good health you may be helped by [chemotherapy](#) (chemo) combined with [radiation therapy](#) (known as **chemoradiation**). Some people can even be cured with this treatment. If the cancer stays under control after 2 or more treatments of chemoradiation, the [immunotherapy](#) drug durvalumab (Imfinzi) can be given for up to a year to help keep the cancer stable.

Patients who are not healthy enough for this combination are often treated with radiation therapy alone, or, less often, chemo alone. If surgery, radiation, and chemoradiation aren't likely to be good treatment options, an [immunotherapy](#) drug such as pembrolizumab (Keytruda) or cemiplimab (Libtayo) may be considered as the first treatment.

These cancers can be hard to treat, so taking part in a [clinical trial](#)³ of newer treatments may be a good option for some people.

Treating stage IVA and IVB NSCLC

Stage IVA or IVB NSCLC has already spread when it is diagnosed. These cancers can be very hard to cure. Treatment options depend on where and how far the cancer has spread, whether the cancer cells have certain gene or protein changes, and your overall health.

If you are in otherwise good health, treatments such as [surgery](#), [chemotherapy](#) (chemo), [targeted therapy](#), [immunotherapy](#), and [radiation therapy](#) may help you live longer and make you feel better by relieving symptoms, even though they aren't likely to cure you.

Other treatments, such as photodynamic therapy (PDT) or laser therapy, may also be used to [help relieve symptoms](#). In any case, if you are going to be treated for advanced NSCLC, be sure you understand the goals of treatment before you start.

NSCLC that has spread to only one other site (stage IVA)

Cancer that is limited in the lungs and has only spread to one other site (such as the

have been used, and on the person's health and desire for more treatment. It's important to understand the goal of any further treatment – if it is to try to cure the cancer, to slow its growth, or to help relieve symptoms. It is also important to understand the benefits and risks.

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