

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

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

• Health Professionals Who Are Part of a Cancer Care Team

Making treatment decisions

It's important to discuss all of your treatment options as well as their possible side effects with your family and your treatment team to make the choice that best fits your needs. If there's anything you don't understand, ask to have it explained.

If time permits, it is often a good idea to seek a second opinion. A second opinion can give you more information and help you feel more confident about the treatment plan you choose.

- Questions to Ask About Lung Cancer
- Seeking a Second Opinion

<u>Clinical Trials</u>

Considering complementary and alternative methods

You may hear about alternative or complementary methods to relieve symptoms or treat your cancer that your doctors haven't mentioned. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods are treatments that are used **along with** your regular medical care. **Alternative** treatments are used **instead of** standard medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

<u>Complementary and Integrative Medicine</u>

Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

- Palliative Care
- Programs & Services

Choosing to stop treatment or choosing no treatment at all

For some people, when treatments have been tried and are no longer controlling the cancer, it could be time to weigh the benefits and risks of continuing to try new treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

Surgery for Non-Small Cell Lung Cancer

Surgery to remove the cancer might be an option for early-stage non-small cell lung cancer (NSCLC). It provides the best chance to cure the disease. Still, lung cancer surgery is a complex operation that can have serious consequences, so it should be done by a thoracic surgeon who has a lot of experience operating on lung cancers.

- Tests before lung surgery
- Types of lung surgery
- Ways to do lung surgery
- Possible risks and side effects of lung surgery

- After surgery
- More information about Surgery

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** fgTf 0 0 0 rg /e lymph nod

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. RATS is similar to VATS in terms of less pain, less blood loss, and shorter recovery time.

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 <u>imaging tests</u>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 <u>Cancer</u> Surgery³.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁴.

Hyperlinks

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

References

Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Ch. 69 - Cancer of

the Lung: Non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Chiang A, Detterbeck FC, Stewart T, Decker RH, Tanoue L. Chapter 48: Non-small cell lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa:

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

- 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.

References

Chiang A, Detterbeck FC, Stewart T, Decker RH, Tanoue L. Chapter 48: Non-small cell lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

Dupuy DE. Image-guided ablation of lung tumors. UpToDate website. https://www.uptodate.com/contents/image-guided-ablation-of-lung-tumors. Updated Nov 6, 2023. Accessed Jan 23, 2024.

Iyengar P, All S, Berry MF, Boike TP, Bradfield L, Dingemans AC, Feldman J, Gomez DR, Hesketh PJ, Jabbour SK, Jeter M, Josipovic M, Lievens Y, McDonald F, Perez BA, Ricardi U, Ruffini E, De Ruysscher D, Saeed H, Schneider BJ, Senan S, Widder J, Guckenberger M. Treatment of Oligometastatic Non-Small Cell Lung Cancer: An ASTRO/ESTRO Clinical Practice Guideline. Pract Radiat Oncol. 2023 Sep-Oct;13(5):393-412. doi: 10.1016/j.prro.2023.04.004. Epub 2023 Apr 25. PMID: 37294262.

Jairam V, Park HS, Decker RH. Local Ablative Therapies for Oligometastatic and Oligoprogressive Non-Small Cell Lung Cancer. Cancer J. 2020 Mar/Apr;26(2):129-136. doi: 10.1097/PPO.0000000000000433. PMID: 32205537.

Juan O, Popat S. Ablative Therapy for Oligometastatic Non-Small Cell Lung Cancer. Clin Lung Cancer. 2017 Nov;18(6):595-606. doi: 10.1016/j.cllc.2017.03.002. Epub 2017 Mar 14. PMID: 28377206.

National Cancer Institute. Physician Data Query (PDQ). Health Professional Version. Non-Small Cell Lung Cancer Treatment. 2023. Accessed at https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq on Jan 23, 2024.

Last Revised: January 29, 2024

Radiation Therapy for Non-Small Cell Lung Cancer

Radiation therapy uses high-energy rays or particles to kill cancer cells.

- When is radiation therapy used?
- Types of radiation therapy used for NSCLC
- Possible side effects of radiation therapy for NSCLC
- More information about radiation therapy

When is radiation therapy used?

Depending on the stage stage

• Stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiotherapy (SABR), is most often used to treat early-stage lung 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

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 <u>External Beam Radiation</u> <u>Therapy</u>¹.

Brachytherapy (internal radiation therapy)

In people with NSCLC, <u>brachytherapy</u>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 <u>bronchoscope</u>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

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 caused by cancer that has spread to the brain, but they can affect your quality of life.

More information about radiation therapy

To learn more about how radiation is used to treat cancer, see <u>Radiation Therapy</u>⁴.

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>⁵.

Hyperlinkse 0.50 Ts 0 g /F2 12 Tf 0 0 0 rg /G w 100.32 0 0 0G w 10050or troub.T 0 0

Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Ch. 69 - Cancer of the Lung: Non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Chiang A, Detterbeck FC, Stewart T, Decker RH, Tanoue L. Chapter 48: Non-small cell lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

National Cancer Institute. Physician Data Query (PDQ). Patient Version. Non-Small Cell Lung Cancer Treatment. 2023. Accessed at https://www.cancer.gov/types/lung/patient/non-small-cell-lung-treatment-pdq on Jan 23, 2024.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. V.1.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf on Jan 23, 2024.

Simone CB 2nd, Bradley J, Chen AB, Daly ME, Louie AV, Robinson CG, Videtic GMM, Rodrigues G. ASTRO Radiation Therapy Summary of the ASCO Guideline on Management of Stage III Non-Small Cell Lung Cancer. Pract Radiat Oncol. 2023 May-Jun;13(3):195-202. doi: 10.1016/j.prro.2023.01.005. PMID: 37080641.

Last Revised: January 29, 2024

Chemotherapy for Non-Small Cell Lung Cancer

Chemotherapy (chemo) is treatment with anti-cancer drugs that may be injected into a

More information about chemotherapy

When is chemotherapy used?

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 <u>central venous catheters</u>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 therapy**, seems to help keep the cancer in check and help some people live longer.

If the initial chemo treatment for advanced lung cancer is no longer working, the doctor may recommend second-line treatment with chemo, targeted therapy, immunotherapy,

National Cancer Institute. Physician Data Query (PDQ). Patient Version. Non-Small Cell Lung Cancer Treatment. 2023. Accessed at

https://www.cancer.gov/types/lung/patient/non-small-cell-lung-treatment-pdq on Jan 23, 2024.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. V.1.2024. Accessed at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf on Jan 23, 2024.

Patil PD, Shepherd F, Johnson DH. A Career in Lung Cancer: Pushing Beyond Chemotherapy. Am Soc Clin Oncol Educ Book. 2019 Jan;39:583-589. doi:

Targeted Drug Therapy for Non-Small Cell 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 (see below).

Examples of KRAS inhibitors:

- **Sotorasib (Lumakras)** is used alone for advanced NSCLC with the KRAS G12C mutation if you've already had at least one other type of drug treatment.
- Adagrasib (Krazati) can be used in ways similar to sotorasib.

Side effects of KRAS inhibitors:

- **Common side effects:** Diarrhea, nausea and vomiting, muscle pain, fatigue, cough, decreased white blood cell and red blood cell counts, and changes in other blood tests.
- Rare, but serious side effects: Kidney damage, liver damage, lung damage called interstitial lung disease (ILD)/ pneumonitis, and a heart condition called QTc interval prolongation (see below).

EGFR inhibitors

How they work (mechanism of action): Epidermal growth factor receptor (EGFR) is a protein on the surface of cells. It normally helps the cells grow and divide. Sometimes NSCLC cells have too much EGFR, which makes them grow faster. Drugs called **EGFR inhibitors** can block the signal from EGFR that tells the cancer cells to grow. These drugs are often used to treat advanced NSCLCs that have certain mutations in the *EGFR* gene, although osimertinib can also be used as an adjuvant (additional) treatment after surgery for some earlier-stage lung cancers.

Examples of EGFR inhibitors:

EGFR inhibitors that target cells with either an exon 19 or exon 21 mutation:

- Drugs such afatinib (Gilotrif), erlotinib (Tarceva), dacomitinib (Vizimpro), gefitinib (Iressa), and osimertinib (Tagresso) can be given alone.
- Lazertinib (Lazcluze) in combination with amivantamab (Rybrevant).
- **Osimertinib** in combination with chemotherapy (cisplatin or carboplatin with pemetrexed).
- Erlotinib in combination with a VEGF inhibitor (ramucirumab or bevacizumab).
- Amivantamab in combination with chemo (carboplatin and pemetrexed).

EGFR inhibitors that target cells with S768I, L861Q and/or G719X mutations:

- Drugs such as afatinib (Gilotrif), osimertinib (Tagrisso), erlotinib (Tarceva), dacomitinib (Vizimpro), and gefitinib (Iressa) can be given alone.
- Amivantamab in combination with chemo (carboplatin and pemetrexed).

EGFR inhibitors that target cells with an exon 20 mutation:

- Amivantamab (Rybrevant) in combination with chemo (carboplatin and pemetrexed). Amivantamab 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.
- Amivantamab given alone is also an option after chemotherapy has been tried.

Side effects of EGFR inhibitors:

- **Common side effects:** Skin problems, nail changes, fatigue, loss of appetite, nausea, vomiting, and diarrhea.
- Rare, but serious side effects: A lung condition called interstitial lung disease (ILD)/ pneumonitis; damage to the heart muscle; heart rhythm changes; other organ damage including kidney, gut and liver; harm to a fetus; and severe skin rashes.

ALK inhibitors

How they work (mechanism of action): About 5% of NSCLCs have a rearrangement

Examples of ROS1 inhibitors:

- Entrectinib (Rozlytrek), crizotinib (Xalkori), and ceritinib (Zykadia) are often the first treatment options for advanced NSCLC with a *ROS1* rearrangement.
- Lorlatinib (Lorbrena) is an option for patients with *ROS1*-mutated advanced NSCLC who have already been treated with the either entrectinib, crizotinib, or ceritinib.
- **Repotrectinib (Augtyro)** is an option for patients with *ROS1*-mutated advanced NSCLC who have *or* who have not been treated with a ROS1 inhibitor.

Side effects of ROS1 inhibitors:

- **Common side effects:** Vision changes, muscle soreness, swelling in hands and/or feet, nerve damage (called peripheral neuropathy), diarrhea, fatigue, and 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; and 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, and 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, and 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 knowal aglb1BT 1 0 0 1

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; and 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

Noor ZS, Cummings AL, Johnson MM, Spiegel ML, Goldman JW. Targeted Therapy for Non-Small Cell Lung Cancer. Semin Respir Crit Care Med. 2020 Jun;41(3):409-434. doi: 10.1055/s-0039-1700994. Epub 2020 May 25. PMID: 32450595.

Reck M and Rabe KF. Precision Diagnosis and Treatment for Advanced Non-Small-Cell Lung Cancer. *N Engl J Med.* 2017;377(9):849-861.

Immunotherapy for Non-Small Cell Lung Cancer

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.

CTLA-4 inhibitors

To learn about some of the side effects listed here and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

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

References

Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Ch. 69 - Cancer of the Lung: Non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Chiang A, Detterbeck FC, Stewart T, Decker RH, Tanoue L. Chapter 48: Non-small cell lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

Lahiri A, Maji A, Potdar PD, Singh N, Parikh P, Bisht B, Mukherjee A, Paul MK. Lung cancer immunotherapy: progress, pitfalls, and promises. Mol Cancer. 2023 Feb

Sun L, Bleiberg B, Hwang WT, Marmarelis ME, Langer CJ, Singh A, Cohen RB, Mamtani R, Aggarwal C. Association Between Duration of Immunotherapy and Overall Survival in Advanced Non-Small Cell Lung Cancer. JAMA Oncol. 2023 Aug 1;9(8):1075-1082. doi: 10.1001/jamaoncol.2023.1891. PMID: 37270700; PMCID: PMC10240399.

Suresh K, Naidoo J, Lin CT, Danoff S. Immune Checkpoint Immunotherapy for Non-Small Cell Lung Cancer: Benefits and Pulmonary Toxicities. Chest. 2018 Dec;154(6):1416-1423. doi: 10.1016/j.chest.2018.08.1048. Epub 2018 Sep 4. PMID: 30189190; PMCID: PMC6335259.

Last Revised: September 23, 2024

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 <u>chemotherapy</u> 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**

(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 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 <u>Palliative Care²</u>.

To learn about some of the side effects of cancer or treatment and how to manage them, see <u>Managing Cancer-related Side Effects</u>³.

Hyperlinks

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

References

Araujo LH, Horn L, Merritt RE, Shilo K, Xu-Welliver M, Carbone DP. Ch. 69 - Cancer of the Lung: Non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.

Chiang A, Detterbeck FC, Stewart T, Decker RH, Tanoue L. Chapter 48: Non-small cell

lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

Irwin KE, Greer JA, Khatib J, Temel JS, Pirl WF. Early palliative care and metastatic non-small cell lung cancer: potential mechanisms of prolonged survival. Chron Respir Dis. 2013 Feb;10(1):35-47. doi: 10.1177/1479972312471549. PMID: 23355404.

National Cancer Institute. Physician Data Query (PDQ). Health Professional Version.

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

If you smoke: one of the most important things you can do to be ready for treatment is to <u>try to quit</u>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. <u>Bronchoscopy</u>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

Because stage 0 NSCLC is limited to the lining layer of the airways and has not invaded deeper into the lung tissue or other areas, it is usually curable by surgery alone. No chemotherapy or radiation therapy is needed.

If you are healthy enough for surgery, you can usually be treated by segmentectomy or wedge resection (removal of part of the lobe of the lung). Cancers in some locations (such as where the windpipe divides into the left and right main bronchi) may be treated with a sleeve resection, but in some cases, they may be hard to remove completely without removing a lobe (lobectomy) or even an entire lung (pneumonectomy).

For some stage 0 cancers, treatments such as photodynamic therapy (PDT), laser therapy, or brachytherapy (internal radiation) may be alternatives to surgery.

Treating stage I NSCLC

If you have stage I NSCLC, surgery may be the only treatment you need. Surgery will either take out the lobe of the lung that has the tumor (lobectomy) or take out a smaller piece of the lung (sleeve resection, segmentectomy, or wedge resection). At least some lymph nodes in the lung and in the space between the lungs will also be removed and checked for cancer.

Segmentectomy or wedge resection is generally an option only for very small stage I cancers and for patients with other health problems that make removing the entire lobe dangerous. Still, most surgeons believe it is better to do a lobectomy if the patient can tolerate it, as it offers the best chance for cure.

For people with stage I NSCLC that has a higher risk of coming back (based on size,

As with other stages, treatment for stage IV lung cancer depends on a person's overall health. For example, some people not in good health might get only 1 chemo drug instead of 2. For people who can't have chemo, radiation therapy is usually the treatment of choice. Local treatments such as laser therapy, PDT, or stent placement may also be used to help relieve symptoms caused by lung tumors.

Because treatment is unlikely to cure these cancers, taking part in a clinical trial of newer treatments may be a good option.

You can also find more information about living with stage IV cancer in <u>Advanced</u> <u>Cancer</u>⁵.

NSCLC that progresses or recurs after treatment

If cancer continues to grow during treatment (progresses) or comes back (recurs), further treatment will depend on the location and extent of the cancer, what treatments 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.

Smaller cancers that recur locally in the lungs can sometimes be treated again with surgery or radiation therapy (if it hasn't been used before). Cancers that recur in the lymph nodes between the lungs are usually treated with chemo, possibly along with radiation if it hasn't been used before. For cancers that return at distant sites, chemo, targeted therapies, and/or immunotherapy are often the treatments of choice.

For more on dealing with a recurrence, see <u>Understanding Recurrence</u>⁶.

In some people, the cancer may never go away completely. These people may get regular treatments with chemo, radiation therapy, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. <u>Managing Cancer as a Chronic Illness</u>⁷ talks more about this.

Hyperlinks

1. www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html

(https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as editors and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/aboutus/policies/content-usage.html).

cancer.org | 1.800.227.2345