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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

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 Associated with Cancer Care

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

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they're not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

Clinical Trials

Considering complementary and alternative methods

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

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's 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.

Complementary and Integrative Medicine

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.

Whether you are thinking about treatment, getting treatment, or not being treated at all, you can still get supportive care to help with pain or other symptoms. Communicating with your cancer care team is important so you understand your diagnosis, what treatment is recommended, and ways to maintain or improve your quality of life.

Different types of programs and support services may be helpful, and can be an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists.

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 and 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

- Tests before lung surgery
- Types of lung surgery
- Surgery for lung cancer that has spread to other organs
- More information about Surgery

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 surgeon who has a lot of experience operating on lung cancers.

Tests before lung surgery

If your doctor thinks the cancer can be treated with surgery:

- Pulmonary function tests will be done to see if you would still have enough healthy lung tissue left after surgery.
- Tests will be done to check the function of your heart and other organs to be sure you're healthy enough for surgery.
- Your doctor will want to check if the cancer has already spread to the lymph nodes between the lungs. This is often done before surgery with mediastinoscopy or another technique.

To learn more about these tests, see <u>Tests for Lung Cancer</u>¹.

Types of lung surgery

Different operations can be used to treat (and possibly cure) NSCLC. With any of these operations, nearby lymph nodes are also removed to look for possible spread of the cancer. These operations require general anesthesia (where you are in a deep sleep) and are usually done through a large surgical incision between the ribs in the side of the chest or the back (called a **thoracotomy**).

- **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 and 2 on the left). 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 your doctor recommends 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.

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 belly pain, heartburn, itching, chest pain, nausea, vomiting, 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.

After surgery

When you wake up from surgery, you will 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 5 to 7 days in the hospital after the surgery.

Video-assisted thoracic surgery (VATS)

Video-assisted thoracic surgery (VATS), also called <u>thoracoscopy</u>³, is a procedure being used more frequently by doctors to treat early-stage lung cancers. It uses smaller incisions, typically has a shorter hospital stay and fewer complications than a thoracotomy.

Most experts recommend that only early-stage tumors of the lung be treated this way.

The cure rate after this surgery seems to be the same as with surgery done with a larger incision. But it's important that the surgeon doing this procedure is experienced, because it requires a great deal of skill.

Robotically-assisted thoracic surgery (RATS)

In this approach, the thoracoscopy is done using a robotic system. The surgeon sits at a control panel in the operating room and moves robotic arms to operate through several small incisions in the patient's chest.

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

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. While all surgeries carry some risks, these 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.

Surgery for lung cancer that has spread to other organs

If the lung cancer has spread to your brain and there is only one tumor, you may benefit from having the tumor removed. This surgery should be considered only if the tumor in the lung can also be removed or treated (with radiation and/or chemotherapy) completely.

Surgery to remove a tumor in the brain is typically done through a small hole in the skull (called a **craniotomy**). It should only be done if the tumor can be removed without damaging vital areas of the brain.

More information about Surgery

For more general information about surgery as a treatment for cancer, see <u>Cancer</u> <u>Surgery</u>⁴.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁵.

Hyperlinks

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

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

Radiofrequency ablation (RFA) might be considered for some people with small lung tumors that are near the outer edge of the lungs, especially if they can't tolerate surgery.

RFA uses high-energy radio waves to heat the tumor. 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. Once the tip is in place, an electric current is passed through the probe, which heats the tumor and destroys the cancer cells.

RFA 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 as well.

You might have some pain where the needle was inserted for a few days after the procedure. 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

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

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

Depending on the stage of the non-small cell lung cancer (NSCLC) and other factors, radiation therapy might be used:

• As the main treatment (sometimes along with chemotherapy), especially if the lung

tumor can't be removed because of its size or location, if a person isn't healthy enough for surgery, or if a person doesn't want surgery.

- After surgery (alone or along with chemotherapy) to try to kill any small areas of cancer that surgery might have missed.
- Before surgery (usually along with chemotherapy) to try to shrink a lung tumor to make it easier to operate on.
- To treat cancer spread to other areas such as the brain or bone.
- To relieve (palliate) symptoms of advanced NSCLC such as pain, bleeding, trouble swallowing, cough, or problems caused by spread to other organs such as the brain.

Types of radiation therapy used for NSCLC

Different types of radiation therapy can be used to treat NSCLC. There are 2 main types:

- External beam radiation therapy
- Brachytherapy (internal radiation therapy)

External beam radiation therapy

External beam radiation therapy (EBRT) focuses radiation from outside the body onto the cancer. This is the type of radiation therapy most often used to treat NSCLC or its spread to other organs.

Treatment is much like getting an x-ray, but the radiation dose is stronger. The procedure itself is painless and each treatment lasts only a few minutes. Most often, radiation treatments to the lungs are given 5 days a week for 5 to 7 weeks, but this can vary based on the type of EBRT and the reason it's being given.

Newer EBRT techniques have been shown to help doctors treat lung cancers more accurately while lowering the radiation exposure to nearby healthy tissues. These include:

• 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 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.

• 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 <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 bronchoscope, 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.

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 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 Radiation Therapy⁴.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁵.

Hyperlinks

- 1. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-beam-radiation-therapy.html</u>
- 2. <u>www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html</u>
- 3. www.cancer.org/cancer/diagnosis-staging/tests/endoscopy/bronchoscopy.html
- 4. www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html
- 5. www.cancer.org/cancer/managing-cancer/side-effects.html

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Chemotherapy for Non-Small Cell Lung Cancer

- 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

Chemotherapy (chemo) is treatment with anti-cancer drugs that may be injected into a vein or taken by mouth. These drugs travel through the bloodstream and reach most parts of the body.

When is chemotherapy used?

Not all people with non-small cell lung cancer (NSCLC) will need chemo, but depending on the cancer's <u>stage</u>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 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 even on imaging tests².
- 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 so that 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. Sometimes other combinations that do not include these drugs, such as gemcitabine with vinorelbine or paclitaxel, may be used.

Advanced lung cancer though may be treated with a single chemo drug especially for people who might not tolerate combination chemotherapy well, such as those in poor overall health or who are elderly.

For some people with advanced lung cancer, a targeted therapy drug or an immunotherapy drug may be given along 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 2 most common types are the port and the PICC line.

Doctors give chemo in cycles, with each 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 had a good response 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 a single chemo drug such as docetaxel or pemetrexed, or with a targeted therapy or immunotherapy drug.

Possible side effects of chemo for NSCLC

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long they are taken. Some common side effects include:

- Hair loss
- Mouth sores
- Loss of appetite or weight changes

- · Nausea and vomiting
- Diarrhea or constipation

Chemo can also affect the blood-forming cells of the bone marrow, which can lead to:

- Increased chance of infections (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue (from low red blood cell counts)

These side effects usually go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Some drugs can have specific side effects. For example, drugs such as cisplatin, vinorelbine, docetaxel, or paclitaxel can cause nerve damage (*peripheral neuropathy*). This can sometimes lead to symptoms (mainly in the hands and feet) such as pain, burning or tingling sensations, sensitivity to cold, or weakness. In most people this goes away or gets better once treatment is stopped, but it may last a long time in others.

Be sure to report any side effects you notice during chemo to your medical team so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced or treatment may need to be delayed or stopped to prevent the effects from getting worse.

More information about chemotherapy

For more general information about how chemotherapy is used to treat cancer, see Chemotherapy⁴.

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

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/staging-nsclc.html</u>
- 2. www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-

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- 3. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html</u>
- 4. www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html
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Targeted Drug Therapy for Non-Small Cell Lung Cancer

- Drugs that target tumor blood vessel growth (angiogenesis)
- Drugs that target cells with KRAS gene changes
- Drugs that target cells with EGFR gene changes
- Drugs that target cells with ALK gene changes
- Drugs that target cells with ROS1 gene changes
- Drugs that target cells with BRAF gene changes
- Drugs that target cells with RET gene changes
- Drugs that target cells with MET gene changes
- Drugs that target cells with HER2 gene changes
- Drugs that target cells with NTRK gene changes
- More information about targeted therapy

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. 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.

Drugs that target tumor blood vessel growth (angiogenesis)

For tumors to grow, they need to form new blood vessels to keep them nourished. This process is called **angiogenesis**. Some targeted drugs, called **angiogenesisinhibitors**, block this new blood vessel growth:

- Bevacizumab (Avastin) is used to treat advanced NSCLC. It is a monoclonal antibody (a lab-made version of a specific immune system protein) that targets vascular endothelial growth factor (VEGF), a protein that helps new blood vessels to form. This drug is often used with chemo for a time. Then if the cancer responds, the chemo may be stopped and bevacizumab given by itself until the cancer starts growing again.
- Ramucirumab (Cyramza) can also be used to treat advanced NSCLC. This drug is a monoclonal antibody that targets a VEGF receptor (protein). It helps stop the formation of new blood vessels. This drug is often combined with chemo, typically

after another treatment stops working.

Either of these drugs might also be used along with the targeted drug erlotinib (see below) as the first treatment in people whose cancer cells have certain *EGFR* gene mutations.

Side effects of angiogenesis inhibitors

Common side effects of these drugs include:

- High blood pressure
- Tiredness (fatigue)
- Bleeding
- Low white blood cell counts (with increased risk of infections)
- Headaches
- Mouth sores
- Loss of appetite
- Diarrhea

Rare but possibly serious side effects can include blood clots, severe bleeding, holes (called perforations) in the intestine, heart problems, and slow wound healing. If a hole forms in the intestine it can lead to severe infection and may require surgery to fix.

Because of the risks of bleeding, these drugs typically 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.

Drugs that target cells with KRAS gene changes

Some NSCLCs 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 (13%) with NSCLC have a specific type of *KRAS* gene change called a *KRAS* G12C mutation. NSCLCs with this mutation are often resistant to other targeted drugs such as EGFR inhibitors (see below).

Sotorasib (Lumakras) and **adagrasib (Krazati**) are drugs known as *KRAS inhibitors*. They work by attaching to the KRAS G12C protein, which helps keep cancer cells from growing. One of these drugs may be helpful if you have advanced NSCLC, <u>your blood or cancer tissue is tested</u>¹ and the cancer cells are found to have the *KRAS* G12C mutation, and you've already had at least one other type of drug treatment.

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

Side effects of KRAS inhibitors

Common side effects can include:

- Diarrhea
- Joint and muscle pain
- Nausea and vomiting
- Loss of appetite
- Feeling tired or weak
- Cough
- · Low white blood cell or red blood cell counts
- · Changes in certain other blood tests

Less common but more serious side effects can include liver damage as well as inflammation (swelling) or scarring in the lungs, which can make it hard to breathe.

Drugs that target cells with EGFR gene changes

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 cells to grow. Some of these drugs can be used to treat NSCLC.

EGFR inhibitors used in NSCLC with EGFR gene mutations

- Erlotinib (Tarceva)
- Afatinib (Gilotrif)
- Gefitinib (Iressa)
- Osimertinib (Tagrisso)

Dacomitinib (Vizimpro)

For advanced NSCLC: One of these drugs is often used as the first treatment for advanced NSCLCs that have certain mutations in the *EGFR* gene. Most of these drugs are used alone, although erlotinib can also be used along with a targeted drug that affects new blood vessel growth (see above).

For earlier stage NSCLC: Osimertinib can also be used as an adjuvant (additional) treatment after surgery for some earlier stage lung cancers with certain *EGFR* gene mutations.

All of these medicines are taken as pills.

EGFR inhibitors that target cells with the T790M mutation

EGFR inhibitors can often shrink tumors for several months or more. But eventually these drugs stop working for most people, usually because the cancer cells develop another mutation in the *EGFR* gene. One such mutation is known as T790M.

Osimertinib (Tagrisso) is an EGFR inhibitor that often works against cells with the T790M mutation.

Doctors now commonly get another biopsy when other EGFR inhibitors have stopped working to see if the patient's tumor has developed the T790M mutation (and therefore if this drug might be helpful).

EGFR inhibitors that target cells with an exon 20 mutation

While the EGFR inhibitors listed above can help many people whose cancer cells have *EGFR* gene mutations, they don't help everyone. For example, cancer cells with an *EGFR* gene change known as an **exon 20 insertion mutation** are much less likely to affected by these drugs.

However, other drugs that target cancer cells with an exon 20 mutation are now available.

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*. This drug is given as an infusion into a vein (IV).

Mobocertinib (Exkivity) is a drug that targets the EGFR protein in a slightly different way. This drug is taken as pills, typically once a day.

These drugs can be used to treat advanced NSCLC when the cancer cells have an exon 20 mutation, typically after chemotherapy has been tried.

EGFR inhibitors used for squamous cell NSCLC

Necitumumab (Portrazza) is a monoclonal antibody (a lab-made version of an immune system protein) that targets EGFR. It can be used with chemotherapy as the first treatment in people with advanced squamous cell NSCLC. This drug is given as an infusion into a vein (IV).

Side effects of EGFR inhibitors

Common side effects of all EGFR inhibitors include:

- Skin problems
- Diarrhea
- Mouth sores
- Loss of appetite

Skin problems can include an acne-like rash on the face and chest, which in some cases can lead to skin infections.

Some of these drugs can also cause more serious, but less common, side effects. For example:

- Monoclonal antibodies such as amivantamab and necitumumab can sometimes cause infusion reactions (similar to an allergic reaction) during or shortly after they are given.
- Amivantamab can cause eye problems or serious lung disease in some people.
- Necitumumab can lower the levels of certain minerals in the blood, which can affect the heart rhythm and in some cases might be life-threatening.
- Mobocertinib can cause serious lung disease and can damage the heart muscle. It can also affect the rhythm of the heart, which in some cases might be lifethreatening.

Drugs that target cells with ALK gene changes

About 5% of NSCLCs have a rearrangement in a gene called *ALK*. This change is often seen in people who don't smoke (or people who are light smokers) who are younger and who have the adenocarcinoma subtype of NSCLC. The *ALK* gene rearrangement produces an abnormal ALK protein that causes the cells to grow and spread. Drugs that target the abnormal ALK protein include:

- Crizotinib (Xalkori)
- Ceritinib (Zykadia)
- Alectinib (Alecensa)
- Brigatinib (Alunbrig)
- Lorlatinib (Lorbrena)

These drugs can often shrink tumors in people whose advanced lung cancers have an *ALK* gene change. Although they can help after chemo has stopped working, they are often used instead of chemo in people whose cancers have an *ALK* gene rearrangement.

These drugs are taken as pills.

Side effects of ALK inhibitors

Common side effects of ALK inhibitors include:

- Nausea and vomiting
- Diarrhea
- Constipation
- Fatigue
- Changes in vision

Other side effects are also possible with some of these drugs. Some side effects can be severe, such as inflammation (swelling) in the lungs or other parts of the body, liver damage, nerve damage (*peripheral neuropathy*), and heart rhythm problems.

Drugs that target cells with ROS1 gene changes

About 1% to 2% of NSCLCs have a rearrangement in a gene called *ROS1*. This change is most often seen in people who have the adenocarcinoma subtype of NSCLC and

whose tumors are also negative for *ALK*, *KRAS* and *EGFR* mutations. The *ROS1* gene rearrangement is similar to the *ALK* gene rearrangement, and some drugs can work on cells with either ALK or ROS1 gene changes. Drugs that target the abnormal ROS1 protein include:

- Crizotinib (Xalkori)
- Ceritinib (Zykadia)
- Lorlatinib (Lorbrena)
- Entrectinib (Rozlytrek)

These drugs can often shrink tumors in people whose advanced lung cancers have a *ROS1* gene change. Crizotinib or ceritinib might be used as first treatment, instead of chemo, and lorlatinib may be used when crizotinib or ceritinib have stopped working. Entrectinib can be used in people with metastatic NSCLC that has a *ROS1* gene change.

These drugs are taken as pills.

Side effects of drugs that target cells with ROS1 gene changes

Common side effects of ROS1 inhibitors include:

- Dizziness
- Diarrhea
- Constipation
- Fatigue
- Changes in vision

Other side effects are also possible with some of these drugs. Some side effects can be severe, such as inflammation (swelling) in the lungs or other parts of the body, liver damage, nerve damage (peripheral neuropathy), and heart problems.

Drugs that target cells with BRAF gene changes

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:

Dabrafenib (Tafinlar) is a type of drug known as a BRAF inhibitor, which attacks

the BRAF protein directly.

• Trametinib (Mekinist) is known as a MEK inhibitor, because it attacks the related MEK proteins.

These drugs can be used together to treat metastatic NSCLC if it has a certain type of BRAF gene change.

These drugs are taken as pills or capsules each day.

Side effects of drugs that target cells with BRAF gene changes

Common side effects can include skin thickening, rash, itching, sensitivity to the sun, headache, fever, joint pain, fatigue, hair loss, nausea, and diarrhea.

Less common but serious side effects can include bleeding, heart rhythm problems, liver or kidney problems, lung problems, severe allergic reactions, severe skin or eye problems, and increased blood sugar levels.

Some people treated with these drugs develop skin cancers, especially <u>squamous cell skin cancers</u>². Your doctor will want to check your skin often during treatment and for several months after. You should also let your doctor know right away if you notice any new growths or abnormal areas on your skin.

Drugs that target cells with RET gene changes

In a small percentage of NSCLCs, the cells have certain changes in the *RET* gene that cause them to make an abnormal form of the RET protein. This abnormal protein helps the cells grow.

Selpercatinib (Retevmo) and **pralsetinib (Gavreto)** are drugs known as **RET inhibitors**. They work by attacking the RET protein. These drugs can be used to treat advanced NSCLC if the cancer cells have certain types of *RET* gene changes.

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

Side effects of RET inhibitors

Common side effects can include:

• Dry mouth

- Diarrhea or constipation
- High blood pressure
- Feeling tired
- Swelling in the hands or feet
- Skin rash
- High blood sugar levels
- Muscle and joint pain
- Low white blood cell, red blood cell, or blood platelet counts
- Changes in certain other blood tests

Less common but more serious side effects can include liver damage, lung damage, allergic reactions, changes in heart rhythm, bleeding easily, and problems with wound healing.

Drugs that target cells with MET gene changes

In some NSCLCs, the cells have changes in the *MET* gene that cause them to make an abnormal form of the MET protein. This abnormal protein helps the cells grow and spread.

Capmatinib (Tabrecta) and **tepotinib (Tepmetko)** are types of drugs known as a **MET inhibitors**. They work by attacking the MET protein. These drugs can be used to treat metastatic NSCLC if the cancer cells have certain types of *MET* gene changes.

Capmatinib is taken as pills, typically twice a day. Tepotinib is also taken as pills, but usually once a day.

Side effects of MET inhibitors

Common side effects can include:

- Swelling in the hands or feet
- Nausea or vomiting
- Feeling tired or weak
- Loss of appetite
- Constipation or diarrhea
- Changes in certain blood tests
- Joint and muscle pain

Less common but more serious side effects can include inflammation (swelling) or scarring in the lungs, which can make it hard to breathe, as well as liver damage.

Some people might become more sensitive to sunlight (or other sources of UV rays) while being treated with capmatinib, so it's important to protect yourself during treatment (for example, by using sunscreen or wearing clothes that cover your skin).

Drugs that target cells with *HER2* gene changes

In a small percentage of NSCLCs, the cancer cells have certain changes in the *HER2* gene that help them grow.

Trastuzumab deruxtecan (Enhertu) is a type of medicine known as an *antibody-drug conjugate (ADC)*. It's composed 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.

This drug can be used to treat NSCLC that can't be removed by surgery or that has spread, if the cancer cells have certain types of *HER2* gene changes, and if at least one other drug treatment has already been tried.

This drug is infused into a vein (IV). It is typically given once every 3 weeks.

Side effects of trastuzumab deruxtecan

This drug can cause **low blood cell counts**, which can increase a person's risk of infections and bleeding.

Other common side effects can include nausea, vomiting, diarrhea or constipation, loss of appetite, fever, feeling tired, and hair loss.

This drug can cause **serious lung disease** in some people, which might even be life threatening. It's very important to let your doctor or nurse know right away if you're having symptoms such as coughing, wheezing, trouble breathing, or fever.

This drug can also rarely cause **heart damage**. Before and during treatment with this drug, your doctor may test your heart function with an echocardiogram or a MUGA scan.

Drugs that target cells with NTRK gene changes

A very small number of NSCLCs have changes in one of the *NTRK* genes. Cells with these gene changes can lead to abnormal cell growth and cancer. **Larotrectinib** (Vitrakvi) and **entrectinib** (Rozlytrek) target and disable the proteins made by the *NTRK* genes. These drugs can be used in people with advanced lung cancer that is still growing despite other treatments and whose tumor has an *NTRK* gene change.

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

Side effects of drugs that target cells with NTRK gene changes

Common side effects include dizziness, fatigue, nausea, vomiting, constipation, weight gain, and diarrhea.

Less common but serious side effects can include abnormal liver tests, heart problems, and confusion.

More information about targeted therapy

To learn more about how targeted drugs are used to treat cancer, see <u>Targeted Cancer</u> <u>Therapy</u>³.

To learn about some of the side effects listed here and how to manage them, see Managing Cancer-related Side Effects⁴.

Hyperlinks

- 1. <u>www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 2. www.cancer.org/cancer/types/basal-and-squamous-cell-skin-cancer.html
- 3. www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html

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Immunotherapy for Non-Small Cell Lung

Cancer

- Immune checkpoint inhibitors
- More information about immunotherapy

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

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, <u>lab tests</u>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).

 Nivolumab can be used along with chemotherapy as a first treatment before surgery (known as neoadjuvant treatment) in some people with early-stage NSCLC.

- Pembrolizumab, atezolizumab, or cemiplimab can be used (sometimes with chemo) as part of the first treatment in some people with metastatic NSCLC.
- Nivolumab can be an option as part of the first treatment in some people with metastatic NSCLC, along with CTLA-4 inhibitor ipilimumab (Yervoy), which is described below. Similarly, durvalumab can be given along with the CTLA-4 inhibitor tremelimumab (Imjudo). Chemo is often given along with these treatments as well.
- Nivolumab, pembrolizumab, and atezolizumab can also be used in people with certain types of advanced NSCLC whose cancer starts growing again after chemotherapy or other drug treatments.
- For people with stage III NSCLC who cannot have surgery or chemotherapy with radiation, pembrolizumab or cemiplimab can be given as the first treatment.
- Durvalumab can be used in people with stage III NSCLC whose cancer cannot be removed with surgery and has *not* gotten worse after they have received chemotherapy with radiation (chemoradiation). The goal of treatment with this drug (also called **consolidation therapy**) is to keep the cancer from getting worse for as long as possible.
- Atezolizumab or pembrolizumab can be used in people with some earlier stages of NSCLC who have already been treated with surgery followed by chemotherapy.
 This known as adjuvant therapy.

All of these drugs are given as an intravenous (IV) infusion. 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 doctor or nurse right away if you have any of these symptoms while getting these drugs.

Autoimmune reactions: These drugs work by basically 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 health 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 chemo as well.

These drugs are given by intravenous (IV) infusion, usually once every 3 or 6 weeks.

Possible side effects

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.

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.

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 health 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.

More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see <u>Cancer Immunotherapy</u>².

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. www.cancer.org/cancer/managing-cancer/side-effects.html

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Palliative Procedures for Non-Small Cell Lung Cancer

- 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

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

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

Thoracentesis is a procedure done to drain the fluid. The doctor will numb an area in the lower back, and then place a hollow needle into the space between the ribs to drain the fluid around the lung. An ultrasound may be used to guide the needle into the fluid.

Pleurodesis

Pleurodesis is a procedure done to remove the fluid and keep it from coming back. The 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 Therapy¹.

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 <u>Palliative Care</u>².

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. www.cancer.org/cancer/managing-cancer/side-effects.html

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

- 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

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.

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. If your cancer is truly stage 0, these treatments should cure you.

Treating stage I NSCLC

If you have stage I NSCLC, <u>surgery</u> may be the only treatment you need. This may be done either by taking out the lobe of the lung that has the tumor (lobectomy) or by taking 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, location, or other factors), adjuvant chemotherapy (and possibly immunotherapy) after surgery may lower the risk that cancer will return. But doctors aren't always sure how to determine which people are likely to be helped by adjuvant treatment. New lab tests that look at the patterns of certain genes in the cancer cells may help with this.

After surgery, the removed tissue is checked to see if there are cancer cells at the edges of the surgery specimen (called **positive margins**). This could mean that some cancer has been left behind, so a second surgery might be done to try to ensure that all

the cancer has been removed. (This might be followed by chemotherapy as well.) Another option might be to use radiation therapy after surgery.

For stage I cancers that are 4 centimeters across, another treatment option is immunotherapy with nivolumab along with chemotherapy before surgery. Additional therapy after surgery might be needed depending on what is found at the time of surgery.

If you have serious health problems that prevent you from having surgery, you may get stereotactic body radiation therapy (SBRT) or another type of radiation therapy as your main treatment. Radiofrequency ablation (RFA) may be another option if the tumor is small and in the outer part of the lung.

Treating stage II NSCLC

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 adjuvant (additional) treatment with chemotherapy (chemo), possibly followed by adjuvant immunotherapy for up to a year. Another option is to treat with radiation, sometimes with chemo.

Even if positive margins are not found, adjuvant chemo (and possibly immunotherapy) might be recommended after surgery to try to destroy any cancer cells that might have been left behind. Newer lab tests now being studied may help doctors find out which patients need this adjuvant treatment and which are less likely to benefit from it.

For stage II cancers that are larger than 4 centimeters across, another treatment option is immunotherapy with nivolumab along with chemotherapy before surgery (known as *neoadjuvant therapy*). Additional therapy after surgery might be needed depending on what is found at the time of surgery.

For people whose cancer cells have certain mutations in the *EGFR* gene, adjuvant

treatment with the targeted drug osimertinib might be an option at some point as well.

If you have serious medical problems that would keep you from having surgery, you may get only radiation therapy as your main treatment.

Treating stage IIIA NSCLC

The initial treatment for stage IIIA NSCLC may include some combination of radiation therapy, chemotherapy (chemo), and/or surgery. For this reason, planning treatment for stage IIIA NSCLC often requires input from a medical oncologist, radiation oncologist, and a thoracic surgeon. Your treatment options depend on the size of the tumor, where it is in your lung, which lymph nodes it has spread to, your overall health, and how well you are tolerating treatment.

For patients who can tolerate it, treatment usually starts with chemo, often combined with radiation therapy (also called *chemoradiation*). Surgery may be an option after this if the doctor thinks any remaining cancer can be removed and the patient is healthy enough.

For certain stage IIIA cancers, another treatment option is immunotherapy with nivolumab along with chemotherapy first and then surgery. Additional therapy after surgery might be needed depending on what is found at the time of surgery.

In some cases, surgery may be an option as the first treatment. This is often followed by adjuvant chemo, which in turn might be followed by adjuvant immunotherapy for up to a year in some cases. Adjuvant radiation therapy might also be an option if it hasn't been given before. For people whose cancer cells have certain mutations in the *EGFR* gene, adjuvant treatment with the targeted drug osimertinib might be an option at some point as well.

For people who are not healthy enough for surgery, radiation therapy, which may be combined with chemo, is often used.

If surgery, radiation, and chemoradiation are not likely to be good treatment options, an immunotherapy drug such as pembrolizumab (Keytruda) or cemiplimab (Libtayo) may be considered as the first treatment.

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 <u>clinical trial</u>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 brain) is not common, but it can sometimes be treated (and even potentially cured) with surgery and/or radiation therapy to treat the area of cancer spread, followed by treatment of the cancer in the lung. For example, a single tumor in the brain may be treated with surgery or stereotactic radiation, or surgery followed by radiation to the

whole brain. Treatment for the lung tumor is then based on its T and N stages, and may include surgery, chemo, radiation, or some of these in combination.

NSCLC that has spread widely (stage IVB)

For cancers that have spread widely throughout the body, before any treatments start, your <u>tumor will be tested</u>⁴ for certain gene mutations (such as in the *KRAS*, *EGFR*, *ALK*, *ROS1*, *BRAF*, *RET*, *MET*, or *NTRK* genes). If one of these genes is mutated in your cancer cells, your first treatment will likely be a <u>targeted therapy</u> drug:

- For people whose cancer has the *KRAS G12C gene* change, a KRAS inhibitor such as sotorasib (Lumakras) or adagrasib (Krazati) might be used, after another drug has already been tried.
- For tumors that have the *ALK gene* change, an ALK inhibitor can often be the first treatment. Another ALK inhibitor can be used if one or more of these drugs stops working or is not well tolerated.
- For people whose cancers have certain changes in the *EGFR gene*, an EGFR inhibitor may be used as the first treatment (sometimes along with a targeted drug that affects new blood vessel growth).
- For people whose cancers have changes in the *ROS1 gene*, drugs such as crizotinib (Xalkori), entrectinib (Rozlytrek), or ceritinib (Zykadia) might be used.
- For people whose cancers have a certain change in the *BRAF gene*, a combination of the targeted drugs dabrafenib (Tafinlar) and trametinib (Mekinist) might be used.
- For people whose cancers have certain changes in the *RET gene*, selpercatinib (Retevmo) or pralsetinib (Gavreto) might be used.
- For people whose cancers have certain changes in the *MET gene*, capmatinib (Tabrecta) or tepotinib (Tepmetko) might be options.
- For people whose cancers have a change in the *NTRK gene*, larotrectinib (Vitrakvi) or entrectinib (Rozlytrek) may be an option.

Your tumor cells might also be tested for the **PD-L1 protein**. Tumors with higher levels of PD-L1 are more likely to respond to certain immunotherapy drugs (known as immune checkpoint inhibitors), which might be an option either alone or along with chemo.

For most other cancers that have spread, chemo is usually at least part of the main treatment, as long as the person is healthy enough for it. Often it is used along with other types of drugs:

• Chemo might be used along with an **immunotherapy drug** such

as pembrolizumab (Keytruda), atezolizumab (Tecentriq), or cemiplimab (Libtayo), in some situations. Another option might be a combination of immunotherapy drugs, such as nivolumab (Opdivo) along with ipilimumab (Yervoy), or durvalumab (Imfinzi) along with tremelimumab (Imjuno).

- For people who are not at high risk for bleeding (that is, they do not have squamous cell NSCLC and have not coughed up blood), the targeted drug bevacizumab
 (Avastin) might be given with chemo. Some people with squamous cell cancer might still be given bevacizumab, as long as the tumor is not near large blood vessels in the center of the chest. If bevacizumab is used, it is often continued even after chemo is finished.
- An option for people with squamous cell NSCLC is to get chemo along with the targeted drug necitumumab (Portrazza).

If the cancer has caused fluid buildup in the space around the lungs (a malignant pleural effusion), the fluid may be drained. If it keeps coming back, options include pleurodesis or placement of a catheter into the chest through the skin to let the fluid drain out. (Details of these are discussed in Palliative Procedures for Non-Small Cell Lung Cancer.)

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 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.

If cancer continues to grow during initial treatment such as radiation therapy, chemotherapy (chemo) may be tried. If a cancer continues to grow during chemo as the first treatment, second-line treatment most often consists of a single chemo drug such as docetaxel or pemetrexed, or targeted therapy. If a targeted drug was the first treatment and is no longer working, another targeted drug or combination chemo might be tried. For some people with certain types of NSCLC, treatment with an immunotherapy drug such as nivolumab (Opdivo), sometimes along with ipilimumab (Yervoy); pembrolizumab (Keytruda); or atezolizumab (Tecentriq) might be an option.

Smaller cancers that recur locally in the lungs can sometimes be retreated 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. Managing Cancer as a Chronic Illness⁷ talks more about this.

Hyperlinks

- 1. www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html
- 2. www.cancer.org/cancer/diagnosis-staging/tests/endoscopy/bronchoscopy.html
- 3. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html</u>
- 4. <u>www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html</u>
- 5. www.cancer.org/cancer/managing-cancer/advanced-cancer.html
- 6. www.cancer.org/cancer/survivorship/long-term-health-concerns/recurrence.html
- 7. <u>www.cancer.org/cancer/survivorship/long-term-health-concerns/cancer-as-a-chronic-illness.html</u>

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