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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:



- [Clinical Trials](#)

## Considering complementary, integrative, 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.

- [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 they 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 Cancer Knowledge Hub at 1-800-227-2345 and speak with one of our caring, trained cancer helpline specialists. Or, if you prefer, you can use our chat feature on cancer.org to

connect with one of our 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 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.

People who have advanced cancer and who are expected to live less than 6 months may want to consider hospice care. Hospice care is designed to provide the best possible quality of life for people who are near the end of life. You and your family are encouraged to talk with your doctor or a member of your supportive care team about hospice care options, which include hospice care at home, a special hospice center, or other health care locations. Nursing care and special equipment can make staying at home a workable option for many families.

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

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

## Ways to do lung surgery

There are 2 main ways to do lung surgery: open lung surgery (thoracotomy) and minimally invasive surgery. Minimally invasive surgery includes mainly 2 types: video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracoscopic surgery (RATS). With any of these surgeries, the goal could be to diagnose (to get more tissue for diagnosis), stage (to look at nearby lymph nodes for possible spread of cancer), and/or treat lung cancer (to remove all known cancer in the lung). All surgeries require general anesthesia, which puts you in a deep sleep.

### Open lung surgery (thoracotomy)

In a thoracotomy, the surgeon makes a large cut between the ribs. Where the cut is depends on which part of the lung needs to be removed. In general, the surgeon will spread the ribs to see the lung and nearby organs inside.

### Video-assisted thoracic surgery (VATS)

Video-assisted thoracoscopic surgery (VATS) is a procedure being used more frequently to treat early-stage lung cancers. It uses smaller incisions, typically has a shorter hospital stay and fewer complications than a thoracotomy.

Many 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 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.

### **Robotic-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, 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 [imaging tests](#)<sup>2</sup> (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.





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

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

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

## Types of ablation for lung cancer

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

## Ways to do ablation for lung cancer

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

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# Radiation Therapy for Non-Small Cell Lung Cancer





might be eligible for surgery.

- **Stereotactic radiosurgery (SRS)** isn't really surgery, but a type of stereotactic radiation therapy that is given in only one session. It can sometimes be used instead of or along with surgery for single tumors that have spread to the brain. In one version of this treatment, a machine focuses about 200 beams of radiation on the tumor from different angles over a few minutes to hours. Your head is kept in the same position with a rigid frame. In another version, a linear accelerator (a machine that creates radiation) that is controlled by a computer moves around your head to deliver radiation to the tumor from many different angles. These treatments can be repeated if needed.

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

### **Brachytherapy (internal radiation therapy)**

In people with NSCLC, [brachytherapy](#)<sup>2</sup> 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](#)<sup>3</sup>, but it may also be done during surgery. The radiation travels only a short distance from the source, limiting the effects on surrounding healthy tissues. The radiation source is usually removed after a short time. Less often, small radioactive “seeds” are left in place permanently, and the radiation gets weaker over several weeks.

### **Proton therapy**

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

## **Possible side effects of radiation therapy for NSCLC**

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

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

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

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

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

Radiation therapy to large areas of the brain can sometimes cause memory loss, headaches, or trouble thinking. Usually these symptoms are minor compared with those 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 Therapy](#)<sup>4</sup>.

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

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation/external-)

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2. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation/internal-radiation-therapy-brachytherapy.html)
  3. [www.cancer.org/cancer/diagnosis-staging/tests/endoscopy/bronchoscopy.html](http://www.cancer.org/cancer/diagnosis-staging/tests/endoscopy/bronchoscopy.html)
  4. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html)
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# Chemotherapy for Non-Small Cell Lung Cancer

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

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

## When is chemotherapy used?

Chemotherapy travels through the bloodstream and reaches most parts of the body. Not all people with non-small cell lung cancer (NSCLC) will need chemo, but depending on the cancer's [stage](#)<sup>1</sup> and other factors, chemo may be recommended in different situations:

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

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

## Chemotherapy drugs used to treat NSCLC

The chemo drugs most often used for NSCLC include:

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

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

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

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

## How is chemotherapy given?

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

Often, a slightly larger and sturdier IV is required in the vein system to administer chemo. They are known as [central venous catheters](#)<sup>3</sup> (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, or a clinical trial.

## 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 and weight loss
- 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 might last a long time in others.

Be sure to report any side effects you notice during chemo to your cancer care 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 keep the side effects from getting worse.

## More information about chemotherapy

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

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

## Hyperlinks

1. [www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/staging-nsclc.html](http://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/staging-nsclc.html)
2. [www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html)
3. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/tubes-lines-ports-catheters.html)
4. [www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html)
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## **Targeted Drug Therapy for Non-Small Cell Lung Cancer**

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

## When is targeted therapy used?

Targeted drugs work differently from standard [chemotherapy](#) (chemo) drugs. They sometimes work when chemo drugs don't, and they often have different side effects. At

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

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

## KRAS inhibitors

**How they work (mechanism of action):** In some NSCLCs, the cancer cells have changes in the *KRAS* gene that cause them to make an abnormal form of the KRAS protein. This abnormal protein helps the cancer cells grow and spread. About 1 in 8 people with NSCLC have a specific type of *KRAS* gene change called a **KRAS G12C mutation**. KRAS inhibitors attach to the KRAS G12C protein, which helps keep cancer cells from growing.

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

NSCLCs with this mutation are often resistant to other targeted drugs, such as EGFR inhibitors (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 target cells with either an **exon 19** or **exon 21** mutation: 156 mg / GS914 qd ( ) T1006u0.g

## 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)** for NSCLCs that have certain mutations (S768I, L861Q, T790M, D790Y, G790S, G790V, G790A, G790E, G790L, G790F, G790C, G790G, G790H, G790I, G790K, G790M, G790N, G790P, G790Q, G790R, G790S, G790T, G790V, G790W, G790X, G790Y, G790Z, G790AA, G790AB, G790AC, G790AD, G790AE, G790AF, G790AG, G790AH, G790AI, G790AJ, G790AK, G790AL, G790AM, G790AN, G790AO, G790AP, G790AQ, G790AR, G790AS, G790AT, G790AU, G790AV, G790AW, G790AX, G790AY, G790AZ, G790BA, G790BB, G790BC, G790BD, G790BE, G790BF, G790BG, G790BH, G790BI, G790BJ, G790BK, G790BL, G790BM, G790BN, G790BO, G790BP, G790BQ, G790BR, G790BS, G790BT, G790BU, G790BV, G790BW, G790BX, G790BY, G790BZ, G790CA, G790CB, G790CC, G790CD, G790CE, G790CF, G790CG, G790CH, G790CI, G790CJ, G790CK, G790CL, G790CM, G790CN, G790CO, G790CP, G790CQ, G790CR, G790CS, G790CT, G790CU, G790CV, G790CW, G790CX, G790CY, G790CZ, G790DA, G790DB, G790DC, G790DD, 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**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 in a gene called *ALK*. This change is often seen in people who don't smoke (or 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 inhibit this ALK protein are called **ALK inhibitors** and are taken as an oral pill.

### **Examples of ALK inhibitors:**

- **Third-generation ALK inhibitor [Lorlatinib (Lorbrena)] and second-generation ALK inhibitors [alectinib (Alecensa), brigatinib (Alunbrig), ceritinib (Zykadia), and ensartinib (Ensacove)]** are often the preferred first treatment for advanced NSCLC with the ALK rearrangement mutation. These later generation ALK inhibitors tend to get into the brain better than crizotinib, a first-generation ALK inhibitor.
- **Alectinib (Alecensa)** can be given to patients with early stage ALK-positive NSCLC in the adjuvant setting (after the lung tumor has been removed).
- **First-generation ALK inhibitor: Crizotinib (Xalkori)** was the first ALK inhibitor approved for advanced NSCLC with an *ALK* rearrangement. It is still given in certain situations.

### **Side effects of ALK inhibitors:**

- **Common side effects:** Vision changes, nausea, vomiting, diarrhea, swelling in

hands and/or feet, tiredness, muscle soreness, rash, cough, nerve damage (peripheral neuropathy), and changes in lab values.

- **Rare, but serious side effects:** Liver damage; a lung condition called interstitial lung disease (ILD)/pneumonitis; changes in heart rhythm; and harm to a fetus.

## ROS1 inhibitors

**How they work (mechanism of action):** 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. These drugs, called **ROS1 inhibitors**, can often shrink tumors in people whose advanced lung cancers have a *ROS1* gene change. They are taken as a pill.

### 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

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

#### Side effects of RET inhibitors:

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

## MET inhibitors

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

#### Examples of MET inhibitors:

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

#### Side effects of MET inhibitors:

- **Common side effects:** Nausea, vomiting, diarrhea, tiredness, swelling in hands and/or feet, muscle and joint pain, low blood cell counts, or changes in other blood tests.
- **Rare, but serious side effects:** A lung condition called **interstitial lung disease (ILD)/pneumonitis**; liver damage; harm to a fetus; 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 to the HER2 protein on cancer cells, bringing the chemo directly to them. It can be used to treat NSCLC with HER2 mutations if you've already had at least one other type of drug treatment.
- **Ado-trastuzumab emtansine (Kadcyla)** is also a HER2-targeted ADC. It can be used to treat HER2-mutated NSCLC in certain situations.
- **Zenocutuzumab-zbco (Bizengri)** is a bispecific antibody that binds to HER2 and HER3 and prevents a protein called neuregulin 1 (NRG1) from binding to HER3. It can be used to treat NSCLC with a NRG1 gene fusion mutation, if you've already had at least one other type of drug treatment.

### Side effects of HER2 inhibitors:

- **Common side effects:** Low white blood cell, red blood cell, and platelet counts; tiredness; hair loss; nausea and vomiting; muscle and joint pain; and changes in other blood tests.
- **Rare, but serious side effects, specific to fam-trastuzumab deruxtecan:** Changes in heart function and a severely low white blood cell count, which increases your risk of infection.

## TRK inhibitors

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

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

### Examples of TRK inhibitors:

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

### Side effects of *NTRK* inhibitors:

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

## More information about targeted therapy

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

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

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html)
2. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)

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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,



# **Immunotherapy for Non-Small Cell Lung Cancer**

- [More information about immunotherapy](#)

## Immune checkpoint inhibitors

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

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

### PD-1/PD-L1 inhibitors

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

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

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

All of these drugs are given as intravenous (IV) infusions. Depending on the drug, they might be given every 2, 3, 4, or 6 weeks. Atezolizumab can also be given (as **Tecentriq Hybreza**) as an injection under the skin (subcutaneously) over several minutes, typically once every 3 weeks.

### ***Possible side effects***



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

Other, more serious side effects occur less often.

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

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

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

## **CTLA-4 inhibitors**

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

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

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

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

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

## More information about immunotherapy

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

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

## Hyperlinks

1. [www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/how-diagnosed.html)
2. [www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html)
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## Tumor Treating Fields (TTF) Therapy for Non-small Cell Lung Cancer

Researchers have found that exposing some types of cancer cells to alternating electric fields, also known as **tumor treating fields** (or **TFields**), can interfere with the cells' ability to grow and spread.

A wearable device known as **Optune Lua** is a TFields treatment that creates such electric fields. It is an option to help treat some people with non-small cell lung cancer (NSCLC).

- [When might TFields be used to treat NSCLC?](#)
- [How is TFields therapy given?](#)
- [Possible side effects of TFields therapy](#)

## When might TFields be used to treat NSCLC?

Optune Lua can be used along with either an [immune checkpoint inhibitor](#) or with the [chemotherapy](#) drug docetaxel to treat some people with metastatic NSCLC that has grown during or after treatment with chemotherapy.

## How is TFields therapy given?

For this treatment, the chest and/or back is shaved (if needed), and pads containing sets of electrodes are placed on the skin, usually 2 on the chest and 2 on the back.

The electrodes are attached to a battery pack (kept in a backpack) and are worn for most of the day - typically at least 18 hours. They create mild electric currents that are thought to affect cancer cells more than normal cells.

## Possible side effects of TFields therapy

Side effects of the device are usually limited to the electrode sites. They can include:

- Skin irritation
- Allergic reactions
- Local warmth and tingling sensations
- Muscle twitching
- Infections
- Breakdown of the skin (ulcers)

## References

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# Palliative Procedures for Non-Small Cell Lung Cancer

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

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

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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**

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

the tumor. The doctor then aims the laser beam at the tumor to burn it away. This treatment can usually be repeated, if needed. You are usually asleep (under general anesthesia) for this type of treatment.

### Stent placement

If a lung tumor has grown into an airway and is causing problems, sometimes a bronchoscope is used to put a hard silicone or metal tube called a stent in the airway to help keep it open. This is often done after other treatments such as PDT or laser therapy.

### More information about palliative care

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

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

### Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation/photodynamic-therapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation/photodynamic-therapy.html)
2. [www.cancer.org/cancer/managing-cancer/palliative-care.html](http://www.cancer.org/cancer/managing-cancer/palliative-care.html)
3. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)

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

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

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

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

## Treating occult cancer

For these cancers, malignant cells are seen on sputum cytology, but no obvious tumor can be found with bronchoscopy or imaging tests. They are usually early-stage cancers. [Bronchoscopy](#)<sup>2</sup> 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

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





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)**

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treatment choice. Localth, treatments such or laser therapPDT,ery or g bxaac eatmou.

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.



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

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