



What you need to know about...

squamous cell lung cancer





foreword

About LUNGevity

LUNGevity is the largest national lung cancer-focused nonprofit, changing outcomes for people with lung cancer through research, education, and support.

About the LUNGevity PATIENT EDUCATION SERIES

LUNGevity has developed a comprehensive series of materials for patients/survivors and their caregivers, focused on understanding how lung cancer develops, how it can be diagnosed, and treatment options. Whether you or someone you care about has been diagnosed with lung cancer, or you are concerned about your lung cancer risk, we have resources to help you.

The medical experts and lung cancer survivors who provided their valuable expertise and experience in developing these materials all share the belief that well-informed patients make their own best advocates.

In addition to this and other brochures in the LUNGevity patient education series, information and resources can be found on LUNGevity's website at www.LUNGevity.org, under "About Lung Cancer" and "Support & Survivorship."

This patient education booklet was produced through charitable donations from:



table of contents

01 Understanding Squamous Cell Lung Cancer	2
What is squamous cell lung cancer?	2
Diagnosis of squamous cell lung cancer.....	3
How is squamous cell lung cancer diagnosed?	3
Stages of lung cancer.....	9
Biomarker profile.....	16
02 Treatment Options for Squamous Cell Lung Cancer	18
What are currently approved treatment options for squamous cell lung cancer?	18
Surgery	19
Radiation therapy.....	23
Chemotherapy.....	25
Angiogenesis inhibitors	28
Immunotherapy.....	30
What clinical research study (clinical trial) treatment options are available for squamous cell lung cancer?	32
Immunotherapy.....	32
Targeted cancer therapy	32
New approaches to existing treatments	34
Finding a clinical trial that might be right for you.....	34
03 Managing Symptoms and Side Effects.....	37
04 Glossary	39
05 My Healthcare Team.....	47
06 Notes	50

introduction

Squamous cell lung cancer, also called squamous cell carcinoma of the lung, accounts for about 30% of all lung cancers. This type of lung cancer tends to be found in the middle of the lungs. There are numerous treatment options available to people affected by squamous cell lung cancer, and doctors are working hard to develop and improve these treatments.

This brochure will help you:

- Learn about squamous cell lung cancer
- Understand the treatment options available for squamous cell lung cancer
- Consider whether participating in a clinical trial might be right for you
- Understand how to manage the side effects associated with lung cancer treatment

YOU'LL FIND A GLOSSARY TOWARD THE END OF THIS BROCHURE.

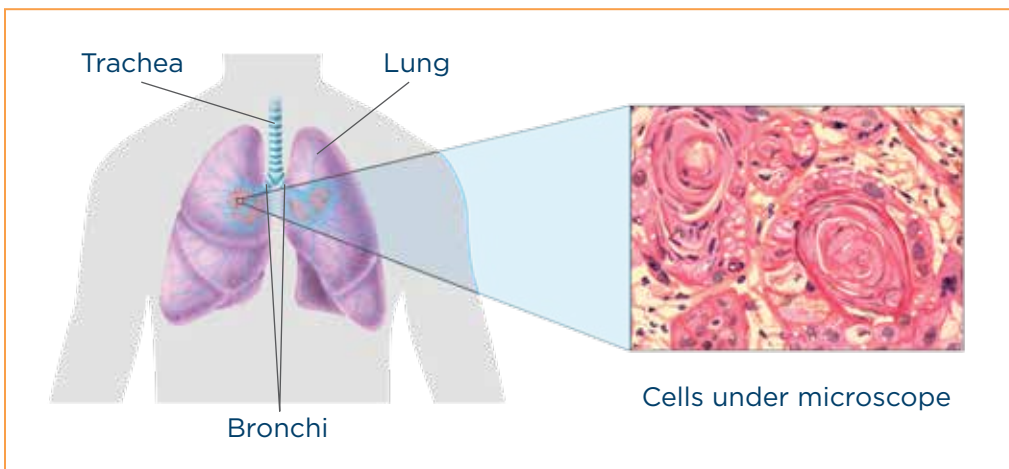
Words included in the glossary appear **blue** the first time that they are used in the text.

01 understanding squamous cell lung cancer

What is squamous cell lung cancer?

Squamous cell lung cancer, or squamous cell carcinoma of the lung, is one type of **non-small cell lung cancer (NSCLC)**. It is also called **epidermoid carcinoma**. This type of lung cancer begins in the squamous cells—thin, flat cells that look like fish scales when seen under a microscope. They line the inside of the airways in the lungs.

SQUAMOUS CELL LUNG CANCER



Squamous cells are also found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the lining of the digestive tract. Only squamous cell carcinoma that begins in the lungs is considered lung cancer.

Squamous cell lung **tumors** usually occur in the central part of the lung or in one of the main airway branches (left or right bronchus). The tumor's location is responsible for symptoms, such as cough, trouble breathing, chest pain, and blood in the **sputum**. If the tumor grows to a large size, a **chest X-ray** or computed tomography (CT or CAT) scan may detect a cavity in the lung. A cavity is a gas- or fluid-filled space within a tumor mass or **nodule** and is a classic sign of squamous cell lung cancer. Squamous cell lung cancer can spread to multiple sites, including the brain, spine and other bones, adrenal glands, and liver.

Squamous cell carcinoma makes up about 30% of all lung cancers. It is more strongly associated with smoking than any other type of non-small cell lung cancer. Other risk factors for squamous cell lung cancer include age, family history, and exposure to secondhand smoke, mineral and metal dust, **asbestos**, or **radon**.

Diagnosis of squamous cell lung cancer

How is squamous cell lung cancer diagnosed?

Your doctors may use many different tests to diagnose lung cancer and determine whether it has spread to other parts of the body. Some can also help to decide which treatments might work best. The steps and tests used in diagnosing squamous cell lung cancer include:

- Imaging tests
- Laboratory tests
- Biopsies

Not all of these will be used for every person. The approaches used for an individual will depend on your medical history and condition, symptoms, location of the nodule(s), and other test results.

Imaging tests

Imaging tests create pictures of the inside of the body using **X-rays**, magnetic fields, sound waves, or radioactive particles.

Imaging tests cannot confirm that a person has lung cancer. However, they provide a lot of information to help put the whole picture together for the doctor. Imaging tests may be done before a diagnosis of lung cancer, during treatment for lung cancer, and after treatment. They are done for a number of reasons, including:

- To get more specific information about a suspicious area that might be cancerous
- To determine how far cancer may have spread
- To find out if treatment has been effective
- To monitor for possible signs of cancer coming back after treatment

Various imaging types are available.

Chest X-ray

A chest X-ray takes pictures of the bones and organs in the chest. A chest X-ray is often the first test a doctor uses to look for a mass when symptoms are more general.

Computed tomography (CT or CAT) scan

Computed tomography (CT) uses a computer linked to an X-ray machine to make detailed pictures of the inside of the body. Unlike a conventional X-ray, which takes one picture, a CT scanner takes multiple pictures as it rotates around the patient, in order to get

images from different angles. A CT scan can provide specific information about the size, shape, and position of masses or nodules in the lung. It also can help find enlarged **lymph nodes** or masses in other organs that might be caused by the spread of lung cancer. A **low-dose CT (LDCT) scan** is most commonly used to look for lung cancer and follow up on changes in lung nodules.

Magnetic resonance imaging (MRI) scan

Magnetic resonance imaging (MRI) scans provide detailed pictures of areas inside the body by using radio waves and strong magnets. MRI is used in lung cancer to find out whether the cancer has spread to the brain or spinal cord.

Positron emission tomography (PET) scan

A positron emission tomography (PET) scan is used to help determine whether an abnormal area on a chest X-ray or CT scan may be cancer. It is also used to check whether cancer has spread to lymph nodes, bones, or other organs in the body. For a PET scan, a form of radioactive sugar is given **intravenously** to the patient. Because cancer cells grow rapidly, they absorb more of the sugar than most healthy cells. A scanner then creates images of the inside of the body to show what “lights up” with the sugar.

Some hospitals and radiology centers have a special scan called a positron emission tomography-computed tomography (PET-CT) scan that is able to do a PET and a CT scan at the same time. This allows the doctor to compare areas of radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Bone scan

A bone scan also uses a small amount of a radioactive **tracer**, which is injected into a vein. The tracer settles in areas of the bone that have suffered injury, such as injury caused by cancer. The scanner then creates a picture of the skeleton. The injured parts look darker. Since PET scans also pick up cancer in the bones, they are usually used in place of a bone scan in lung cancer.

Laboratory tests

Doctors may also order one or more kinds of laboratory tests to help determine if a person has lung cancer.

Blood tests

Blood tests do not diagnose lung cancer, but they provide a doctor with information on a patient's overall health and on how well the organs of the body are functioning. For example, **blood chemistry tests** are used to check whether a patient's liver or kidneys are working well. The results from these blood tests help the doctor decide on treatment options.

Sputum cytology

If lung cancer is suspected, testing of the sputum for cancer cells may be performed. The patient may be asked to cough up **phlegm** so a **pathologist** can look at it under a microscope. A pathologist can locate cancer cells in the mucus, but most of the time there are not enough cells to make a final diagnosis of lung cancer. Sputum cytology is more likely to help diagnose lung cancers that start in the major airways of the lung, such as most squamous cell lung cancers. It does not provide information on how far the disease has spread, so if it shows lung cancer, other diagnostic tests must be performed.

Biopsies

There are many different ways doctors can obtain tissue to find out if a person has lung cancer and, if so, which type of lung cancer. Depending on which method is used, the doctor can also determine whether the cancer has spread to lymph nodes or other organs. The tissue or fluid that is removed is sent to a pathologist, who examines it and then issues a **pathology report** with his or her findings.

Having enough tissue available for **molecular testing** (which you may also hear called **biomarker** testing, genetic testing, or **mutation** testing) can also be an important consideration. Several targeted cancer therapies for squamous cell lung cancer are available through clinical trials. These tests can help identify whether your cancer is a match for any of them. Before a biopsy is done, the patient should speak with his or her doctor about having the tumor sample molecularly profiled.

Bronchoscopy

During a bronchoscopy, a surgeon or **pulmonologist** inserts a bronchoscope (a thin, flexible tube) into the patient's mouth or nose, down the **trachea**, or windpipe, and into the lungs. A light and a camera at the end of the tube allow the doctor to look for abnormal areas. Tiny tools can be passed down through the bronchoscope to take samples of tissue.

Transthoracic needle biopsy

If a suspicious mass is in the **periphery** of the lungs, a needle can be passed through the chest wall with CT or **ultrasound** guidance to sample tissue or remove suspicious fluid. A specialist called an **interventional radiologist** performs the procedure. When a small needle is inserted through the skin of the chest wall, it is called a **fine needle aspiration (FNA)**. If a larger sample is needed, a **core biopsy** is done with a larger needle.

Note: A core biopsy is usually preferred for molecular testing.

Thoracentesis

If a patient has a **pleural effusion**, doctors can perform a thoracentesis to see if it was caused by cancer that spread to the linings of the lungs. In this procedure, a doctor numbs the skin and then inserts a hollow needle between the ribs to drain the fluid, which can then be sent to the pathologist.

Thoracoscopy

A surgeon makes a small incision in the skin of the chest wall and inserts a special instrument with a small video camera on the end to examine the lungs and inside of the chest and to remove samples of tissue. This procedure is also referred to as video-assisted thoracoscopic surgery (VATS) and is performed in the operating room under general anesthesia.

A thoracoscopy can be used:

- To sample tumors and lymph nodes on the outer parts of the lungs
- To see if lung cancer has spread to the spaces between the lungs and the chest wall
- To check if the tumor has spread to nearby lymph nodes and organs
- As part of the treatment to remove part of a lung in some early-stage lung cancers

Mediastinoscopy

This procedure is performed to get biopsies from the **mediastinum**.

A surgeon makes a small incision in the front of the neck at the top of the breastbone. Then a thin, hollow tube with a light and a lens for viewing is inserted through the incision, along the front edge of the windpipe. Instruments are passed through the tube to take samples from the lymph nodes along the trachea. A mediastinoscopy requires general anesthesia and is performed in an operating room, but typically as an outpatient procedure.

Stages of lung cancer

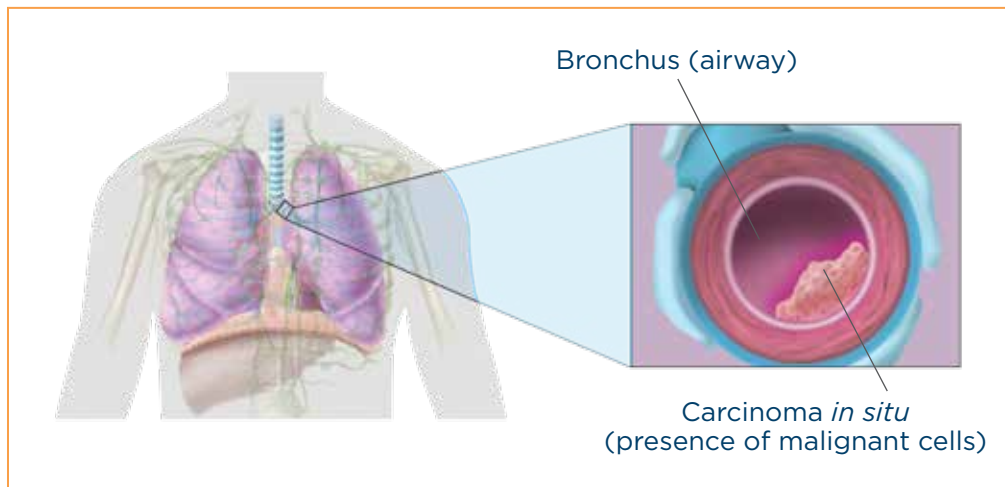
Staging is a way of describing where the cancer is located, if or where it has spread, and whether it is affecting other parts of the body. Doctors use diagnostic tests to determine the cancer's stage, so staging may not be complete until all of the tests are finished. Knowing the stage helps the doctor to recommend a treatment plan.

The stage of non-small cell lung cancer is described by a number, zero through four (Roman numerals I through IV are usually used).

Stage 0

Also called *in situ* disease, meaning the cancer is “in place” and has not invaded nearby tissues and spread outside the lung.

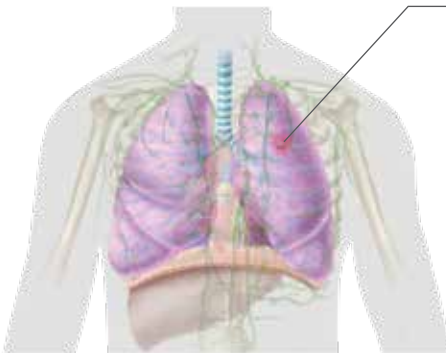
LUNG CANCER: STAGE 0



Stage one (I)

A small lung cancer tumor that has not spread to any lymph nodes. This tumor may be surgically removed, if the patient is healthy enough. Stage one (I) is divided into two sub-stages: stage IA and stage IB, based on the size of the tumor. Smaller tumors, such as those less than 3 centimeters (cm) wide, are stage IA, and slightly larger ones (more than 3 cm but less than 5 cm wide) are stage IB.

LUNG CANCER: STAGE IA

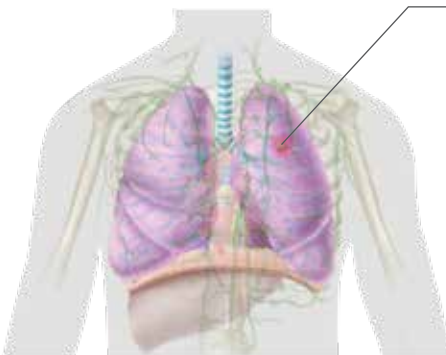


Tumor **less than 3 cm**
in the greatest dimension

AND

Cancer **has not spread**
to any lymph nodes

LUNG CANCER: STAGE IB



Tumor **more than 3 cm**
but less than 5 cm in the
greatest dimension

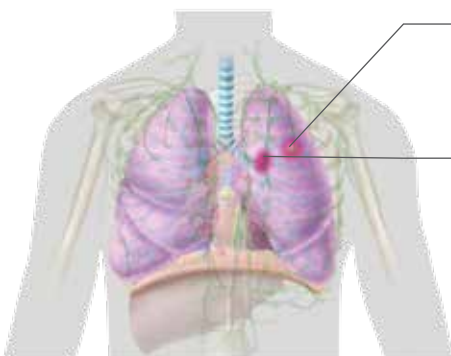
AND

Cancer **has not spread**
to any lymph nodes

Stage two (II)

Stage two (II) is divided into two sub-stages: stage IIA and stage IIB. Stage IIA is characterized by a small tumor (less than 5 cm wide) that has spread to the nearby lymph nodes, or by a tumor that is larger than 5 cm but less than 7 cm wide that has not spread to the nearby lymph nodes.

LUNG CANCER: STAGE IIA

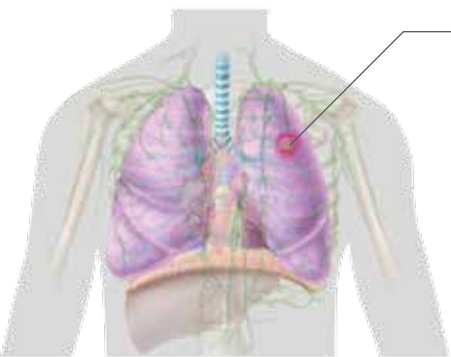


Tumor **less than 5 cm**
in the greatest dimension

AND

Cancer **has spread** to
regional lymph nodes

OR



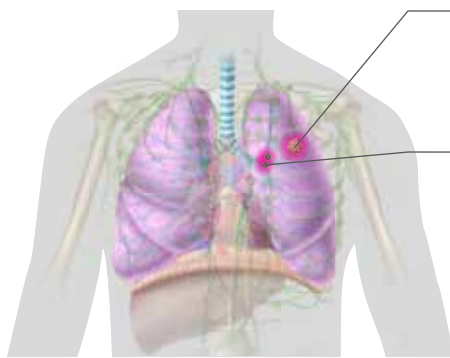
Tumor **more than 5 cm**
but less than 7 cm in the
greatest dimension

AND

Cancer **has not spread**
to any lymph nodes

Stage IIB is characterized by a tumor that is larger than 5 cm but less than 7 cm wide that has spread to the lymph nodes, or by a larger tumor (more than 7 cm wide) that may or may not have invaded nearby structures in the lung but has not spread to the lymph nodes.

LUNG CANCER: STAGE IIB

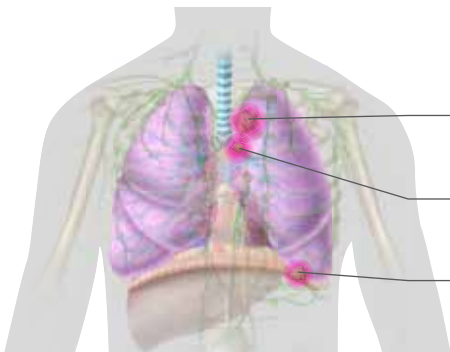


Tumor **more than 5 cm but less than 7 cm** in the greatest dimension

AND

Cancer **has spread** to regional lymph nodes

OR



Cancer **has not spread** to any lymph nodes

AND

Tumor **more than 7 cm**

OR

Tumor in the **main bronchus**

OR

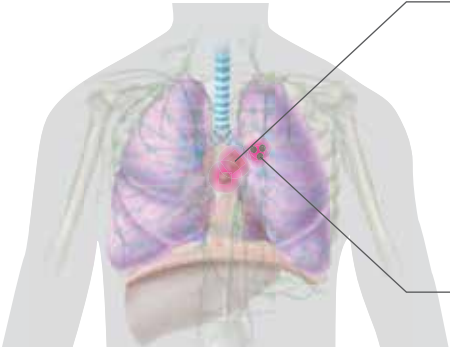
Tumor **directly invades diaphragm** (or any other nearby organs)

Sometimes stage II tumors can be removed with surgery, and other times other treatments are needed.

Stage three (III)

Stage three (III) cancers are classified as either stage IIIA or stage IIIB. Many stage IIIA cancers and nearly all stage IIIB cancer tumors are difficult, and sometimes impossible, to remove through surgery alone. For example, the lung cancer may have spread to the lymph nodes located in the center of the chest, or the tumor may have invaded nearby structures in the lung. Patients with stage III cancers will usually need a combination of at least two treatments, such as surgery, chemotherapy, or radiation.

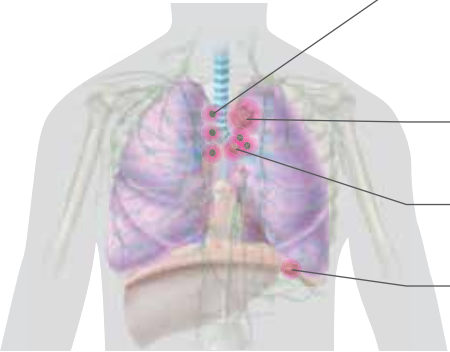
LUNG CANCER: STAGE IIIA



Tumor of any size that **invades the heart** (and/or the great vessels, mediastinum, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe)

AND

Cancer **has spread** to regional lymph nodes



Cancer **has spread** to lymph nodes in center of the chest and outside and inside the lung

AND

Tumor **more than 7 cm**

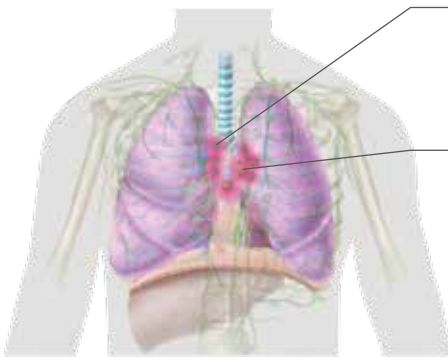
OR

Tumor in the **main bronchus**

OR

Tumor **directly invades diaphragm** (or any other nearby organs)

LUNG CANCER: STAGE IIIB

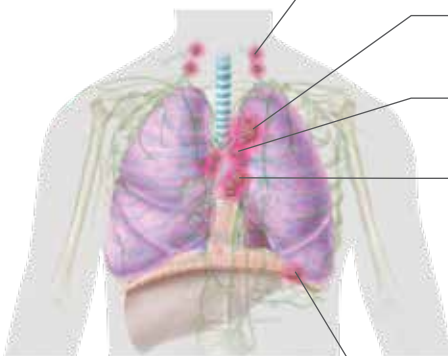


Cancer **has spread** to lymph nodes in center of the chest and inside the lung

AND

Tumor of any size that **invades the heart** (and/or the great vessels, mediastinum, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe)

OR



Cancer **has spread** to contralateral lymph nodes above the clavicle and inside and outside of lungs

AND

Tumor **more than 7 cm**

OR

Tumor in the **main bronchus**

OR

Tumor of any size that **invades the heart** (and/or the great vessels, mediastinum, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe)

OR

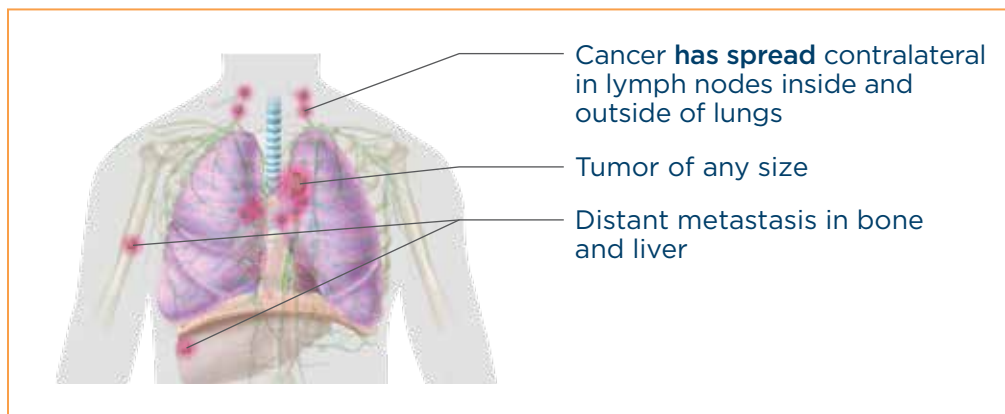
Tumor directly **invades diaphragm** (or any other nearby organs)

Stage four (IV)

The stage four (IV) lung cancer has spread to either:

- The opposite lung
- The fluid surrounding the lung or the heart
- Distant parts of the body by way of the bloodstream

LUNG CANCER: STAGE IV



Once released in the blood, lung cancer can spread anywhere in the body, but it is more likely to spread to the brain, bones, liver, and adrenal glands. It is classified as stage IVA when the cancer has spread within the chest and IVB when it has spread outside of the chest.

In general, surgery is not successful for stage IV lung cancers. Lung cancer can also be impossible to remove if it has spread to the lymph nodes above the collarbone, or if the cancer has grown into vital structures within the chest, such as the heart, large blood vessels, or the main breathing tubes leading to the lungs. In cases like these, the doctor will recommend other treatment options.

Recurrent lung cancer is lung cancer that has come back after treatment. If there is a recurrence, the cancer may need to be staged again (called restaging) using the system above.

Usually, patients with recurrent cancer are treated like patients with stage IV cancer.

Note: You may also hear about the TNM classification, because the stages mentioned previously have been developed based on a combination of T (the size of the primary tumor), N (whether and how regional lymph nodes are affected by the cancer), and M (whether there is distant **metastasis**).

Biomarker profile

Lung cancer describes many different types of cancer that start in the lung or related structures. There are two different ways of describing what kind of lung cancer a person has:

- Histology—what the cells look like under a microscope. Squamous cell lung cancer is a histological subtype of non-small cell lung cancer. Other subtypes of NSCLC include **adenocarcinoma**, **large cell carcinoma**, and some rarer types. **Small cell lung cancer (SCLC)** is the other major type of lung cancer
- Biomarker profile (also called molecular, genetic, or signature profile)—the genetic characteristics or mutations, as well as any other unique biomarkers, found in a person's cancer that allowed the cancer to grow

Note: Genetic biomarkers can be:

- Acquired—present only in the tumor and not passed on to children
- Inherited—present in all cells of the body and passed on to children

Most of the biomarkers that are helpful to making treatment decisions in lung cancer are acquired. These are sometimes also called somatic mutations.

A person's lung cancer may or may not have one of the many known mutations. And, two patients may be treated with two different therapies because of their own cancer's specific mutation or lack of a mutation.

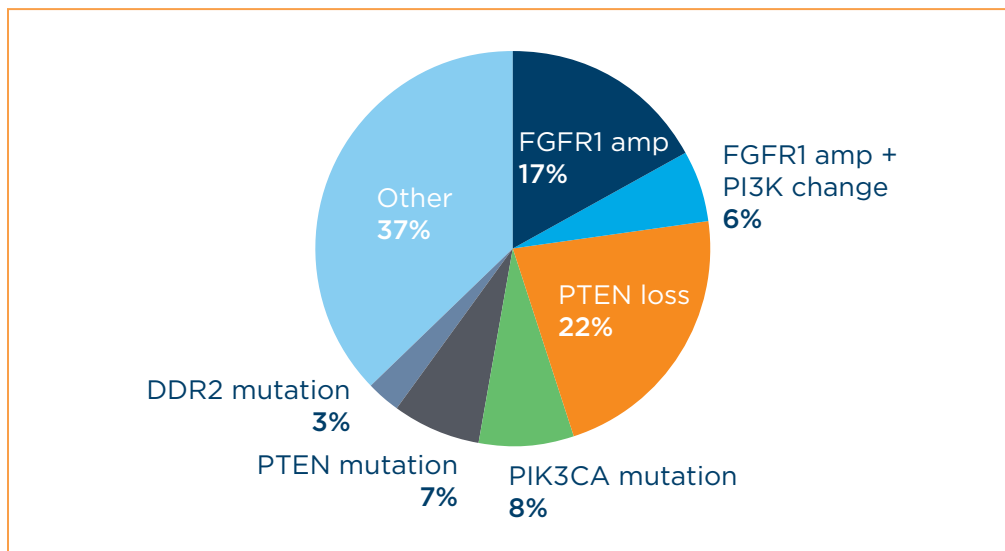
Non-genetic biomarkers are also important and can help determine the best treatment. In particular, your doctor may want to look at a **protein** called **PD-L1**, which may be helpful in choosing immunotherapies.

Researchers are making progress in understanding mutations in squamous cell lung cancer. While no targeted therapies are approved yet for use in squamous cell lung cancer, several are being studied in clinical trials.

The decision to test for mutations should be made together by you and your **oncologist**.

Here are the mutations that have been identified at this time.

MOLECULAR PROFILE OF SQUAMOUS CELL LUNG CANCER



02 treatment options for squamous cell lung cancer

What are currently approved treatment options for squamous cell lung cancer?

There are a number of currently approved treatment options for squamous cell lung cancer. These include:

- Surgery
- Chemotherapy
- Immunotherapy
- Radiation therapy
- Angiogenesis inhibitors

The treatments chosen for a specific patient's lung cancer will depend on the stage of the cancer and the patient's overall health and preferences. The stage indicates where the cancer is in the lung and whether it has spread to other parts of the body.

It is important to note that a patient's age has never been useful in predicting whether that patient will benefit from treatment. A patient's age should never be used as the only reason for deciding what treatment is best. This is especially true for older patients who are otherwise physically fit and have no medical problems besides lung cancer.



QUESTIONS TO DISCUSS WITH YOUR HEALTHCARE TEAM WHEN PLANNING YOUR TREATMENT APPROACH:

- What are my treatment options?
- What treatment plan do you recommend for me?
- What is our goal with these treatment(s)?
To eliminate my cancer? To slow its growth?
To treat symptoms?
- How long will my treatment take?
- When do I need to decide on my treatment plan?
- What are the risks and potential side effects of the different treatment options?
- Will my insurance cover these treatment options?

The following is more information about treatment options that are currently approved for squamous cell lung cancer.

Surgery

Lung cancer that is only in one lung and that has not spread to other organs is often treated with surgery, if the patient can tolerate it. Patients should discuss with their healthcare team whether surgery is the best option for them. Lung cancer surgery is a complex operation that can have serious consequences. Therefore, it should be done by a thoracic surgeon—a surgeon specially trained in operating on people with lung cancer. Patients often seek a second opinion with a thoracic surgeon when considering surgery.

Lung cancer surgery may be used in combination with chemotherapy and/or radiation therapy. Chemotherapy and/or radiation therapy

may be given either before surgery (**neoadjuvant**), or after surgery (**adjuvant**) in order to eliminate any small amount of cancer that was not detected and removed by surgery.

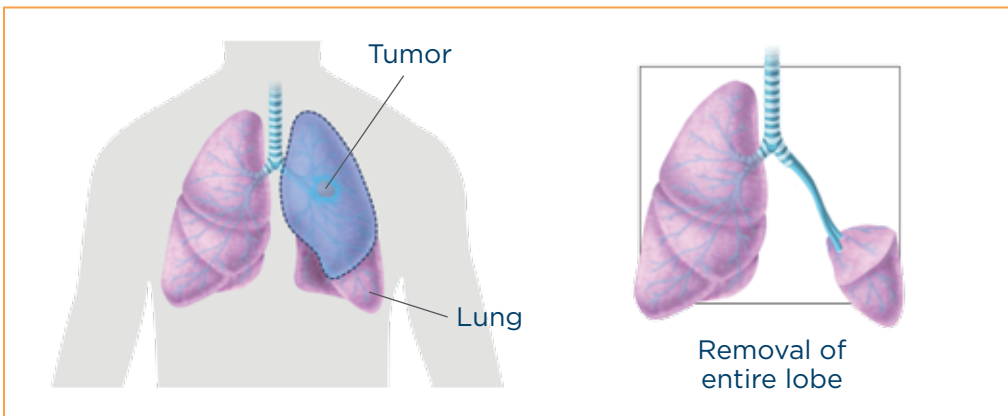
The type of surgery the doctor recommends depends on the size and location of the tumor and on how well the patient's lungs are working. If a patient's lungs are healthy, a lobectomy is most commonly the preferred operation. Removing more of the lung tissue may provide a better chance to cure the lung cancer.

Other types of surgeries may also be performed to treat lung cancer that is only in one lung and has not spread to other organs. Removal of part or all of a lung will decrease your lung function. Talk to your healthcare team about what you can do before and after surgery to manage that for best quality of life. Pulmonary rehabilitation, for example, may be an option for you.

Lobectomy

Lobectomy is the removal of one of the five lobes of the lung. When non-small cell lung cancer is detected at a very early stage, a lobectomy is the most effective type of surgery, even when the lung tumor is very small.

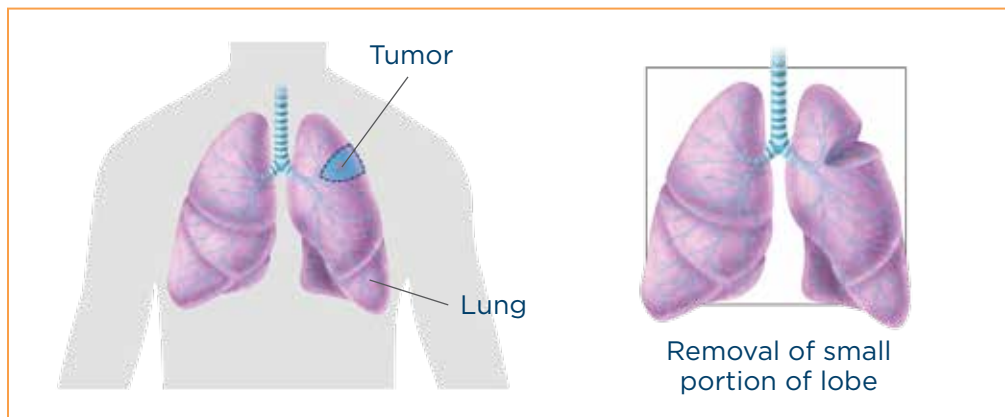
LOBECTOMY



Wedge resection

In a wedge resection, the surgeon removes the tumor and a small rim of normal tissue surrounding it. This is done if the surgeon is unable to remove an entire lobe of the lung. A wedge resection may also be performed if the patient has a peripheral lesion.

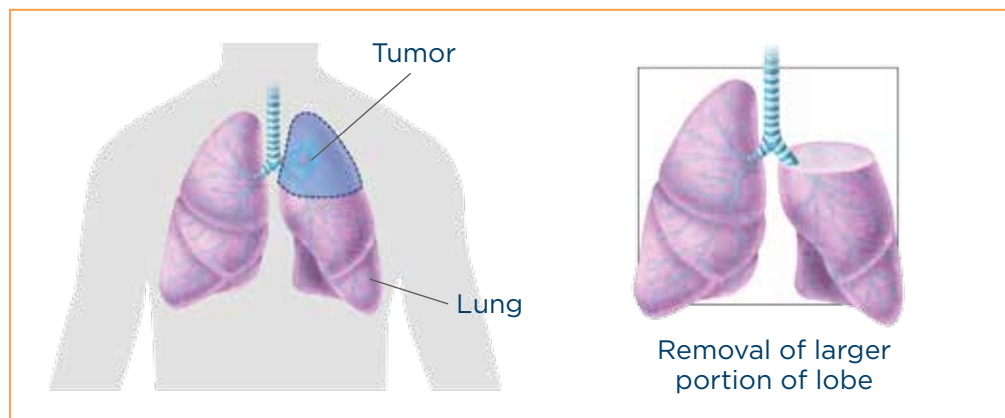
WEDGE RESECTION



Segmentectomy

A segmentectomy removes one of the small segments within the lobes of the lung that contains a cancer. The amount of lung tissue

SEGMENTECTOMY

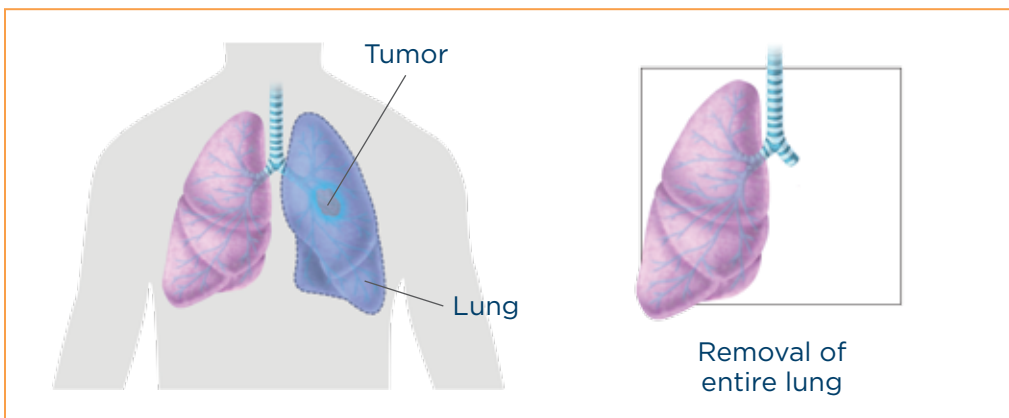


removed is between what is removed in a lobectomy and in a wedge resection. Like wedge resection, segmentectomy is recommended only for treating stage I lung cancers that are less than 2 cm wide and for elderly patients or those with other medical conditions that make removing the entire lobe dangerous.

Pneumonectomy

Pneumonectomy is the surgical removal of the entire lung. This type of surgery is sometimes required if the tumor is very large or is close to the center of the chest.

PNEUMONECTOMY



Sleeve resection

This surgery is used for tumors that involve the large airways. The tumor and a portion of the airway are removed and the ends of the airway are rejoined so the remaining lobes can be left in place. A surgeon may do this operation instead of a pneumonectomy to preserve more lung function.

SLEEVE RESECTION



Radiation therapy

Radiation therapy is a type of cancer treatment that uses high-powered energy beams, such as X-rays, to kill cancer cells. Depending on the individual patient's situation, radiation therapy may be used when trying to cure cancer, control cancer growth, or relieve symptoms caused by the tumor, such as pain. Radiation treatment can be given as the main treatment in early-stage squamous cell lung cancer if surgery is not possible. In that case, it may be given either with or without chemotherapy. In some cases, radiation therapy is used before or after surgery.

Radiation therapy is administered by a radiation oncologist, a doctor who specializes in using radiation treatments to treat cancer.

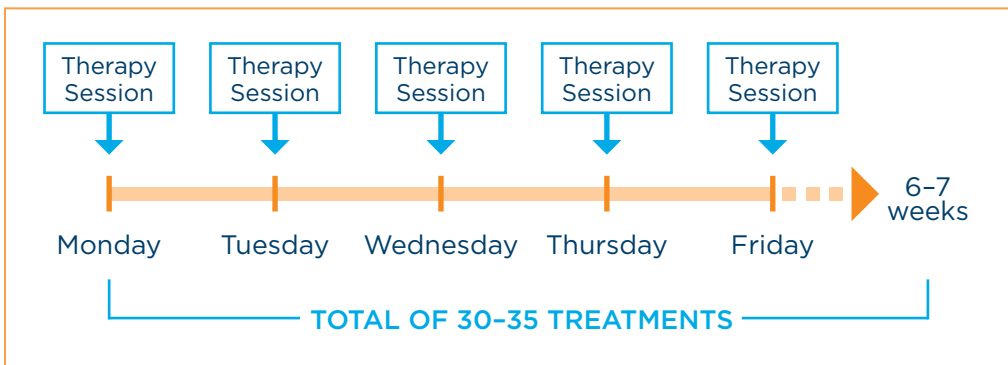
Radiation therapy can be roughly classified by the position of the radiation source. Radiation can come from a machine outside the body (external beam radiation therapy, or EBRT) or from radioactive material placed in the body (internal radiation therapy, more commonly called brachytherapy). EBRT is more commonly used to treat lung cancer, so we will discuss it in more detail.

For EBRT, the radiation oncologist takes careful measurements to determine the proper dose of radiation and the correct angles for aiming the radiation beams. Treatment is similar to getting an X-ray, but the radiation dose is stronger.

Each radiation therapy session is usually painless and only lasts a few minutes.

A radiation therapy schedule usually consists of a specific number of treatments given over a set period of time. For example, a standard course for lung cancer may consist of sessions 5 days per week (Monday-Friday) for 6 to 7 weeks, for a total of 30 to 35 treatments.

RADIATION THERAPY TO TREAT LUNG CANCER



In patients with early-stage non-small cell lung cancer, in which there is only a single small nodule in the lung without any spread to nearby lymph nodes, a type of EBRT called **stereotactic body radiation therapy (SBRT)**, or stereotactic ablative radiotherapy (SABR), is typically given. SBRT is the standard of care for patients who cannot be treated surgically.

Various devices can be used to deliver these treatments, including Accuray's CyberKnife and TomoTherapy, as well as linear accelerators by Varian (e.g., Novalis Tx, Trilogy, and TrueBeam) and Elekta (e.g., Versa HD). Your radiation oncologist can tell you which device their facility uses.

In more advanced stages of non-small cell lung cancer, EBRT can be given alone or along with chemotherapy as the main treatment. EBRT can be used prior to surgery, as neoadjuvant therapy, typically along with chemotherapy, to try to shrink a lung tumor to make it

easier to operate on. It is also used after surgery, alone or along with chemotherapy, to try to kill any small deposits of cancer that surgery may have missed.

Both external beam and internal radiation therapies are used to shrink tumors to relieve symptoms of advanced lung cancer, such as pain, bleeding, trouble swallowing, cough, and shortness of breath.

Common side effects from radiation treatment for lung cancer may include:

- Tiredness
- Sunburn-like skin changes, such as dryness, itching, or peeling
- Hair loss (in the area where the radiation enters the body)
- Sore throat and trouble swallowing
- Cough, difficulty breathing, and shortness of breath
 - These symptoms can develop as “radiation pneumonitis.” When it happens, it usually happens months after radiation was finished and may require anti-inflammatory medication
- Loss of appetite and weight loss
- Nausea and vomiting (when the treated area is near the stomach)

Most of these side effects go away within a few weeks after radiation treatment is done.

Chemotherapy

Chemotherapy is a word that describes many different cancer treatments that are given in drug form. Here, chemotherapy is used specifically to describe intravenous drugs that are designed to kill cancer cells. We will discuss other drug therapy options, like targeted therapies, angiogenesis inhibitors, and immunotherapy, in different

sections. Your doctor will help to select the best treatment based on your medical history and fitness.

Chemotherapy is used in two main ways for patients with lung cancer:

- For those patients with cancer that involves the lung and some lymph nodes (stages II or III), chemotherapy is used to improve the chance of cure.

For patients with stage II or III lung cancer who have had a surgery for their lung cancer, patients typically receive chemotherapy after surgery for a defined period of time (usually 4 cycles, which can last anywhere from 12 to 16 weeks). This treatment after surgery is called adjuvant therapy. If their doctors recommend it, patients sometimes receive this chemotherapy before surgery, as neoadjuvant. In either case, platinum-based chemotherapy is usually used.

In other patients with stage III lung cancer, chemotherapy is combined with radiation therapy. Many different chemotherapies can be combined with radiation therapy.

- For patients with stage IV lung cancer, chemotherapy is used to shrink the cancer, reduce symptoms from cancer, and prolong life.

As with other types of non-small cell lung cancer, patients with squamous cell carcinoma are often given two chemotherapy agents as **first-line therapy**. Which drugs are chosen will depend in part on the patient's overall health and ability to tolerate different possible side effects.

Most often, the platinum-based drugs, cisplatin or carboplatin, are combined with another chemotherapy drug. Two combinations that have been shown to work particularly well in squamous cell lung cancer are:

- Cisplatin and gemcitabine
- Carboplatin and nab-paclitaxel (Abraxane®)

Another type of chemotherapy was recently approved as first-line treatment of people with metastatic squamous cell lung cancer. The drug, necitumumab (Portrazza™), was approved to be used in combination with cisplatin and gemcitabine.

Whereas squamous cell lung cancer has not been shown to have **epidermal growth factor receptor (EGFR)** mutations, this drug seems to work by blocking EGFR protein expression, which **is** seen in squamous cell lung cancer.

General side effects of chemotherapies as a group are listed below.

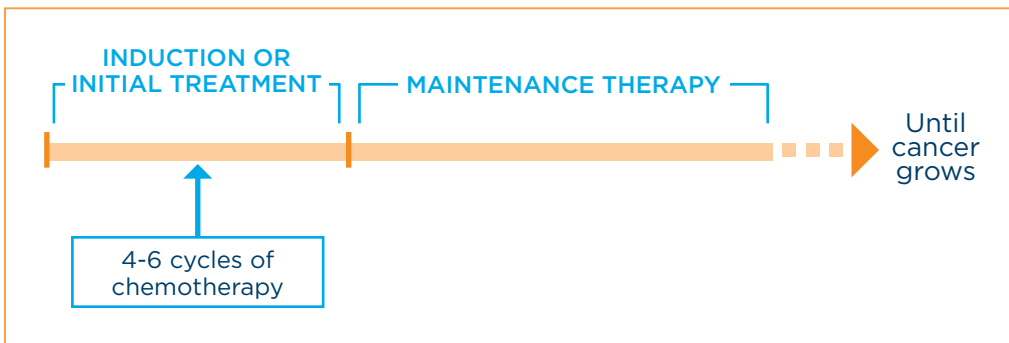
Each drug has a different set of most common side effects. It's important to remember that just because a side effect is possible doesn't mean that it will happen to you. Some side effects don't happen with some drugs. In general, these side effects include:

- Diarrhea
- Constipation
- Tiredness
- Hair loss
- Dehydration
- Nausea and vomiting
- Skin and nail changes
- Muscle or joint pain
- Numbness, tingling, pain, or weakness in the hands or feet
- Low red blood cell or platelet count
- Loss of appetite or ability to taste food
- Swelling in the hands or feet

In addition to the side effects commonly seen with cisplatin and gemcitabine, necitumumab-treated patients in clinical trials were more likely to have rashes and low levels of magnesium in the blood. Levels of calcium, magnesium, and potassium should be monitored during and after treatment.

You may hear the term **maintenance therapy**. This is sometimes used in people with late-stage (stage IV) lung cancer whose cancer shrank or stopped growing after initial chemotherapy treatment. The goal of maintenance therapy is to help keep the cancer from growing again. The benefit of maintenance therapy is still being studied in squamous cell lung cancer, as discussed in the “Clinical Trials” section.

MAINTENANCE THERAPY TO TREAT LUNG CANCER



Another approach after induction/initial therapy is to stop treatment. Then the cancer is carefully monitored by the oncologist, and **second-line treatment** is given if there is **disease progression**.

There are a number of post-first-line therapy options for squamous cell lung cancer, such as chemotherapy, with or without the angiogenesis inhibitor ramucirumab, or immunotherapy.

Your doctor will help you select the best treatment based on your medical history and fitness.

Angiogenesis inhibitors

As the body develops and grows, it makes new blood vessels to supply all of the cells with blood. This process is called angiogenesis. When the new blood vessels provide oxygen and nutrients to cancer cells, they help the cancer cells grow and spread.

Angiogenesis inhibitors help stop or slow the growth or spread of tumors by stopping them from making new blood vessels. The tumors then die or stop growing because they cannot get the oxygen and nutrients they need. The inhibitors work by blocking the cancer cells' **vascular endothelial growth factor (VEGF)** receptors.

Angiogenesis inhibitors are not effective given alone, but are most effective when combined with additional therapies, usually chemotherapy. Angiogenesis inhibitors do not kill tumors; they instead may prevent tumors from growing. Therefore, this type of therapy may need to be administered over a long period.

Currently, two angiogenesis inhibitors are FDA-approved for patients with non-small cell lung cancer, but only one of them is approved for treating squamous cell lung cancer:

- Ramucirumab (Cyramza®): Approved in combination with docetaxel for the second-line treatment of patients with metastatic non-small cell lung cancer, including squamous cell lung cancer. Ramucirumab is considered a VEGF receptor 2 **antibody**. The most common side effects are high blood pressure, diarrhea, fatigue, **neutropenia**, bleeding from the nose, and **stomatitis**/mucosal inflammation
- The other angiogenesis inhibitor, bevacizumab (Avastin®), is **not** an option for squamous cell lung cancer

Note: Bevacizumab is thought to have a different way of blocking VEGF than ramucirumab and is approved only in non-squamous cell lung cancer. It has been found to cause life-threatening and fatal bleeding in the lungs of patients with squamous cell carcinoma. The high risk of bleeding is thought to be due to the central location of these tumors.

Immunotherapy

Immunotherapy aims to strengthen the natural ability of the patient's immune system to fight cancer. Some squamous cell carcinomas may grow and spread by avoiding the immune response that would otherwise help to keep cancer cells in check. Instead of targeting the person's cancer cells directly, immunotherapy attempts to trigger a person's natural immune system to recognize cancer cells and selectively target and kill them.

Currently, there are two immunotherapy drugs available outside clinical trials for people with non-small cell lung cancer, including squamous cell lung cancer. Many more are being studied for lung cancer at this time.

Nivolumab (Opdivo®) and pembrolizumab (Keytruda®) are both FDA-approved for people who have:

- Metastatic non-small cell lung cancer
- Disease progression during or after treatment with platinum-based chemotherapy

Note: Platinum-based chemotherapies include carboplatin and cisplatin.

Pembrolizumab's approval also requires the following:

- The patient's tumors must express PD-L1
- And, for patients with **anaplastic lymphoma kinase (ALK)**-positive or EGFR-positive non-small cell lung cancer, the lung cancer should have progressed on an approved ALK or EGFR inhibitor before they are treated with pembrolizumab

Both drugs belong to the type of immunotherapy called **immune checkpoint inhibitors**. The immune checkpoint inhibitors work by targeting and blocking the fail-safe mechanisms of the immune system. Their goal is to block the immune system from limiting itself, so they can target the cancer cells.

The most common side effects seen with these immunotherapy drugs are:

- Trouble breathing
- Cough
- Fatigue
- Musculoskeletal pain
- Nausea
- Constipation
- Decreased appetite

A side effect sometimes seen with immune checkpoint inhibitors is pneumonitis, which is inflammation of the lung tissues that may lead to difficulty breathing if not treated early and correctly.

Pneumonitis and some of the other side effects seen with immune checkpoint inhibitors are related to “turning on” the immune system, which then may also attack some healthy cells and cause inflammation. These are all relatively rare, but can be serious if left untreated. Other examples of this include:

- **Arthritis**
- **Nephritis**
- **Colitis**
- Inflammation of the **endocrine glands**, like the thyroid
- **Hepatitis**

Note: It’s important to let your doctor or nurse know if you are experiencing any problems while on treatment, so they can sort out whether the side effects are related to treatment or not. It is also important to let your doctor or nurse know if you have a history of an autoimmune disease. This is because immune checkpoint inhibitors may make autoimmune diseases worse.

More information on immunotherapy can be found in LUNgevity’s Immunotherapy brochure.

What clinical research study (clinical trial) treatment options are available for squamous cell lung cancer?

Clinical trials are an important option for people thinking about lung cancer treatments because the newest treatment approaches are being tested in them. A lot of promising research is going on now in squamous cell lung cancer. *More information on clinical trials can be found in LUNgevity's Clinical Trials brochure.*

The following describe some, but by no means all, of the clinical trials available for people with squamous cell lung cancer.

Immunotherapy

Three main types of immunotherapy are currently being studied in people with non-small cell lung cancer:

- Immune checkpoint inhibitors by themselves or combined with other drugs
- **Therapeutic cancer vaccines**
- **Adoptive T cell transfer**

Nivolumab, pembrolizumab, and other immunotherapies continue to be studied in clinical trials for all types and stages of lung cancer.

Targeted cancer therapy

Drugs that target certain DNA mutations in a tumor are called targeted cancer therapies. As discussed earlier, a number of these mutations have been found in squamous cell lung cancer. Currently, researchers are still working to develop drugs that target most of these mutations.

Note that ALK rearrangements and EGFR mutations, which are seen in adenocarcinoma, have not been seen in pure squamous cell lung cancer. Cases where they seem to occur in squamous cell lung cancer may be **adenosquamous carcinoma** or misdiagnosed solid adenocarcinoma. In those cases, ALK inhibitors or EGFR inhibitors may be a treatment option.



CLINICAL TRIALS STUDYING TARGETED CANCER THERAPIES FOR SQUAMOUS CELL CARCINOMA INCLUDE:

- The Lung-MAP clinical trial is focused on patients with recurrent stage IIIB–IV squamous cell lung cancer. This large research study looks at DNA from each patient’s tumor for changes that may be driving the growth of that cancer. Based on those results, patients are matched with one of a number of new treatments being researched. Lung-MAP treatments are being studied as second-line therapy or later. More information can be found at www.lung-map.org
- New drugs targeting mutations that are frequently seen in squamous cell carcinoma, including: PIK3CA, PTEN, FGFR1, DDR2, AKT1, CCND1, and CDK6

New approaches to existing treatments

In addition to new treatments, doctors are also trying new approaches to existing treatments. Some examples include:

- Chemotherapy agents given in combination with radiation therapy, surgery, immunotherapy, and targeted cancer therapy
- The chemotherapy nab-paclitaxel (Abraxane®) given as maintenance therapy in patients with advanced squamous cell lung cancer to keep the cancer from coming back
- Radiation therapy given in combination with chemotherapy and surgery—doctors are also looking at which type of radiation therapy is best to use in squamous cell carcinoma. For example, there is a study comparing stereotactic body radiation therapy with **proton therapy**

Finding a clinical trial that might be right for you

If you are considering participating in a clinical trial, start by asking your healthcare team whether there is one that might be a good match for you in your geographic area. In addition, there are several other resources to help you find one that may be a good match.

Information about available clinical trials may be found through the resources detailed on the next page.

In addition, if you are interested in a specific drug or other treatment that is being developed, you can often find information about studies for that drug on the website of the company developing it.



RESOURCES TO HELP YOU NAVIGATE YOUR CLINICAL TRIALS SEARCH:

- **EmergingMed:**
www.emergingmed.com/networks/LUNgevity
 - LUNgevity partners with this **free** clinical trials matching service to help you with the decision of whether to participate in a clinical trial
 - EmergingMed helps you identify lung cancer clinical trials for which you may be eligible
 - Clinical trial navigators are available Monday through Friday from 8:30am to 6:30pm ET at 800-698-0931
- **LUNgevity Clinical Trial Finder:**
www.LUNgevity.org/clinicaltrialfinder
 - Makes it easier to find available clinical trials by type of lung cancer and geographic location, and provides information and links to the medical centers at which these studies are taking place
 - This site gets its information from www.clinicaltrials.gov
- **Lung Cancer Master Protocol (Lung-MAP):**
www.lung-map.org
 - For patients with squamous cell carcinoma
 - Lung-MAP is a collaboration of many research sites across the country. They use a unique approach to match patients to one of several drugs being developed
- **U.S. National Institutes of Health:**
www.clinicaltrials.gov
 - Includes publicly and privately supported clinical studies of human participants conducted in the U.S. and 186 other countries around the world in all different disease states

continued >

RESOURCES TO HELP YOU NAVIGATE YOUR CLINICAL TRIALS SEARCH (CONTINUED):

- **National Cancer Institute (NCI):**
www.cancer.gov/clinicaltrials/search
 - This site has all of the 12,000+ clinical trials in the U.S. in all cancer types
- **Coalition of Cancer Cooperative Groups:**
www.cancertrialshelp.org/cancer-trial-search
 - This site gets its information from www.clinicaltrials.gov, but organizes the search and results in a different way



03 managing symptoms and side effects

As already noted, lung cancer treatments can cause side effects. Some cancer therapy side effects are temporary, while others can be more long-term. When you start a new treatment, you should discuss with your doctor which potential side effects to expect, what can be done to manage them, and which side effects are serious and need to be reported immediately. Often, drugs can be prescribed to help reduce many of these side effects.

In addition to the side effects of lung cancer treatment, lung cancer itself can result in a number of symptoms.

The most common symptoms of lung cancer itself include:

- Pain in the chest, upper back, or shoulder
- Cough that doesn't go away or gets worse
- Coughing up blood or rust-colored sputum
- Frequent infections such as bronchitis and pneumonia
- Weight loss and loss of appetite
- Hoarseness
- New wheezing
- Shortness of breath
- Fatigue and weakness

To help reduce the severity and duration of most side effects and alleviate the cancer's symptoms, you may want to request palliative care, also called "supportive care" or "symptom management." There is sometimes confusion about the difference between palliative care and hospice care. Hospice care is a form of palliative care given only to patients whose life expectancy is six months or less, while palliative care in general is an extra layer of support that can be initiated alongside other standard medical care.

The goal of palliative care is to improve the patient's quality of life while he or she is receiving standard medical care by anticipating, preventing, and treating suffering. Palliative care can be provided from the time of diagnosis, and also addresses the emotional, social, practical, and spiritual issues that a patient faces. Scientific evidence is starting to emerge that shows that palliative care may actually help patients live longer.

Note: Your oncology team can answer your questions about palliative care.

04 glossary

Adenocarcinoma—A type of non-small cell lung cancer that usually develops in the cells lining the lungs. It is the most common type of lung cancer seen in non-smokers

Adenosquamous carcinoma—A type of cancer that contains two types of cells: squamous cells (thin, flat cells that line certain organs) and gland-like cells

Adjuvant—Cancer treatment given after the primary treatment in order to kill unseen cancer cells or to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, or biological therapy

Adoptive T cell transfer—Therapy that involves removing some of a patient’s own immune system cells—often altering and increasing their ability to recognize and kill cancer cells—growing billions of them in the laboratory, and infusing the cultured cells into the patient. The idea is to provide an invading force of immune cells that can attack tumors at a level that the immune system is not capable of doing on its own. Also called “adoptive T cell therapy”

ALK—See anaplastic lymphoma kinase

Anaplastic lymphoma kinase (ALK)—A gene that the body normally produces but, when it fuses with another gene, produces an abnormal protein that leads to cancer cell growth

Antibody—A protein made by B cells in response to an antigen. Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen

Arthritis—A disease that causes inflammation and pain in the joints

Asbestos—A group of minerals that take the form of tiny fibers. Asbestos has been used as insulation against heat and fire in buildings. Loose asbestos fibers breathed into the lungs can cause several serious diseases, including lung cancer and malignant mesothelioma (cancer found in the lining of lungs, chest, or abdomen)

Biomarker—A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease

Blood chemistry tests—A common panel of blood tests that measures the amounts of electrolytes and other chemicals made in the body. It provides information on how the body's organs, such as kidneys, liver, and heart, are functioning

Chest X-ray—A type of high-energy radiation that can go through the body and onto film, making pictures of areas inside the chest, which can be used to diagnose disease

Colitis—An illness that causes pain and swelling in the colon

Core biopsy—The removal of a tissue sample with a wide needle for examination under a microscope. Also called “core needle biopsy”

Disease progression—Continued growth or spread of cancer

EGFR—See epidermal growth factor receptor

Endocrine gland—A gland (for example, the thyroid or the pituitary) that produces an endocrine secretion

Epidermal growth factor receptor (EGFR)—The protein found on the surface of some cells and to which epidermal growth factor binds, causing the cells to divide. It is found at abnormally high levels on the surface of many types of cancer cells, so these cells may divide excessively in the presence of epidermal growth factor

Epidermoid carcinoma—Cancer that begins in squamous cells. Also called “squamous cell carcinoma.” When it starts in the lungs, it is considered a type of non-small cell lung cancer

Fine needle aspiration (FNA)—The removal of tissue or fluid with a thin needle for examination under a microscope, usually to determine if cancer is present or what the cancer cell type is

First-line treatment or therapy—The first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. When used by itself, first-line therapy is the one accepted as the best treatment. If it doesn’t cure the disease or it causes severe side effects, other treatment may be added or used instead

Genetic mutation—Any change in the gene sequence of a cell. Mutations may be caused by mistakes during cell division, or they may be caused by exposure to gene-damaging agents in the environment. Certain mutations may lead to cancer or other diseases

Hepatitis—Disease of the liver causing inflammation. Symptoms include an enlarged liver, fever, nausea, vomiting, abdominal pain, and dark urine

Immune checkpoint inhibitors—Agents that target the pathways that tumor cells use to evade recognition and destruction by the immune system

Interventional radiologist—A medical doctor who is specially trained to use minimally invasive image-guided procedures to diagnose and treat diseases, with the goal of minimizing risk to the patient and improving health outcomes

Intravenous (IV)—Into or within a vein. Intravenous usually refers to a way of giving a drug or other substance through a needle or tube inserted into a vein. Also called “IV”

Large cell carcinoma—Lung cancer in which the cells are large and look abnormal when viewed under a microscope

Low-dose CT (LDCT) scan—A newer form of CT scan that uses less radiation than a standard chest CT and takes less than one minute to complete. It continuously rotates in a spiral motion and takes several three-dimensional, very detailed X-rays of the lungs. This type of CT uses no dyes and no injections, and requires nothing to swallow by mouth. Also known as “low-dose spiral (or helical) CT scan”

Lymph node, lymph gland—A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph, the clear fluid that carries cells to fight infections and other diseases, and they store lymphocytes (white blood cells)

Maintenance therapy—Treatment that is given to help keep cancer from growing after it has shrunk or stabilized following initial therapy. It may include treatment with drugs, vaccines, or antibodies that kill cancer cells, and it may be given for a long time

Mediastinum—The space in the chest that is between the lungs. The organs in this area include the heart and its large blood vessels, the trachea, the esophagus, the thymus, and lymph nodes, but not the lungs

Metastasis—The spread of cancer from the primary site, or place where it started, to other places in the body

Molecular testing (biomarker, genetic, or mutation testing)—

Analyzing DNA to look for a change in the DNA that may indicate an increased risk for developing a specific disease or disorder. Also known as “genetic testing,” “biomarker testing,” or “mutation testing”

Mutation—See genetic mutation

Neoadjuvant—Treatment given prior to the main treatment in order to shrink a tumor. Examples of neoadjuvant therapy include chemotherapy and/or radiation therapy prior to surgery

Nephritis—Acute or chronic inflammation of the kidney caused by infection, degenerative process, or vascular disease

Neutropenia—A condition in which there are fewer than normal neutrophils (a type of white blood cell), leading to increased susceptibility to infection

Nodule—A growth or lump that may be malignant (cancer) or benign

Non-small cell lung cancer (NSCLC)—A group of lung cancers that are named for the kinds of cells found in the cancer and how the cells look under a microscope. The three main types of non-small cell lung cancer are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. Non-small cell lung cancer is the most common kind of lung cancer

Oncologist—A doctor who specializes in treating cancer. Some oncologists specialize in a particular type of cancer or cancer treatment. For example, a thoracic oncologist specializes in treating lung, esophageal, pleural, mediastinal, and chest wall tumors. A radiation oncologist specializes in treating cancer with radiation

Pathologist—A doctor who identifies diseases by studying cells and tissues under a microscope or with other equipment

Pathology report—The description of cells and tissues made by a pathologist based on what is seen under a microscope. This is sometimes used to make a diagnosis of lung cancer or another disease. May also be referred to in short form as “path report” or even “the path”

PD-L1 (programmed death ligand 1)—Part of the immune system mechanism that keeps T cells from functioning

Periphery—The outermost part or region within a precise boundary

Phlegm—Thick mucus made by the cells lining the upper airways and lungs

Pleural effusion—Fluid around the lungs

Protein—A molecule made up of amino acids that is needed for the body to function properly. Proteins are the basis of body structures, such as skin and hair, and of other substances such as enzymes, cytokines, and antibodies

Proton therapy—A type of radiation therapy that uses streams of protons (tiny particles with a positive charge) to kill tumor cells. This type of treatment can reduce the amount of radiation damage to healthy tissue near a tumor. It is used to treat cancers of the head and neck and organs, such as the brain, eye, lung, spine, and prostate

Pulmonologist—A doctor who specializes in lung disease

Radon—A radioactive gas that is released by uranium, a substance found in soil and rock. Breathing in too much radon can damage lung cells and may lead to lung cancer

Second-line treatment or therapy—Treatment that is usually started after the first set of treatments doesn’t work, has stopped working, or has side effects that are not tolerated

Small cell lung cancer (SCLC)—A fast-growing cancer that forms in tissues of the lung and can spread to other parts of the body. Named “small” for how the cancer cells look under a microscope

Sputum—Mucus and other matter brought up from the lungs by coughing

Stereotactic body radiation therapy (SBRT)—A type of external beam radiation therapy that uses special equipment to position a patient and precisely deliver extremely high doses of radiation to the tumor while decreasing the dose to healthy tissue nearby. Instead of giving small doses of radiation each day for several weeks, SBRT can be given in two to five treatments

Stomatitis—Inflammation or irritation of the mucous membranes in the mouth

T cell, T lymphocyte—A type of white blood cell. T cells are part of the immune system and develop from stem cells in the bone marrow. They help protect the body from infection and may help fight cancer

Therapeutic cancer vaccine—A type of treatment using a vaccine that is usually made from a patient’s own tumor cells or from substances taken from tumor cells. A cancer vaccine may help the immune system kill cancer cells

Tracer—A substance used in imaging procedures so that certain structures can be identified or the substance can be followed

Trachea—The airway that leads from the larynx (voice box) to the bronchi (large airways that lead to the lungs). Also called “windpipe”

Tumor—An abnormal mass of tissue that results when cells divide more than they should or do not die when they should

Ultrasound—A procedure that uses high-energy sound waves to look at tissues and organs inside the body

Vascular endothelial growth factor (VEGF)—A protein made by cells that stimulates new blood vessel formation

VEGF—See vascular endothelial growth factor

X-ray—A type of radiation used in the diagnosis and treatment of cancer and other diseases. In low doses, X-rays are used to diagnose diseases by making pictures of the inside of the body. In high doses, X-rays are used to treat cancer

05 my healthcare team

Please use the space below to write down the contact information of the members of your healthcare team.

MEDICAL ONCOLOGIST _____

Contact Information _____

THORACIC SURGEON _____

Contact Information _____

RADIATION ONCOLOGIST _____

Contact Information _____

PULMONOLOGIST _____

Contact Information _____

PRIMARY CARE DOCTOR _____

Contact Information _____

ONCOLOGY NURSE _____

Contact Information _____

ONCOLOGY SOCIAL WORKER _____

Contact Information _____

COUNSELOR/THERAPIST _____

Contact Information _____

NUTRITIONIST/DIETITIAN _____

Contact Information _____

PHARMACIST _____

Pharmacy _____

Contact Information _____

OTHER TEAM MEMBERS

Name _____ Specialty _____

Contact Information _____

Name _____ Specialty _____

Contact Information _____

Name _____ Specialty _____

Contact Information _____

06 notes

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Find it. Treat it. Live.

CHICAGO OFFICE

228 S. WABASH AVENUE, SUITE 700
CHICAGO, IL 60604

PH: 312.407.6100 **F:** 312.464.0737

BETHESDA OFFICE

6917 ARLINGTON ROAD, SUITE 352
BETHESDA, MD 20814

PH: 240.454.3100 **F:** 240.497.0034

EMAIL: INFO@LUNGEVITY.ORG

www.LUNgevity.org

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