



What you need to know about...

biomarker testing



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 "For Patients and Caregivers" and "For Supporters and Advocates."

This patient education booklet was produced through charitable donations from:



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introduction

Lung cancer treatment options now include a number of targeted therapies aimed at particular driver mutations and several immunotherapies aimed at a person's own immune system. Each of these treatments can provide substantial benefits—but not to all patients. For doctors to know whether to prescribe any of these treatments to a lung cancer patient requires a type of testing known as biomarker testing.

Biomarker testing is used among diagnosed lung cancer patients to determine the presence of particular mutations or of a particular protein, how aggressive the disease is, and how well a patient is likely to respond to a particular treatment. It is the first step in precision medicine—ensuring that a patient gets matched to the right treatment at the right time, based on the patient's biomarker profile.

This brochure will help you:

- Understand what a biomarker is
- Learn how biomarkers are used to make lung cancer treatment decisions
- Understand how biomarker testing is done
- Consider whether you should have biomarker testing

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 biomarkers

What is a biomarker?

A **biomarker** is any **molecule** that can be measured in blood, other bodily fluids, or tissues. Presence of a biomarker may be a sign of an abnormal bodily process or condition or a disease. Your doctors may also use the terms molecular marker, genotype, or signature molecule.

Biomarkers can be used to:

- Determine whether a disease or condition is present
- Tell you how aggressive the disease is
- Predict how well the body will respond to a treatment for a disease or condition

What is biomarker testing? Why is it important?

Biomarker testing (also known as **mutation**, genomic, or molecular testing) is a way for your doctors to gather as much information as possible about your unique **lung cancer**. Your doctors may suggest biomarker testing to discover whether you have a treatable **driver mutation** or to establish your **PD-L1 protein** level. The results of these tests help determine whether any of the **Food and Drug Administration (FDA)**-approved **targeted therapies** or **immunotherapies** are right for you as part of your treatment plan. Biomarker testing is used to plan these treatments for **metastatic** lung cancers. It may also be useful for certain **early-stage** lung cancers.

Before any treatment for your lung cancer can begin, your doctors may test your tumor tissue for biomarkers. If your cancer comes back after treatment, they may suggest another tissue biopsy of your tumor or a liquid biopsy (a blood- or urine-based biomarker test that doesn't require a tissue sample).

What types of biomarkers are used to determine the best treatment for lung cancer patients?

There are two types of biomarkers currently used to help doctors optimize a lung cancer patient's treatment plan: driver mutations to determine whether a targeted therapy is appropriate and biomarkers in the patient's tumor to determine whether an immunotherapy drug is appropriate.

Driver mutations

All the organs and tissues in our bodies are made up of cells, and each of these cells contains thousands of **genes**. Genes are made up of **DNA**, which is a specific code that is used to ultimately make proteins that have specific functions for the cell. It is essential for each gene to have the correct DNA code, or instructions, for making its protein. When the DNA is correct, the protein is able to perform the correct function.

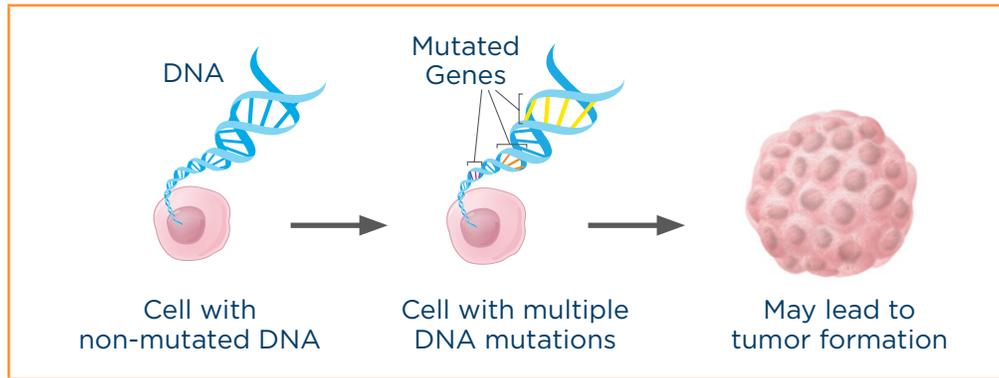
When a gene has an error in its DNA, it is said to be changed or mutated. Mutations can be:

- **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

Virtually all of the biomarkers that are helpful to making treatment decisions in lung cancer are acquired (sometimes called somatic). Inherited biomarkers are still being researched. **In this booklet, we are only talking about acquired mutations.**

Mutations occur often, and normally the body can correct them. However, depending on where in a gene the change occurred, the small change may go undetected by the body and become part of the cell's blueprint. Over time, an accumulation of mutations can result in the formation of a tumor. Mutations that cause cancer are called driver mutations.

DRIVER MUTATIONS

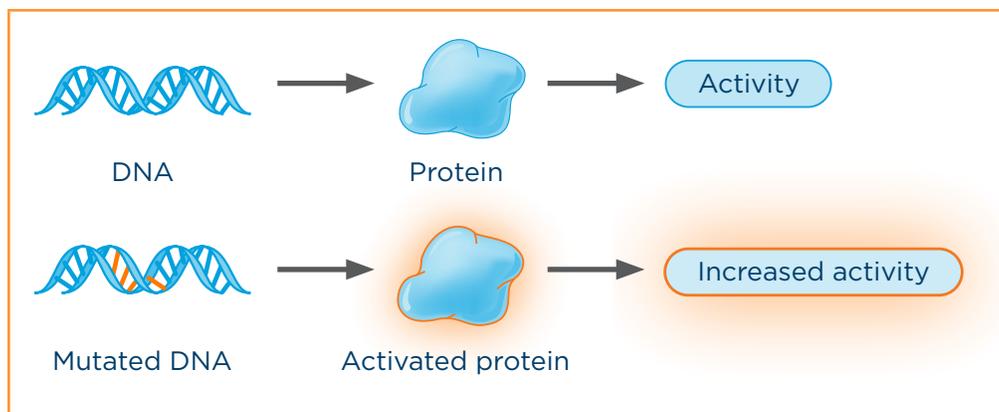


Types of driver mutations

Activating mutation

An **activating mutation** is a change in the DNA sequence that can cause changes in the protein made by the gene so that the protein is always active, leading to uncontrolled cell growth.

ACTIVATING MUTATION

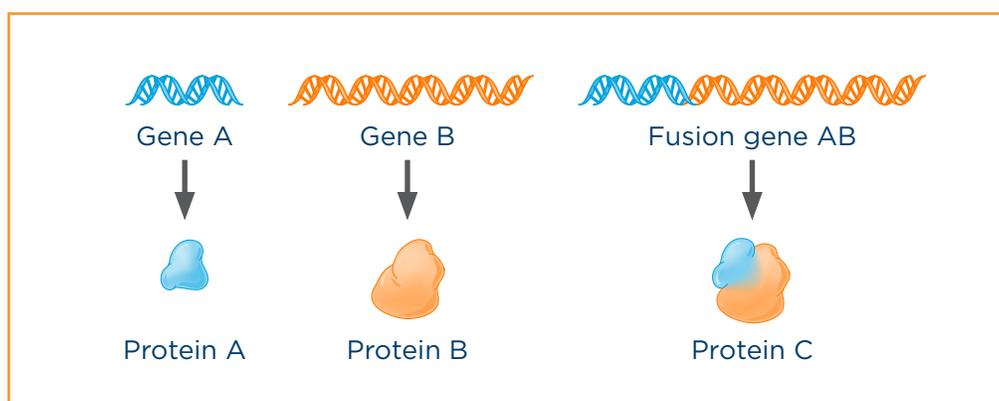


Examples of an activating mutation in lung **adenocarcinoma** are the **epidermal growth factor receptor (EGFR)** and **BRAF V600E**.

Fusion

Fusion, or rearrangement, occurs when a part of one gene fuses with, or attaches to, a part of another gene. The fused gene then produces a unique protein that promotes abnormal, unchecked cell growth.

FUSION PROTEIN

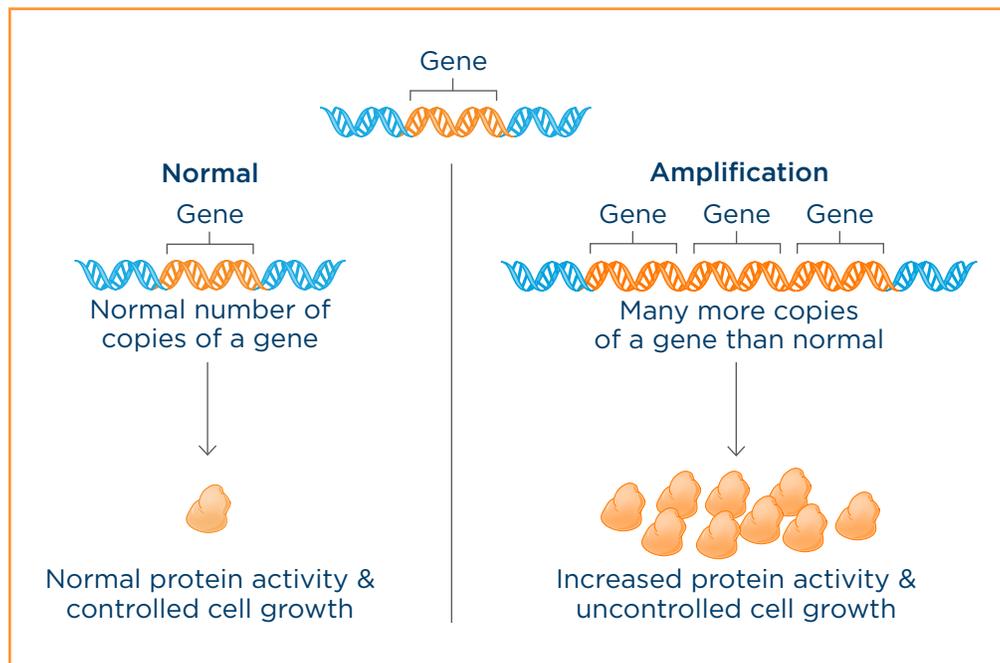


Examples of fusion genes in lung adenocarcinoma include the **ALK-EML4** and the CD74-**ROS1** fusion genes.

Amplification

Amplification means there are many more copies of a gene than normal. The **overexpression** then leads to increased protein activity and uncontrolled cell growth.

AMPLIFICATION

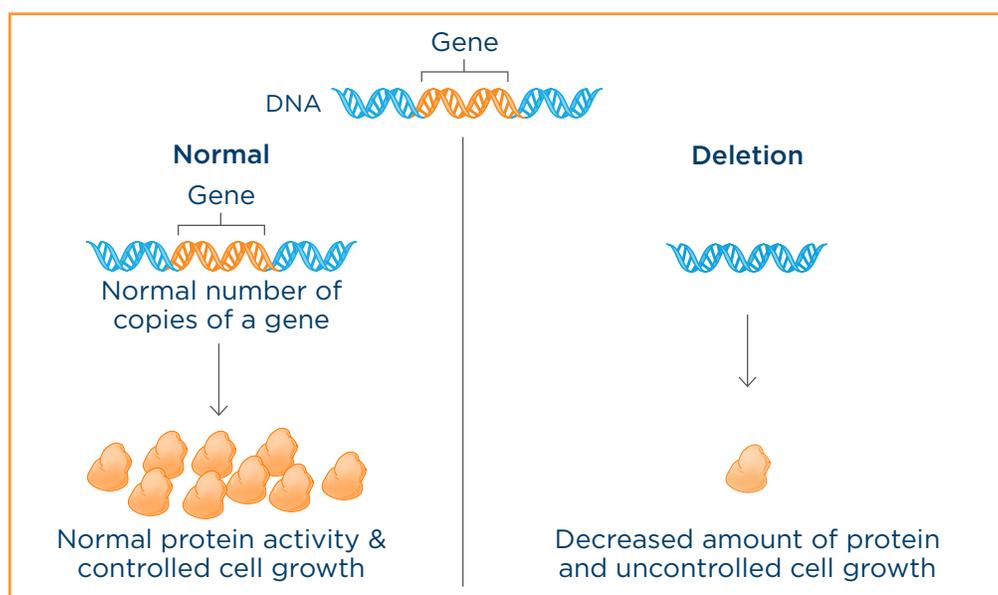


Examples of amplified genes in lung adenocarcinoma include the HER2 and the MET genes.

Deletion

Deletion means part of or the entire gene is missing in the cancer cells. The deletion then leads to reduced levels of protein being produced by the cancer cell.

DELETION



Examples of deleted genes in **small cell lung cancer (SCLC)** include the TP53 and the RB genes.

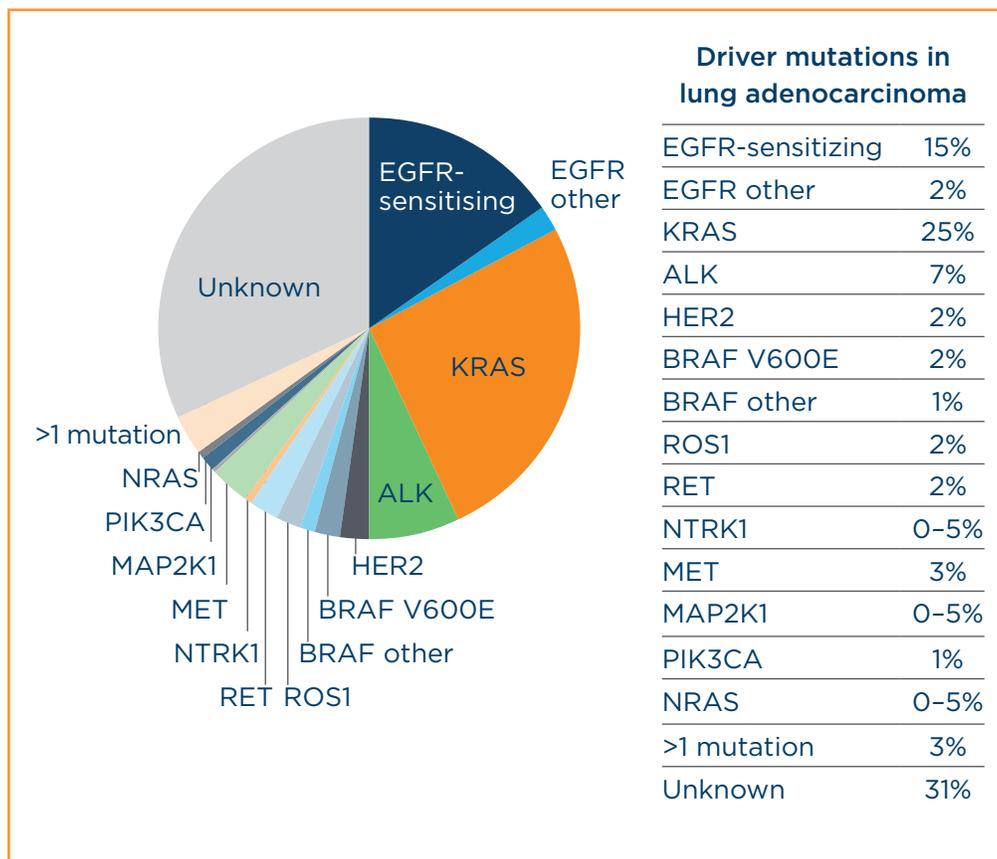
A person's lung cancer may or may not have one of the many known driver mutations. So far, scientists have identified more than 20 different driver mutations sometimes found in **non-small cell lung cancer (NSCLC)** and small cell lung cancer, and they are continuing to look for more.

These driver mutations are biomarkers that are used in biomarker testing in lung cancer; their presence may determine whether a patient will be prescribed one of several approved targeted therapies or be potentially eligible for a **clinical trial**.

A targeted therapy is a treatment that targets specific parts of cells and the signals that proteins send to cells that cause them to grow and divide uncontrollably. However, not all driver mutations have an available targeted therapy.

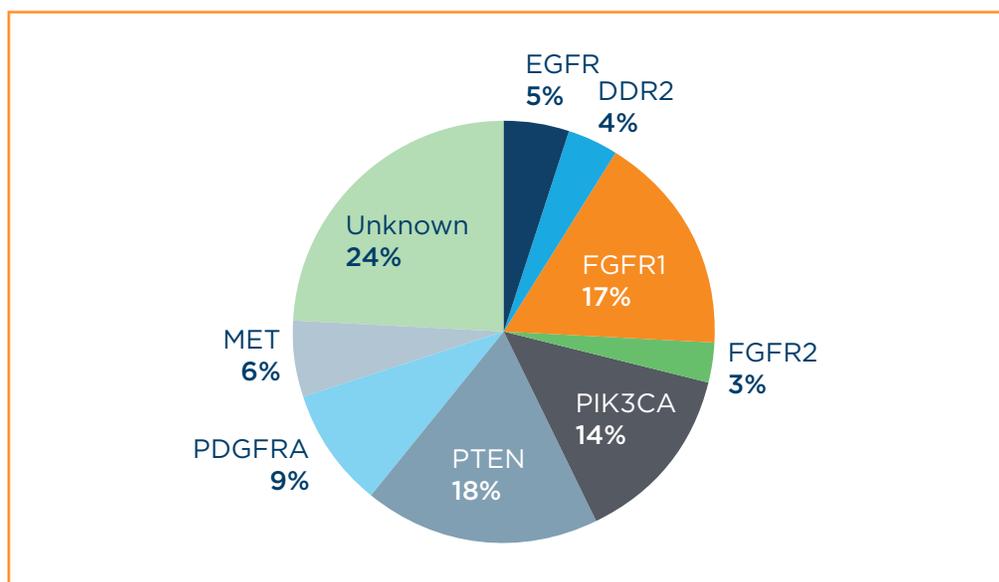
Right now, scientists have the most information about driver mutations in the subtype of non-small cell lung cancer called adenocarcinoma. The driver mutations that currently have FDA-approved targeted therapy drugs available are EGFR, ALK, ROS1, and BRAF V600E.

DRIVER MUTATIONS IN LUNG ADENOCARCINOMA



Scientists are also making progress in understanding mutations in **squamous cell lung cancer**, although there are no FDA-approved drugs for these yet.

DRIVER MUTATIONS IN SQUAMOUS CELL LUNG CANCER



Driver mutations in small cell lung cancer are also being studied. No biomarker testing is currently recommended for small cell lung cancer patients because there are no targeted therapy drugs FDA-approved for a small cell mutation. However, if you are participating in a clinical trial for small cell lung cancer, your doctors may recommend biomarker testing.

Immunotherapy biomarkers

PD-L1: PD-L1 is a protein biomarker used to determine whether a lung cancer patient is likely to benefit from treatment with a type of immunotherapy called **immune checkpoint inhibitors**. Immune checkpoint inhibitors are drugs that help the patient's own **immune system** fight the cancer. They do this by overriding the immune system's fail-safe mechanisms, which are designed to suppress the immune response at appropriate times to minimize damage to healthy tissue.

Patients who have a high level of PD-L1 expression are more likely to respond to immune checkpoint inhibitors. However, even those with tumors that do not express PD-L1 may respond to these treatments.

Other immunotherapy biomarkers: While they are not yet used in the clinic for lung cancer, scientists are also studying types of immunotherapy biomarkers other than PD-L1, such as **tumor mutation burden (TMB)**, CTLA-4 expression, and micro-satellite instability (MSI).

02 biomarker testing in lung cancer

Is biomarker testing appropriate for you?

Biomarker testing may be appropriate:

- If your doctors suspect lung cancer and have recommended a biopsy
- If you are already diagnosed with lung cancer
- If your lung cancer recurs (comes back) after treatment

If you have a diagnosis of lung cancer, you should discuss biomarker testing with your doctors.

How is biomarker testing performed with tumor tissue?

Biomarker testing requires a sample of the tumor. Your doctors will remove either part of the tumor (biopsy) or an entire tumor (surgery). Your doctors will suggest the best approach for you depending on the stage and the location of your tumor as well as your overall health.

Be sure to discuss with your doctors that adequate tissue be gathered so that all necessary biomarkers tests can be performed.

Samples from the biopsy or surgery will be sent to a **pathologist**. A pathologist is a doctor who is an expert in testing cells to find disease. All lab results are recorded in a **pathology report**. It is a good idea to get a copy of your pathology report to have available to show other doctors. The test results are generally available within 10 to 14 days. Biomarker testing can be done on both **primary tumors** and **metastatic tumors**. If the tumor sample is too small to run it through multiple tests, priority should be given to testing for mutations that are the most likely to be present, have an FDA-approved drug treatment, or otherwise help with treatment decisions. Therefore, at this time, if there is only a limited amount of tumor sample, tumors should be tested for the EGFR, ALK, KRAS, ROS1, and BRAF V600E mutations and the PD-L1 protein.

Multiplex testing—testing for multiple gene mutations at the same time from the same sample of tumor tissue—is currently used in some laboratories. This allows more testing to be done on a small tumor sample. An example of multiplex testing is next-generation sequencing, or NGS.

How is tumor tissue collected for diagnosis and biomarker testing?

There are many different techniques doctors can use to obtain the tumor tissue. The technique is determined by the location and size of the tumor.

Your doctor will discuss the best option with you as well as the risks and benefits of the procedure.

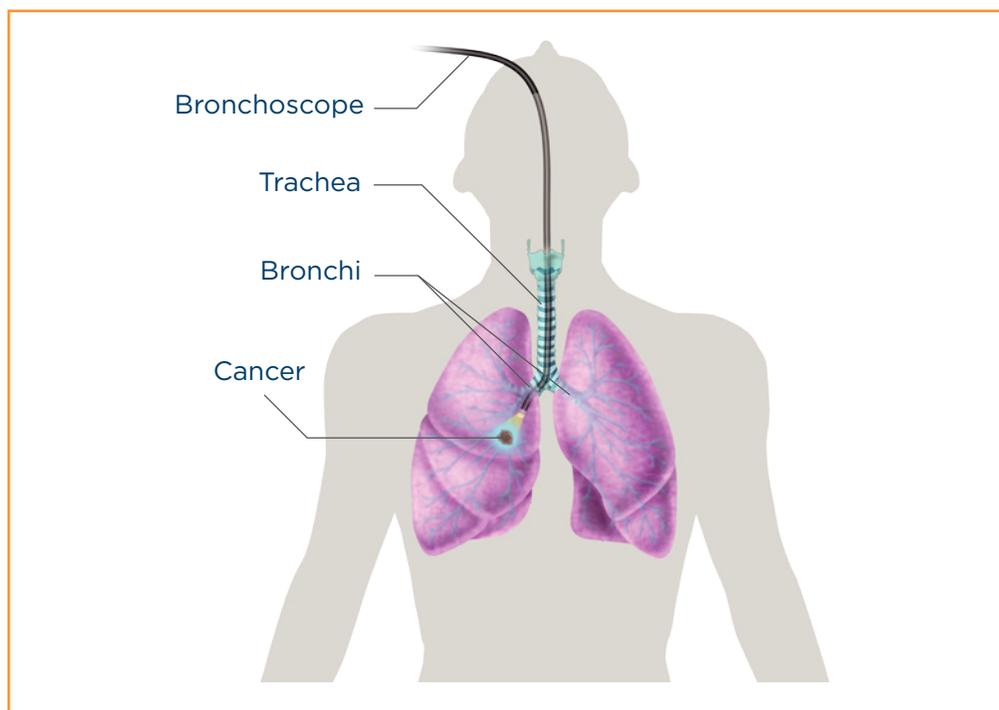
Be sure to discuss with your doctors that adequate tissue be gathered so that all necessary biomarkers tests can be performed.

Tissue collection techniques include:

Bronchoscopy

During a **bronchoscopy**, your doctors will insert a bronchoscope (a thin, flexible tube) into your mouth or nose, down the trachea, and into the lungs. A light and a camera at the end of the tube allow the doctors to look for abnormal areas. Tiny tools can be passed down through the bronchoscope to take samples of tissue, which are checked under a microscope for signs of cancer. Prior to a bronchoscopy, a numbing medicine is sprayed in the mouth and throat. Sometimes you may also be given sedation through an intravenous (IV) line to help you relax or to prevent pain.

BRONCHOSCOPY



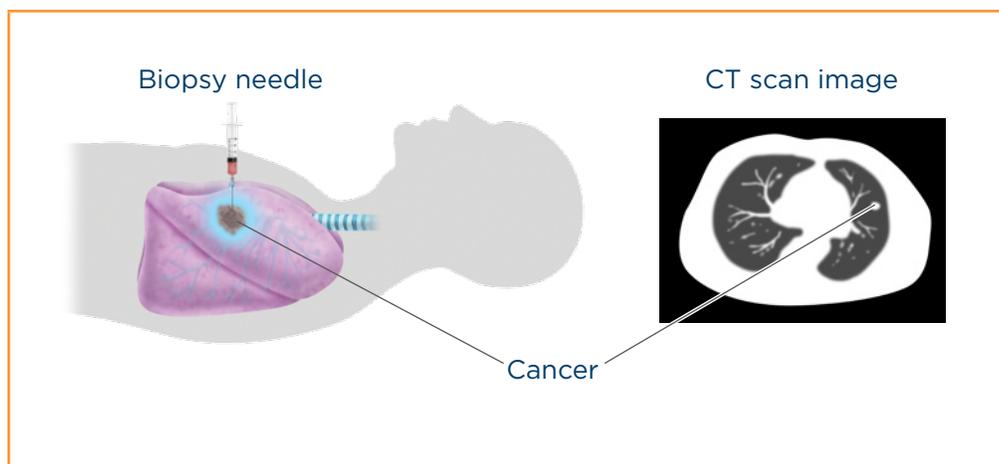
Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

Your doctors may use EBUS-TBNA to access mediastinal **lymph nodes**. A flexible bronchoscope fitted with an **ultrasound** device will be guided down your trachea. Once the bronchoscope is in place, a needle will be inserted through the bronchus and into a lymph node to obtain a sample. EBUS-TBNA requires local anesthesia.

Transthoracic needle biopsy

If a suspicious mass is found in the edges of the lungs, a needle can be passed through the chest wall with CT or ultrasound guidance to biopsy tissue or remove suspicious fluid. When a small needle is inserted through the skin of the chest wall, it is called a **fine needle aspiration (FNA)** or transthoracic needle aspiration. If a larger sample is needed, a core biopsy is done with a larger needle. The only difference between an FNA and a core biopsy is in the diameter of the needle used.

FINE NEEDLE ASPIRATION BIOPSY OF THE LUNG



For a transthoracic needle biopsy, your skin will be numbed and your doctors will insert a needle through the chest wall. A chest **CT scan** or a special X-ray machine called a fluoroscope is used to help the doctors guide the needle toward the suspicious area. A sample of the mass is then aspirated, or sucked out, and sent to the lab to check for cancer cells.

An advantage of this type of biopsy is that it does not require a surgical incision, and usually local numbing medicine is all a patient needs. Disadvantages of a transthoracic needle biopsy are that sometimes it can miss small nodules or might not provide enough of a sample to make a diagnosis and perform biomarker testing.

There is also a risk that air may leak out of the lung at the biopsy site and into the space between the lung and the chest wall. This complication, called a **pneumothorax**, can lead to trouble breathing and may cause part of the lung to collapse. A chest tube can be inserted to treat the pneumothorax, or the air may be sucked out of the space with a needle.

Thoracoscopy

A thoracoscopy is a surgical procedure performed in the operating room under general anesthesia. A surgeon will make a small incision in the skin of the chest wall and insert a special instrument with a small video camera on the end to examine the lungs and inside of the chest. Samples of tissue are removed for a pathologist to look at under the microscope. This procedure is also referred to as VATS (video-assisted thoracoscopic surgery).

A thoracoscopy can be used for multiple reasons:

- 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

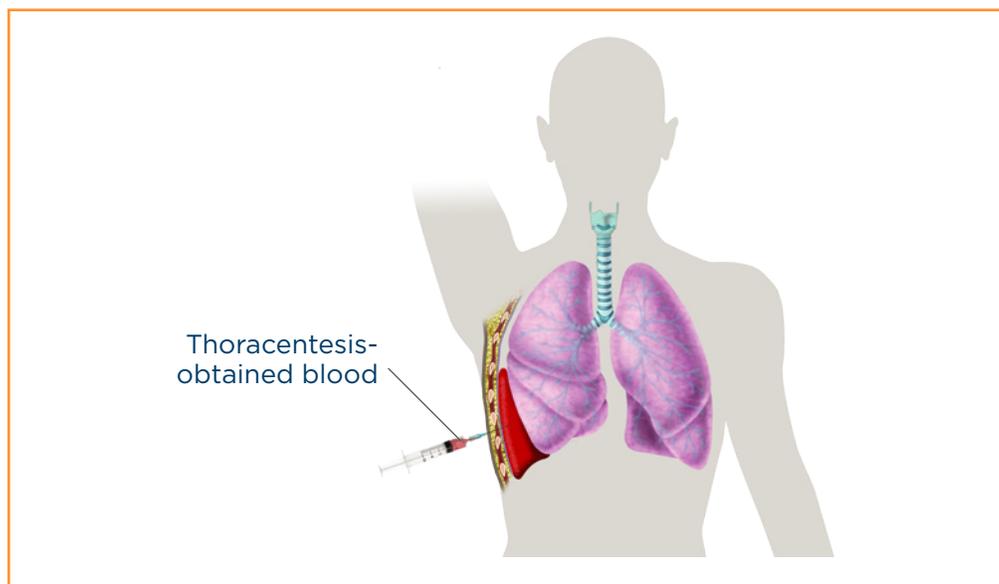
- To check if the tumor has spread to nearby lymph nodes and organs
- As part of the treatment to remove part of a lung in some early-stage lung cancers

Because thoracoscopy is more invasive and requires general anesthesia, it is not usually the first procedure used to get tissue to diagnose lung cancer if a less invasive procedure can be used. Thoracoscopy is sometimes used for diagnosis if tests such as transthoracic needle biopsies are unsuccessful in getting enough tissue for the diagnosis.

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. The fluid is sent to a laboratory to be checked for cancer cells.

THORACENTESIS



Will you need multiple biopsies?

Sometimes, your doctors may recommend an additional biopsy. This could happen when:

- Not enough tissue was obtained during the initial, diagnostic biopsy.
- A targeted therapy that worked well against the cancer has stopped working and the cancer has recurred. Testing the resistant cancer for additional mutations that may have evolved or rare changes in **histology** is indicated to help guide your doctors toward the next best treatment.
- New drugs are approved for the treatment of lung cancer from which you might possibly benefit. The new drug or treatment might require biomarker testing.

Therefore, your doctors may recommend additional biopsies and biomarker testing at several points in your treatment process. The ultimate decision to recommend another biopsy depends on the location of the cancer and your health status and lung function, and should be jointly made by you and your doctors.

What is a liquid biopsy? How is it used?

Currently, tissue biopsies are the only way to confirm a diagnosis of lung cancer and to detect driver mutations or levels of the PD-L1 protein. However, your doctors may also use a liquid biopsy instead of a tissue biopsy to decide if certain targeted therapies are right for you.

Liquid biopsies, the technique of testing blood or urine for biomarkers to determine the DNA changes in a patient's tumor, are a promising alternative to tumor biopsies but are not yet widely used.

- When cancer cells die, they release DNA. The DNA then enters the bloodstream and can be detected in the liquid part of the blood (plasma) or in urine. This is called a circulating tumor DNA or ctDNA test.
- As cancer cells grow, the tumor “sheds” cells just the way our skin sheds cells every day. These cells, called circulating tumor cells (CTCs), can be captured and tested for specific mutations.

At this time, liquid biopsies may help your doctors:

- Check if your cancer has become resistant to a targeted therapy and decide the next treatment option
- Follow your response to a particular targeted therapy

Currently, only ctDNA-based liquid biopsy tests are available for use in the clinic. If a liquid biopsy test is negative, your doctors will recommend a tissue biopsy. It is important to know that not all cancer cells shed DNA so not all patients can be successfully tested via liquid biopsy.

03 how biomarker testing impacts treatment

For which biomarkers should you be tested?

Biomarker testing should be an ongoing part of the discussions with your doctors. Any decision to test for biomarkers should be made together by you and your doctors, and depends on a number of factors, including your type and stage of lung cancer, your current treatment plan, and your overall health.

Current guidelines recommend that all patients diagnosed with **advanced-stage NSCLC** be tested for the EGFR, ALK, KRAS, ROS1, and BRAF V600E mutations, and the PD-L1 protein.

When discussing biomarker testing with your doctors, you may also want to consider that driver mutations other than EGFR, ALK, KRAS, ROS1, and BRAF V600E have been found in both adenocarcinoma and squamous cell lung cancer. Drugs that target many of those mutations are being tested through clinical trials, so it is important for people with non-small cell lung cancer to consider multiplex biomarker testing that includes many mutations, rather than just the five mutations listed above.

Note: Currently, no drug targeting the KRAS mutation is available. However, KRAS testing can be informative because cancers with KRAS mutations are very unlikely to have other driver mutations. KRAS mutations are associated with resistance to EGFR targeted therapy. Finding a KRAS mutation can help you and your doctor decide about whether testing for very rare mutations makes sense.

If you have small cell lung cancer, your doctors may test for the expression of PD-L1 and small cell-specific biomarkers such as DLL3 to determine if you are eligible for specific clinical trials.

The tables below display common recommendations for biomarker testing for targetable driver mutations and immunotherapy. Again, any decision about biomarker testing should be made together by you and your doctor.

Adenocarcinoma

COMMON RECOMMENDATIONS FOR BIOMARKER TESTING

Stage of Lung Cancer	Recommendations for Biomarker Testing
Stage I, II, or III	Testing for the EGFR, ALK, KRAS, ROS1, and BRAF V600E mutations and PD-L1 protein levels at the time of diagnosis and surgical resection is not always recommended but may be considered. The decision should be made on an individual basis with your doctors
Stage IV adenocarcinoma or adenocarcinoma that has recurred or progressed after an initial diagnosis of stage I, II, or III lung cancer in patients who were not previously tested	Tumors should be tested for EGFR, ALK, KRAS, ROS1, and BRAF V600E mutations at the time of diagnosis. Testing for other biomarkers may be helpful in deciding eligibility for clinical trials PD-L1 immunohistochemistry is recommended to determine whether you will benefit from immunotherapy in the first-line setting

Squamous cell lung cancer

COMMON RECOMMENDATIONS FOR BIOMARKER TESTING

Stage of Lung Cancer	Recommendations for Biomarker Testing
Stage I, II, and III	Currently, biomarker testing is performed only for clinical trials
Stage IV	<p>Currently, biomarker testing is performed only for clinical trials</p> <p>PD-L1 immunohistochemistry is recommended to determine whether you will benefit from immunotherapy in the first-line setting</p> <p>Testing for EGFR and ALK mutations is recommended ONLY if your doctors suspect that the tumor may have adenocarcinoma cells (this type of lung cancer is referred to as mixed lung cancer with an adenocarcinoma component)</p>

Small cell lung cancer

COMMON RECOMMENDATIONS FOR BIOMARKER TESTING

Stage of Lung Cancer	Recommendations for Biomarker Testing
All stages	Currently, biomarker testing is performed only for clinical trials

What do the results of your biomarker test(s) mean?

The results of your test(s) will tell you and your doctors if your lung cancer has a driver mutation that makes it likely that you will benefit from a targeted therapy or if your PD-L1 protein level is high enough that you are likely to benefit from immunotherapy.

How do the test results impact your treatment?

If your cancer tests positive for the EGFR, ALK, ROS1, or BRAF V600E mutation and you have advanced-stage NSCLC, there are FDA-approved targeted therapies that you should discuss with your doctors. The drugs listed below are currently available, **but check with your doctor because new drugs may be available at the time of your treatment.**

EGFR:

- Afatinib (Gilotrif®), erlotinib (Tarceva®), or gefitinib (Iressa®) in the first-line setting or second-line setting
- Osimertinib (Tagrisso™) in the second-line setting in those patients who have progressed on an **EGFR tyrosine kinase inhibitor (EGFR TKI)** and have a T790M mutation at the time of progression

ALK:

- Crizotinib (Xalkori®), or alectinib (Alecensa®) in the first-line setting
- Ceritinib (Zykadia™) in the second-line setting after progression on crizotinib in the first-line setting
- Brigatinib (Alunbrig™) in the second-line setting for patients who have progressed on crizotinib in the first-line setting or who are intolerant to crizotinib

ROS1:

- Crizotinib (Xalkori®) in the first-line setting

BRAF V600E:

- Combination treatment of dabrafenib (Tafinlar®) with trametinib (Mekinist®) in first- and subsequent-line settings

PD-L1:

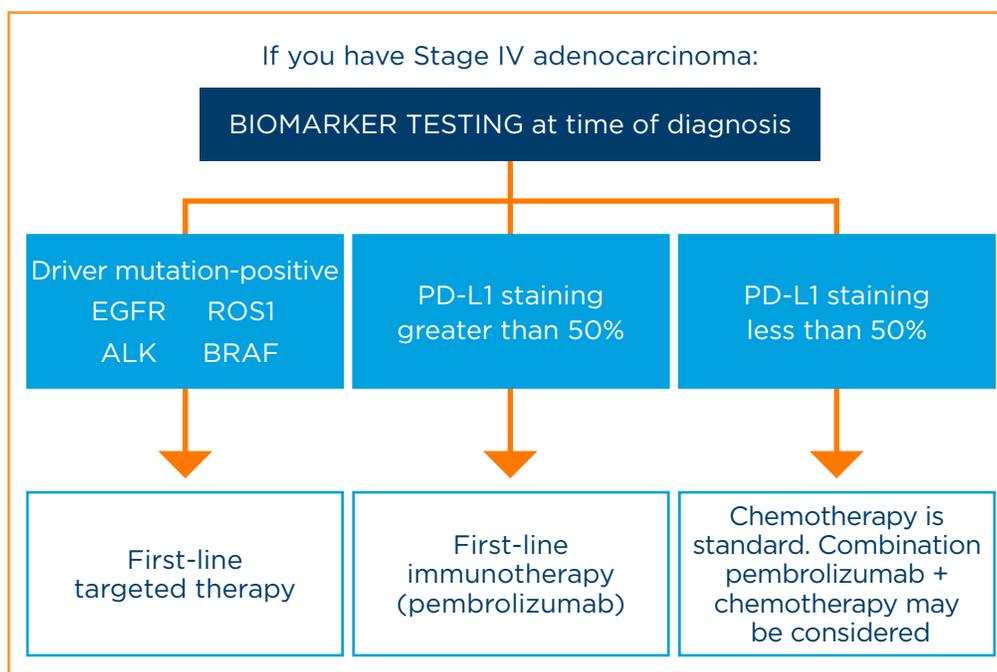
In addition, presence of the PD-L1 protein biomarker will help your doctors determine whether you will benefit from immunotherapy. Current FDA-approved immunotherapy drugs include:

- **Nivolumab (Opdivo®):** Approved in the second-line setting for patients diagnosed with metastatic NSCLC whose lung cancer has progressed on or after platinum-based chemotherapy
- **Pembrolizumab (Keytruda®):** Approved for patients diagnosed with metastatic non-small cell lung cancer (NSCLC) in the following situations:
 - As **first-line treatment** for patients whose tumors have a high PD-L1 expression, and with no EGFR or ALK mutation and no prior systemic chemotherapy treatment for metastatic NSCLC. High PD-L1 expression is defined as Tumor Proportion Score (TPS) greater than or equal to 50%. TPS is the number of cancer cells that are positive for the PD-L1 protein
 - As **second-line treatment** for patients who have progressed on platinum-containing chemotherapy and whose tumors express PD-L1 (TPS greater than or equal to 1%)
 - As second-line treatment for patients with EGFR or ALK mutations who have progressed on FDA-approved therapy and whose tumors express PD-L1 (TPS greater than or equal to 1%)
 - As first-line treatment for patients diagnosed with metastatic non-squamous NSCLC in combination with the chemotherapy drugs pemetrexed and carboplatin, irrespective of PD-L1 expression

- **Atezolizumab (Tecentriq®):** Approved for patients diagnosed with metastatic NSCLC in the following situations:
 - As second-line treatment for patients who have progressed on platinum-containing chemotherapy
 - As second-line treatment for patients with EGFR or ALK mutations who have progressed on FDA-approved therapy

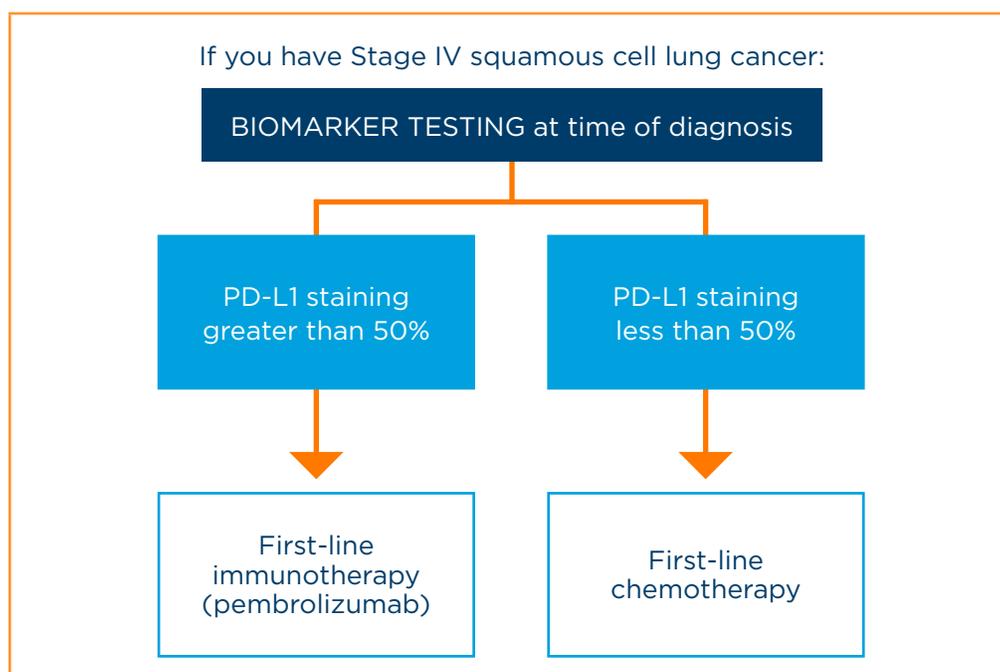
The following chart summarizes the first-line treatment approaches for stage IV lung adenocarcinoma, following biomarker testing.

FIRST-LINE TREATMENT APPROACHES FOR STAGE IV LUNG ADENOCARCINOMA



The following chart summarizes the first-line treatment approaches for stage IV squamous cell lung cancer, following biomarker testing.

FIRST-LINE TREATMENT APPROACHES FOR STAGE IV SQUAMOUS CELL LUNG CANCER



For second-line (and further) treatment options, check with your doctors whether biomarker testing may be needed before deciding the treatment plan.

How will testing help you enroll for clinical trials?

If your cancer tests positive for driver mutations other than EGFR, ALK, ROS1, and BRAF V600E, you should speak with your doctor about participating in clinical trials for new drugs targeting your cancer's driver mutation.

Stage I, II, and IIIA lung cancer: If your stage I, II, or IIIA non-small cell lung cancer tests positive for a driver mutation for which an FDA-approved therapy exists, you may be eligible to enroll for a trial with specific targeted therapies.

Stage IIIB/Stage IV lung cancer or extensive-stage disease-SCLC: If you are stage IIIB/IV advanced-stage NSCLC or extensive-stage disease-SCLC, you may want to consider clinical trials that are open for patients with a variety of driver mutations. These targeted treatments are being studied alone and in combination with other targeted drugs, immunotherapy, chemotherapy, and radiation therapy.

The driver mutations on the following page are currently being actively studied in lung cancer for the development of targeted therapies.

DRIVER MUTATIONS WITH DRUGS IN CLINICAL TRIALS

Driver Mutation	Lung Adenocarcinoma	Squamous Cell Lung Cancer	Small Cell Lung Cancer
TP53	X	X	X
EGFR	X		
KRAS	X		
MEK1 (MAP2K1)	X	X	
RB1	X	X	X
ALK (fusion)	X		
MYC	X	Rare	X
FGFR1 (amp)	X	X	X
RET	X		
MET			
<i>Amplification (de novo)</i>	X		
<i>Amplification (EGFR TKI-resistant)</i>	X		
<i>Exon 14 skipping</i>	X	X	
PTEN	X	X	X
PIK3CA			
<i>Mutation</i>	X	X	
<i>Amplification</i>	X	X	X
BRAF	X		
ROS1	X		
NTRK1	X		
HER2			
<i>Mutation</i>	X		
<i>Amplification</i>	X		
IGR1			X
PARP1		X	X
Notch Signaling			X

New inhibitors of EGFR, ALK, ROS1, and BRAF are also being tested in clinical trials. Make sure to talk to your doctor about these options.

How can you get your tumor tested?

Begin by speaking to your doctors about how to get tested for lung cancer biomarkers. They can arrange for your tumor to be sent for testing or arrange for biopsy if appropriate. Ideally, biomarker testing should be performed at the time of diagnosis.



QUESTIONS TO ASK YOUR HEALTHCARE TEAM ABOUT BIOMARKER TESTING:

Before getting biomarker testing:

- What are you trying to find with biomarker tests?
- Have I already had any biomarker tests? Which ones?
- Who performs these tests?
- How are the tests performed?
- Are there any complications from these tests?
- How long will it take to get the test results?
- Where can I get more information about biomarker testing?
- Are there any limitations of biomarker testing?
- Will insurance pay for these tests?

After getting biomarker testing:

- What tests were done?
- What are the results of these tests?
- How will the results affect my treatment?
- The test results are negative: should I be retested?
- The test results are not clear: should I be retested?
- Are there any medications that target my type of lung cancer?
- Will I need these tests again? If so, why? When?
- Are there any clinical trials open to me based on these results?
- How can I get a copy of my pathology report?

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

Activating mutation—A genetic mutation that causes increased protein activity. This overly active protein may lead to uncontrolled cell growth

Advanced-stage non-small cell lung cancer (advanced-stage NSCLC)—Refers to NSCLC that has spread either locally or to distant parts of the body

ALK—See anaplastic lymphoma kinase

Amplification—A usually massive replication of genetic material and especially of a gene or DNA sequence

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

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

Biomarker testing (mutation, genomic, or molecular testing)—

Analyzing DNA to look for a gene mutation that may indicate an increased risk for developing a specific disease or disorder

Biopsy—The removal of cells or tissues for examination by a pathologist. The pathologist may study the tissue under a microscope or perform other tests on the cells or tissue

BRAF V600E—A mutation in the BRAF gene, which makes a protein that is involved in sending signals in cells and in cell growth. It may increase the growth and spread of cancer cells in non-small cell lung cancer

Bronchoscopy—A procedure that uses a bronchoscope to examine the inside of the trachea, bronchi, and lungs. A bronchoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue; this tissue can then be checked under a microscope for signs of disease. The bronchoscope is inserted through the nose or mouth

Clinical trial—A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called clinical research trial or study

CT scan—A procedure that uses a computer linked to an X-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create 3-dimensional (3-D) views of tissues and organs. A dye may be injected into a vein or swallowed to help the tissues and organs show up more clearly. Also called CAT scan and computed tomography scan

DNA—The molecules inside cells that carry genetic information and pass it from one generation to the next. Also called deoxyribonucleic acid

Driver mutation—A change in the gene sequence of a cell that leads to the development or progression of a tumor

Echinoderm microtubule-associated protein like 4 (EML4)—A gene that, when combined with the anaplastic lymphoma kinase (ALK) gene, produces an abnormal protein that leads to cancer cell growth

EGFR—See epidermal growth factor receptor

EGFR TKI—See epidermal growth factor receptor tyrosine kinase inhibitor

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

Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI)—Drug that blocks the activity of a protein called epidermal growth factor receptor (EGFR). Blocking EGFR may keep cancer cells from growing. Also called EGFR inhibitor and epidermal growth factor receptor inhibitor

Food and Drug Administration (FDA)—The agency in the US federal government whose mission is to protect public health by making sure that food, cosmetics, and nutritional supplements are safe to use and truthfully labeled. The FDA also makes sure that drugs, medical devices, and equipment are safe and effective, and that blood for transfusions and transplant tissue are safe

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 treatments may be added or used instead

Fusion—A gene made by joining parts of two different genes. Once fused together, they produce an abnormal protein that promotes abnormal, uncontrolled cell growth

Gene—Coded instructions within a cell that control how the cell grows in a systematic and precise way

Histology—The study of tissues and cells under a microscope

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

Immune system—A complex network of cells, tissues, organs, and the substances they make that help the body fight infections and other diseases. The immune system includes white blood cells and organs and tissues of the lymph system, such as the thymus, spleen, tonsils, lymph nodes, lymph vessels, and bone marrow

Immunohistochemistry—A lab test that uses antibodies to test for certain antigens (markers) in a sample of tissue. The antibodies are usually linked to an enzyme or a fluorescent dye. When the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be seen under a microscope. Immunohistochemistry is used to help diagnose diseases such as cancer. It may also be used to help tell the difference between different types of cancer

Immunotherapy—A type of cancer therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Some types of immunotherapy only target certain cells of the immune system. Others affect the immune system in a general way

Inhibitor—Any substance that interferes with a chemical reaction, growth, or other biologic activity. For example, an EGFR inhibitor blocks the activity of epidermal growth factor receptors in promoting cancer growth

Liquid biopsy—A test done on a sample of blood to look for cancer cells from a tumor that are circulating in the blood or for pieces of DNA from tumor cells that are in the blood. A liquid biopsy may be used to help find cancer at an early stage. It may also be used to help plan treatment or to find out how well treatment is working or if cancer has come back. Being able to take multiple samples of blood over time may also help doctors understand what kind of molecular changes are taking place in a tumor

Lung cancer—Cancer that begins in tissues of the lung, usually in the cells lining air passages

Lymph node, lymph gland—A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Lymph nodes filter lymph (lymphatic fluid), and they store lymphocytes (white blood cells). They are located along lymphatic vessels

Metastatic—Spread of cancer from the primary site, or place where it started, to other places in the body

Metastatic tumor—A tumor that has metastasized, or spread, from the primary site, or place where it started, to other places in the body

Molecule—The smallest particle of a substance that has all of the physical and chemical properties of that substance. Molecules are made up of one or more atoms. If they contain more than one atom, the atoms can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms

Multiplex testing—The testing for multiple molecular gene mutations at one time

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

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 lung cancer, large cell carcinoma, and adenocarcinoma. Non-small cell lung cancer is the most common kind of lung cancer

NSCLC—See non-small cell lung cancer

Overexpression—The expression of too many copies of a protein or other substance. Overexpression of certain proteins or other substances may play a role in cancer development

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

Pleural effusion—Fluid around the lungs

Pneumothorax—A condition in which air or other gas is present in the pleural cavity, the space enclosed by the pleura, which is a thin layer of tissue that covers the lungs and lines the interior wall of the chest cavity

Precision medicine—A form of medicine that uses information about a person’s genes, proteins, and environment to prevent, diagnose, and treat disease. In cancer, precision medicine uses specific information about a person’s tumor to help diagnose, plan treatment, find out how well treatment is working, or make a prognosis. Examples of precision medicine include using targeted therapies to treat specific types of cancer cells, such as ALK-positive lung cancer cells, or using tumor marker testing to help diagnose cancer. Also called personalized medicine

Primary tumor—The original, or first, tumor in the body

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

ROS1—A gene that makes a protein called ROS1, which is involved in sending signals in cells and in cell growth. Mutated forms of the ROS1 gene have been found in non-small cell 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

Squamous cell lung cancer—A type of non-small cell lung cancer that usually starts near a central bronchus. It begins in squamous cells, which are thin, flat cells that look like fish scales

Stage—The extent of a cancer in the body. In non-small cell lung cancer, early-stage lung cancer is stages I, II, and IIIA, while advanced-stage lung cancer is stages IIIB and IV. In small cell lung cancer, there are two stages, limited-stage disease and extensive-stage disease

Targeted therapy—A type of treatment that uses drugs to attack specific types of cancer cells with less harm to normal cells. Some targeted therapies block the action of certain enzymes, proteins, or other molecules involved in the growth and spread of cancer cells

TKI—See tyrosine kinase inhibitor

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

Tumor mutation burden (TMB)—The number of mutations found in the cancer cell

Tyrosine kinase—A specific enzyme produced by the body to control cell functions, including cell signaling, growth, and division. These enzymes may be too active or found at high levels in some types of cancer cells

Tyrosine kinase inhibitor (TKI)—A type of targeted cancer therapy that blocks the action of enzymes called tyrosine kinases in order to keep cancer cells from growing

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



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