LUNG CANCER TREATMENTS


What you need to know about...

# targeted cancer therapy






LUNGEVITY

# 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."

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# introduction

Targeted cancer therapy is a type of treatment that uses drugs to attack cancer cells, including some kinds of lung cancers. As researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop drugs that directly target some of these changes. These drugs target specific parts of cells and the signals that proteins send to cells that cause them to grow and divide uncontrollably. Targeted cancer therapies are sometimes also called "precision medicines," "molecularly targeted drugs," or "molecularly targeted therapies."

This brochure will help you:

- Learn about the cell changes or mutations that cause some kinds of cancer
- Find out if you should get your tumor tested for mutations and how to go about doing so
- Understand whether targeted cancer therapy might be a good treatment option for you
- Learn which targeted cancer therapy options are available now for people with a genetic mutation

**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

# genetic mutations

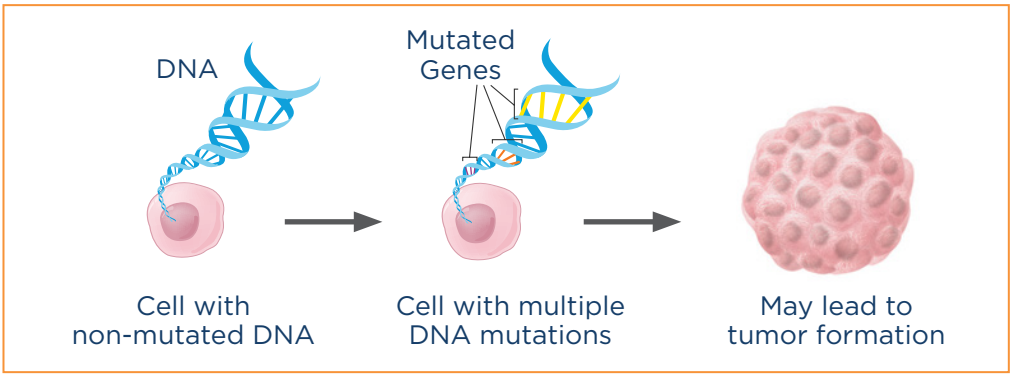
# genetic mutations

All organs and tissues in our body 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 in cells. 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.

## What is a genetic mutation?

When a gene has an error in its DNA code, it is said to be altered or mutated. **Genetic mutations** occur often, and normally the body can correct them. However, depending on where in a gene the change occurred, the small alteration may become part of the cell's blueprint. Over time, an accumulation of genetic mutations can result in the formation of a **tumor**.

MUTATION

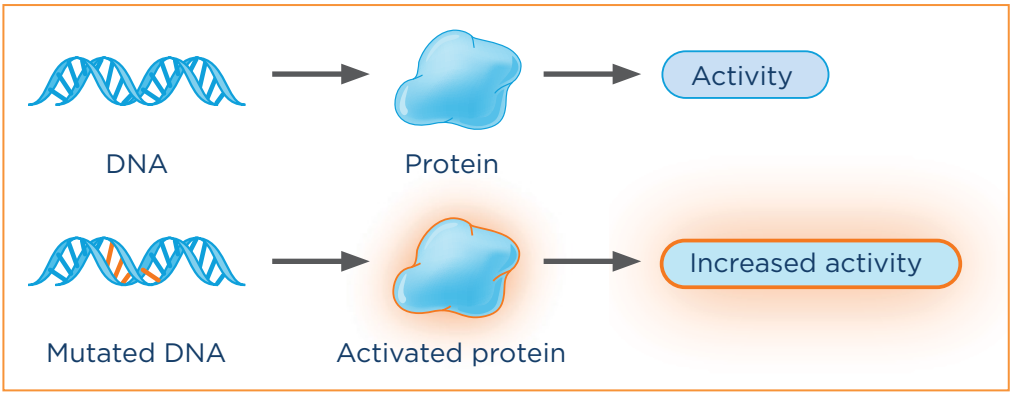



## What are the different types of genetic mutations that are known to cause cancer?

A few different genetic mutations, or alterations, are known to cause cancer. Some of these include:

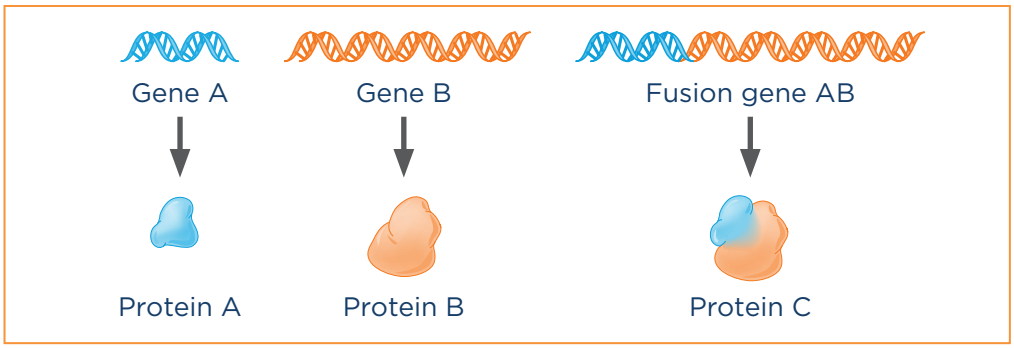
- **Activating mutation**: An activating mutation is a change in the DNA sequence that can cause changes in the protein made by the gene so that it is always active. This may lead to uncontrolled cell growth

ACTIVATING MUTATION



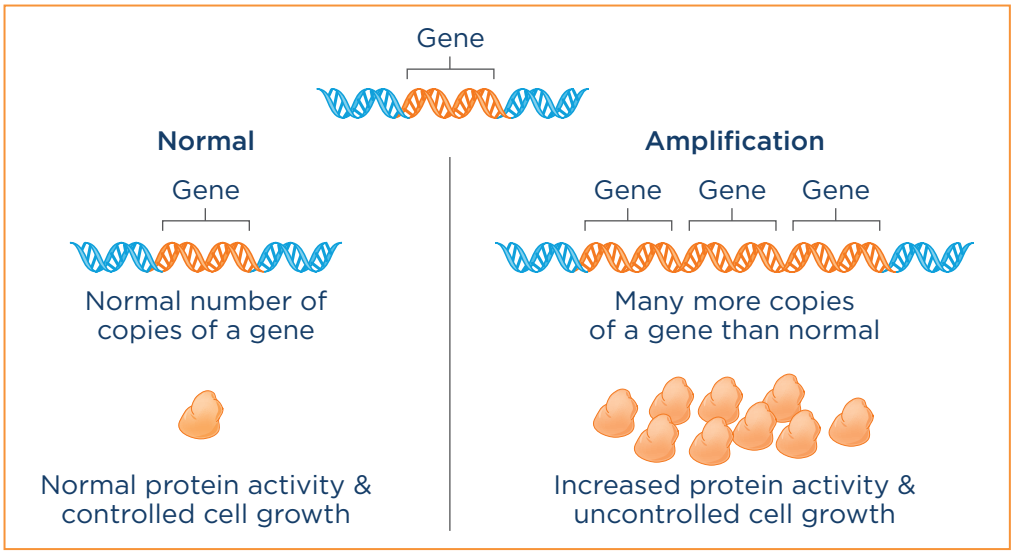
- **Fusion**: Fusion, or rearrangement, occurs when a part of one gene fuses with, or attaches to, a part of another gene. The gene then produces a unique protein that promotes abnormal, uncontrolled cell growth

FUSION




- **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



## Different genetic mutations seen in lung cancers

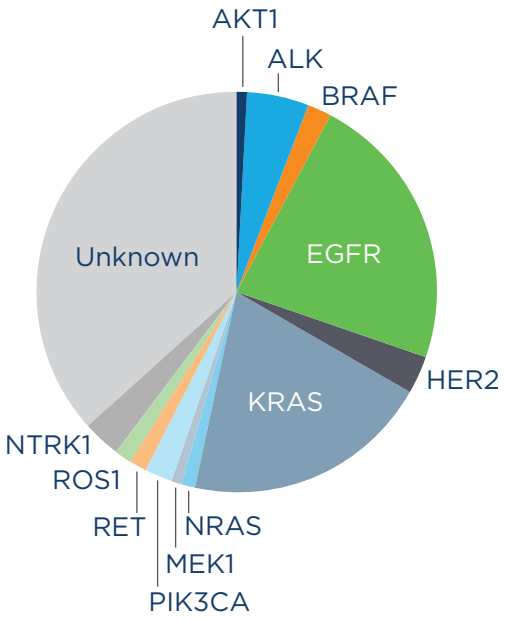
**Lung cancer** describes many different types of cancer that start in the lung or related structures. There are two different ways of describing what kind of lung cancer a person has:

- **Histology**—what the cells look like under a microscope. Histological types include **small cell lung cancer (SCLC)** and **non-small cell lung cancer (NSCLC)**. Subtypes of NSCLC include **adenocarcinoma**, **squamous cell carcinoma**, **large cell carcinoma**, and some rarer types
- **Molecular profile** (also called biomarker profile, genetic profile, or signature profile)—the genetic characteristics, as well as any other unique biomarkers, found in a person's cancer

A person's lung cancer may or may not have one of the many known genetic mutations. For example, two patients may be treated with two different therapies because of their own cancer's specific genetic mutation or lack of a genetic mutation. So far, researchers have identified over a dozen different genetic mutations sometimes found in lung cancer, and they are continuing to look for more.

Right now, scientists have the most information about mutations in the histological subtype of NSCLC called adenocarcinoma.

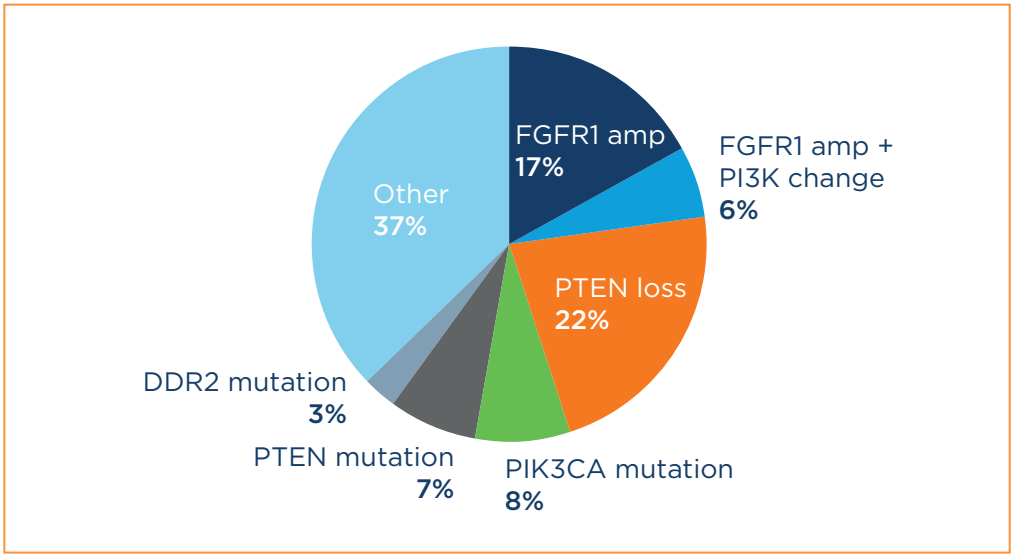
## MOLECULAR PROFILE OF ADENOCARCINOMA




| Frequency of driver mutations in NSCLC | |
|---|---|
| AKT1 | 1% |
| ALK | 3–7% |
| BRAF | 1–3% |
| EGFR | 10–35% |
| HER2 | 2–4% |
| KRAS | 15–25% |
| MEK1 | 1% |
| NRAS | 1% |
| PIK3CA | 1–3% |
| RET | 1–2% |
| ROS1 | 1–2% |
| NTRK1 | ~3% |

Researchers are also making progress in understanding mutations in squamous cell lung cancer.

## MOLECULAR PROFILE OF SQUAMOUS CELL LUNG CANCER




Mutations in small cell lung cancer are also being studied, but at this time there is the least knowledge about mutations in this type of lung cancer, in part because it is less common than the other two.

Genetic mutations are being studied for all lung cancer types, and more information is being presented at every medical conference, so expect more updates.

02

# targeted cancer therapies

# targeted cancer therapies

Researchers are developing drugs that specifically target some of the genetic changes that cause cancer.

## What are targeted cancer therapies?

**Targeted cancer therapies** are a type of **biological therapy** that aims to target cancer cells directly. They target specific parts of cells and the signals that cause cancer cells to grow uncontrollably and thrive. These drugs are often grouped by how they work or what part of the cell they target.

**Targeted cancer therapies are sometimes also called:**

- Precision medicines
- Molecularly targeted drugs
- Molecularly targeted therapies

Targeted cancer therapies are currently approved by the U.S. Food and Drug Administration (FDA) for people who have either **anaplastic lymphoma kinase (ALK)** or **epidermal growth factor receptor (EGFR)** genetic mutations. In addition, **clinical trials** are currently studying promising drugs to target many other genetic mutations.

All of the drugs that have already been studied and FDA-approved belong to a class of drugs called **tyrosine kinase inhibitors (TKIs)**.

## Tyrosine kinase inhibitors (TKIs)

**Tyrosine kinases** are specific **enzymes** (a type of protein) that may signal cancer cells to grow. Tyrosine kinase inhibitors are targeted cancer therapies that block these cell signals. By blocking the signals, they keep the cancer from getting bigger and spreading. TKIs are named based on the enzyme that they block. The first TKIs for which there has been FDA approval are:

- ALK inhibitors
- EGFR inhibitors

### Anaplastic lymphoma kinase (ALK) inhibitors

An anaplastic lymphoma kinase (ALK) rearrangement is a fusion between two genes: ALK and another gene, with the most common being **echinoderm microtubule-associated protein-like 4 (EML4)**. The fusion of these two genes produces an abnormal ALK protein that causes cancer cells to grow and spread. The fusion between ALK and EML4 is more common in younger patients (median age at diagnosis is 52 years), in people who never smoked or light smokers, and in those with adenocarcinomas. It has rarely been

found in patients with squamous cell carcinoma. Similar frequencies of the ALK fusion gene have been reported in Asian and Western populations, unlike what we see with EGFR genetic mutations.

There are currently two marketed ALK inhibitors, which are also known as **anaplastic lymphoma kinase tyrosine kinase inhibitors (ALK TKIs)**:

- **Crizotinib (Xalkori®)**: Approved for patients with **metastatic** NSCLC who are ALK-positive
- **Ceritinib (Zykadia™)**: Approved for patients with metastatic NSCLC who have progressed on or are intolerant to crizotinib

In addition, many other ALK inhibitors are currently being studied in clinical trials.

## *How do ALK inhibitors work?*

ALK inhibitors work by blocking the signals that the abnormal ALK proteins send to cells to grow and divide uncontrollably. This stops the growth and spread of the cancer cells.

## *How are ALK inhibitors administered?*

- **Crizotinib (Xalkori®)**: Given as a pill 2 times a day, with or without food
- **Ceritinib (Zykadia™)**: Given as a pill once a day; cannot be taken within 2 hours of a meal

## *What are the side effects of ALK inhibitors?*

Overall, these drugs are well tolerated with a few key side effects.

The most common side effect that crizotinib causes is difficulty with vision. This includes:

- Trouble looking at light
- Blurred vision
- Double vision
- Seeing flashes of light
- New or increased floaters

**Note**: People don't usually stop treatment because of eye problems.

**Other common side effects of crizotinib include:**

- Nausea
- Diarrhea
- Vomiting
- Constipation
- Swelling of the hands or feet
- Feeling tired

Low testosterone is one source of fatigue in crizotinib patients being treated for ALK-positive NSCLC. This can also lead to sexual dysfunction and depression. Researchers have found that hormone replacement therapy is an effective method of managing these side effects.

Serious side effects of crizotinib include:

- Liver problems
- Lung problems (pneumonitis)
- Slow, fast, or abnormal heartbeats (less common)

**The most common side effects of ceritinib include:**

- Diarrhea
- Nausea
- Elevated transaminases
- Vomiting
- Abdominal pain
- Fatigue
- Decreased appetite
- Constipation

Serious side effects of ceritinib include liver problems and lung problems (**pneumonitis**), as well as severe or long-running gastrointestinal issues. High blood sugar is more likely to be an issue for patients with diabetes or glucose intolerance. Slow, fast, or abnormal heartbeats have also been seen.

### *Where do ALK inhibitors fit in the lung cancer treatment plan?*

Sometimes, treatment with an ALK inhibitor will be the only treatment a patient receives. However, in most cases, ALK inhibitors are used before or after chemotherapy, surgery, and/or **radiation therapy**.

## Epidermal growth factor receptor (EGFR) inhibitors

Epidermal growth factor receptor (EGFR) is a protein found in abnormally high levels on the surface of some cancer cells. Genetic mutations involving EGFR can lead to uncontrolled cancer cell growth and survival.

Approximately 10% of patients with NSCLC in the U.S. and 35% in East Asia have tumors with an EGFR genetic mutation. Regardless of ethnicity, EGFR genetic mutations are more often found in tumors of female nonsmokers. Most commonly, these patients have adenocarcinoma.

There are currently two FDA-approved EGFR inhibitors, which are also known as **epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs)**:

- **Afatinib (Gilotrif™)**: Indicated for **first-line treatment** of patients with metastatic EGFR-positive (mutant) NSCLC
- **Erlotinib (Tarceva®)**: Approved as a first-line treatment for patients with EGFR-mutant NSCLC, and as **maintenance therapy** and second- or third-line treatment for patients with **advanced stage non-small cell lung cancer (advanced stage NSCLC)**

## *How do EGFR inhibitors work?*

EGFR inhibitors work by blocking the signals that activate EGFR. This results in decreased tumor growth and survival.

## *How are EGFR inhibitors administered?*

Most EGFR inhibitors are pills taken by mouth once a day. They should be taken 1 hour before or 2 hours after a meal.

## *What are the side effects of EGFR inhibitors?*

The most common side effect of EGFR inhibitors is an acne-like rash on the scalp, face, neck, chest, and upper back. This occurs because normal skin cells have a lot of EGFR, and they must grow quickly to maintain the skin's surface layer. Drugs that target EGFR also turn off the signal for skin cells to grow normally and make it harder for them to retain moisture.

**The most common side effects of EGFR inhibitors include:**

- Rash
- Pruritus
- Diarrhea
- Stomatitis
- Loss of appetite
- Weakness
- Cough

More serious side effects that have been rarely seen with one or more of the EGFR inhibitors are:

- Interstitial lung disease
- Liver and kidney damage
- Eye inflammation
- Severe skin lesions
- Bleeding problems

### *Where do EGFR inhibitors fit in the lung cancer treatment plan?*

Sometimes, treatment with an EGFR inhibitor will be the only treatment a patient receives. However, in most cases, EGFR inhibitors are used before or after chemotherapy, surgery, and/or radiation therapy.

## Which genetic mutations identified in lung cancer are being studied in clinical trials?

Currently, clinical trials are open for many drugs that inhibit the effect of genetic mutations seen in NSCLC. The targeted treatments are being studied alone, as well as in combination with other targeted agents, chemotherapy, and radiation therapy.

As the number of known genetic mutations in lung cancer tumors increases, so does the number of drugs being developed to target them. Drugs that are currently being studied act against the following genetic mutations:

- AKT1
- ALK
- BRAF (non V600E), KRAS, NRAS, or MEK
- BRAF V600E
- DDR2
- EGFR
- FGFR1
- HER2
- KRAS
- MEK1
- MET
- NTRK1
- PDGFR
- PIK3CA
- PTEN
- RET
- ROS1

## Resistance to tyrosine kinase inhibitors (TKIs)

The biggest challenge of TKIs is that patients with lung cancer who initially benefit from them eventually develop resistance. **Acquired resistance** is defined* as **disease progression** after initial benefit with a targeted cancer therapy.

Cancer cells are clever enough to bypass roadblocks to their survival and often mutate to overcome the effects of targeted drugs. The most common way adenocarcinomas become resistant to EGFR inhibitors is by mutating to a drug-resistant state that stops the drugs from working.

Another way a tumor can become resistant to EGFR inhibitors is by activating a different pathway. In a small number of cases, the adenocarcinoma may transform into small cell lung cancer. Lung cancers with an ALK rearrangement normally have good responses to ALK inhibitors. However, they also eventually become resistant to the effects of the drug. In many cases, resistance arises because of genetic mutations in ALK.

*According to **Response Evaluation Criteria in Solid Tumors (RECIST)** or **World Health Organization (WHO) criteria**

Doctors and researchers are working to overcome resistance in tumors and to keep TKIs effective against cancer for longer periods of time. Their approaches include:

- Simultaneously prescribing multiple **enzyme inhibitors**, in case a different genetic mutation in the cell has been activated
- Developing the next generation of enzyme inhibitors that will inhibit not only the activity of the mutated gene but also the mutant form it could change into. The first treatment of this type to be approved was ceritinib

## How does targeted cancer therapy differ from chemotherapy and radiation therapy?

Targeted cancer therapies are aimed at specific pathways that tumor cells use to thrive, blocking them in the same way that blocking a car's fuel line would keep it from running properly. The advantage of such precise treatments is that they can target the root cause of why a tumor is growing, which may make them more effective.

## QUESTIONS TO ASK YOUR HEALTHCARE TEAM ABOUT TARGETED CANCER THERAPIES:

- Why do you recommend a targeted cancer therapy for me?
- What mutation do I have?
- What kind of targeted cancer therapy will I get?
- Will targeted cancer therapy be my only treatment or will it be combined with another treatment?
- How often will I take this therapy and for how long?
- How and when will I know if the treatment is working?
- How often do I need to be seen between treatments for a physical exam and/or lab work?
- Can I expect to see changes in my lab results while on this treatment?
- Are there any tests or procedures I will need during the treatment?
- What side effects can I expect?
- What can I do to manage these side effects?
- How will this treatment affect my daily life? Will I be able to work, exercise, and perform my usual activities?
- What tests will I need after treatment is completed?
- Are there any long-term health issues I should expect from treatment with targeted cancer therapy?
- How much will my treatment cost?

## Finding a clinical research study 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 resources to help you find one that may be a good match.

Information about available clinical trials may be found through the resources detailed below. The first is a comprehensive resource with trained experts who help you navigate clinical trials. The next three include trials for all cancers, not just lung cancer. The last three focus on people with mutations.

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

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

- **U.S. National Institutes of Health:**
  www.clinicaltrials.gov
- **National Cancer Institute (NCI):**
  www.cancer.gov/clinicaltrials/search
- **Coalition of Cancer Cooperative Groups:**
  www.cancertrialshelp.org/cancer-trial-search
- **My Cancer Genome:**
  www.mycancergenome.org
  - My Cancer Genome gives up-to-date information on what mutations make cancers grow and related treatment options, including available clinical trials
- **Lung Cancer Mutation Consortium (LCMC):**
  www.golcmc.com
  - Composed of 16 leading cancer centers across the country
  - LCMC's goal is to examine the tumors of patients who have a type of advanced (stage IIIB or IV) non-small cell lung cancer called adenocarcinoma, and match those patients to the best possible therapies, including clinical trials
- **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

03

# genetic mutation testing

# genetic mutation testing

To find out if targeted cancer therapy makes sense for an individual with lung cancer, that person's tumor tissue will be tested. The goal is to determine whether or not an appropriate target is present. Patients who do not have the mutation that a specific therapy targets would not be candidates for that treatment.

## How is genetic mutation testing performed?

A sample is taken from either an entire tumor that has been removed by a surgeon, or part of a tumor is collected by **biopsy**. Which approach is used depends on the **stage** of lung cancer and the person's overall health. A tumor sample is sent to a laboratory that can test it for genetic mutations. Test results are generally available within 10 to 14 days. **Genetic mutation testing** can be done on both **primary tumors** and **metastatic tumors**.

**Note that other names for genetic mutation testing include:**

- Biomarker testing
- Genetic testing
- Molecular testing

When there is not enough of a tumor sample to test for multiple mutations, testing should be prioritized based on the most likely mutations and whether there is an available FDA-approved drug treatment. Most insurance plans will only pay for testing related to an FDA-approved treatment. Therefore, at this time, when there is only a limited amount of tumor sample, tumors should be tested for the EGFR mutation and the ALK mutation.

**Multiplex testing** has the ability to identify multiple mutations at the same time. This may allow more tests to be done on a smaller tumor sample than if individual tests are done. For example, one study is looking at a particular laboratory test that has the ability to identify 10 known mutations in NSCLC.

Currently, for patients with a known EGFR mutation, the **EGFR inhibitors**, afatinib (Gilotrif™) and erlotinib (Tarceva®), have been approved by the FDA. The **ALK inhibitors**, crizotinib (Xalkori®) and ceritinib (Zykadia™), are available for patients who test positive for ALK. For patients with these and other mutations, a clinical trial for a new drug targeting that mutation may be an option.

## Who should have their tumor tested and when?

The decision to have your tumor tested and when depends on a number of factors, including your type and stage of lung cancer.

New guidelines* have been developed for deciding which patients should have ALK and EGFR genetic mutation testing. The goal is to match ALK- or EGFR-positive patients with approved drugs that target those mutations.

### GUIDELINES FOR ALK AND EGFR MUTATION TESTING

| Type of Lung Cancer | Guidelines for Genetic Mutation Testing |
|---|---|
| **Stage I, II, or III adenocarcinoma** | Testing for ALK and EGFR genetic mutations at the time of diagnosis is encouraged, but the decision should be made on an individual basis with your physician(s). |
| **Stage IV adenocarcinoma, or adenocarcinoma that has returned after an initial diagnosis of stage I, II, or III lung cancer** | Tumors should be tested for ALK and EGFR mutations. |
| **Any stage squamous cell lung cancer or small cell lung cancer (SCLC)** | If a tumor is completely removed and there is no adenocarcinoma component, testing for ALK and EGFR mutations is not recommended.<br><br>If the specimen is from a more limited sampling technique, such as a biopsy, testing may be performed in cases showing only squamous or small cell lung cancer cells. This is because it is possible that a tumor may have adenocarcinoma cells mixed in that were missed by the biopsy. |

*Jointly developed by the International Association for the Study of Lung Cancer (IASLC), the College of American Pathologists (CAP), and the Association for Molecular Pathology (AMP)

When deciding whether to have your tumor tested, you may also want to consider that mutations in genes other than ALK and EGFR have been found in both adenocarcinoma and squamous cell carcinoma.

Testing to identify other possible mutations in the tumor may help you find clinical research studies. These studies are testing new treatments for mutations in other types of lung cancer. Therefore, you may consider molecular testing for other mutations even if you don't fit into the ALK or EGFR testing categories.

Ultimately, any decision to test for mutations should be made together by you and your physician(s). This should be a part of the discussion with both your **oncologist** and surgeon. Your oncologist may recommend additional testing at different points of your treatment process.

As noted earlier, genetic mutations other than ALK or EGFR have been identified in types of lung cancer other than adenocarcinoma, particularly in squamous cell carcinoma. Drugs that target many of those mutations are being tested through clinical trials, so discussion of genetic testing makes sense for people with pure squamous cell carcinoma, as well.

In addition, multiplex testing to identify other possible mutations in the tumor may help a patient find clinical research studies. These studies are testing new treatments for mutations in both types of lung cancer.

## QUESTIONS TO ASK YOUR HEALTHCARE TEAM IF YOU ARE CONSIDERING GENETIC MUTATION TESTING:

- How long will it take to get the genetic test results, and is waiting for the results to begin treatment an option based on the extent of my disease?
- Will insurance pay for the test?
- What are the side effects of other treatment options that are available?

# 04

# glossary

# glossary

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

**Acquired resistance—**Disease progression after initial benefit with a targeted cancer therapy

**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 nonsmokers

**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

**ALK TKI—**See anaplastic lymphoma kinase tyrosine kinase inhibitor

**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

**Anaplastic lymphoma kinase tyrosine kinase inhibitor (ALK TKI)—** Drugs that block the activity of a protein called anaplastic lymphoma kinase (ALK). Blocking ALK may stop the growth and spread of cancer cells

**Biological therapy—**A type of treatment that uses substances made from living organisms to treat disease. These substances may occur naturally in the body or may be made in the laboratory. Some biological therapies stimulate or suppress the immune system to help the body fight cancer, infection, and other diseases. Other biological therapies attack specific cancer cells, which may help keep them from growing or kill them

**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

**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

**Disease progression—**Cancer that continues to grow or spread

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

**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

**Enzyme—**A special protein that the body produces to control its cells and carry out chemical reactions quickly. Sometimes enzymes signal cancer cells to grow

**Enzyme inhibitor—**A type of targeted cancer therapy that works by blocking the signals an enzyme sends cancer cells to grow

**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

**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

**Floater—**A bit of optical debris (as a dead cell or cell fragment) in the vitreous body or lens that may be perceived as a spot before the eye

**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

**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

**Genetic mutation testing—**Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder

**Histology—**The study of tissues and cells under a microscope

**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

**Interstitial lung disease—**A group of disorders that cause scarring of the lungs, which eventually affects the body's ability to get enough oxygen into the bloodstream and to breathe

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

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

**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

**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

**Molecular profile—**The genetic characteristics, as well as any other unique biomarkers, found in a person's cancer. The information is used to identify and create targeted therapies that are designed to work for a specific cancer tumor profile

**Multiplex testing—**The testing for multiple molecular genetic mutations at one time

**Mutation—**See genetic mutation

**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

**NSCLC—**See non-small cell 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 medical oncologist specializes in treating cancer with chemotherapy. A radiation oncologist specializes in treating cancer with radiation

**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

**Pneumonitis—**Inflammation of the lungs that may be caused by disease, infection, radiation therapy or other therapies, allergy, or irritation of lung tissue by inhaled substance

**Primary tumor—**A term used to describe 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

**Pruritus—**Itching of the skin

**Radiation therapy—**The use of high-energy radiation from X-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy, or brachytherapy). Also called irradiation and radiotherapy

**Response Evaluation Criteria in Solid Tumors (RECIST)—**A standard way to measure how well a cancer patient responds to treatment. It is based on whether tumors shrink, stay the same, or get bigger. To use RECIST, there must be at least one tumor that can be measured on X-rays, CT scans, or MRI scans. The types of response a patient can have are a complete response (CR), a partial response (PR), progressive disease (PD), and stable disease (SD)

**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 carcinoma—**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

**Stage 0 lung cancer in situ—**Abnormal cells found in the lining of the airways. These abnormal cells may become cancer and spread into nearby normal tissue

**Stage I lung cancer—**The lung tumor has grown through the innermost lining of the lung into deeper lung tissue. The tumor is no more than 5 centimeters across. Cancer cells have not spread to nearby tissues or lymph nodes

**Stage II lung cancer—**The lung tumor is smaller than 7 centimeters across and cancer cells have spread to lymph nodes on the same side as the tumor. Or, the lung tumor is more than 5 centimeters across and the cancer did not spread to the lymph nodes, but it did invade nearby tissues, such as the chest wall, diaphragm, pleura, main bronchus, or tissue that surrounds the heart. More than one tumor may be found within the same lobe of the lung

**Stage III lung cancer—**The lung tumor can be any size and more than one tumor may be within the same lung. Cancer cells may have spread to lymph nodes on either side of the chest or the neck. The tumor may have invaded nearby organs, such as the heart, esophagus, or trachea

**Stage IV lung cancer—**Lung tumors are found in both lungs. Or, the lung cancer has spread to other parts of the body, such as the brain, bones, liver, or adrenal glands

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

**Targeted cancer therapy—**A type of treatment that uses drugs to attack specific types of cancer cells with less harm to normal cells. Some targeted cancer 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

**Transaminase—**A type of enzyme that causes the transfer of a chemical substance called an amino group from one molecule to another. Transaminases are involved in many processes in the body, such as making amino acids

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

**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

**World Health Organization (WHO) criteria—**Tumor response criteria, mainly for use in clinical trials, where tumor response is the primary endpoint. Response to therapy is evaluated by the change from baseline while on treatment

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