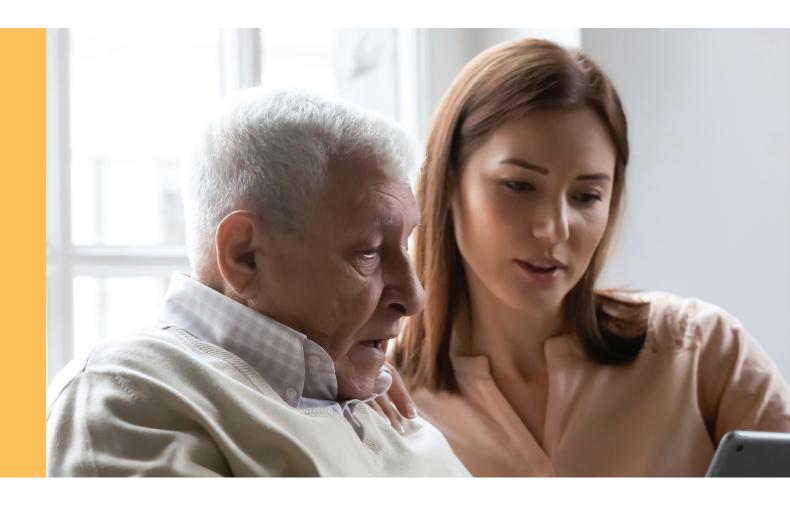
Comprehensive Biomarker Testing for Lung Cancer

A guide for patients and caregivers







You do not need to be a doctor to understand your tumor. Biomarker testing can help.

When your doctors suspected you had cancer, they took a small portion of your tumor tissue (a biopsy) to have it examined. A specialist, called a pathologist, looked at your tumor cells under the microscope and found out you had lung cancer. There are two main types of lung cancer–small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC). If you have NSCLC, the pathologist looks closely at the cancer cells for certain characteristics (features or qualities). Tumors with similar characteristics are referred to as subtypes. Adenocarcinoma (A-deh-noh-KAR-sih-NOH-muh) and squamous cell carcinoma (SKWAY-mus sel KAR-sih-NOH-muh) are the most common subtypes of NSCLC. Once your health care team knows the subtype of your cancer, treatment planning can begin.

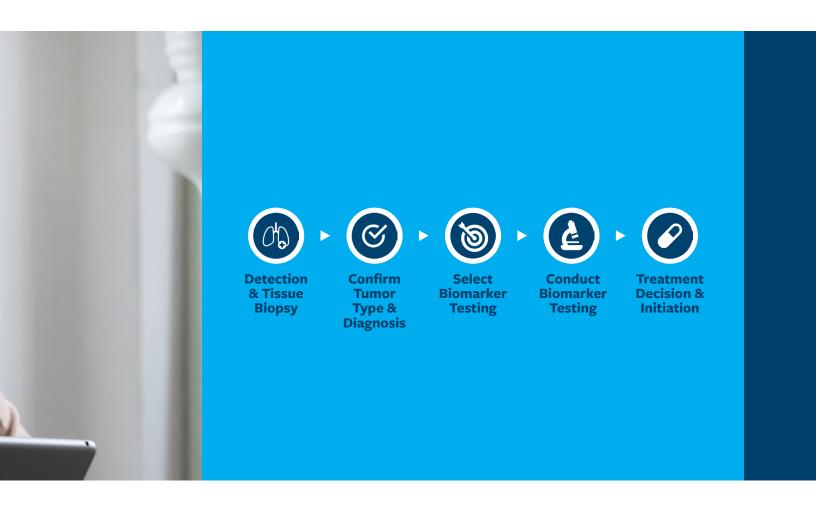
What is a biomarker?

The National Cancer Institute defines a biomarker as a biological molecule— found in blood, body fluids, or tissues that is a sign of a normal or abnormal process, a condition or disease.

Cancer biomarkers can include:

- Proteins
- Gene mutations (changes)
- Gene rearrangements
- Extra copies of genes
- Missing genes
- Other molecules

Cancer biomarkers typically refer to proteins, genes, and other molecules that affect how cancer cells grow, multiply, die, and respond to other substances in the body.



What is biomarker testing?

Your doctor may want more details about your tumor and order biomarker testing to look for mutations (changes) in the DNA of the tumor as well as levels of specific proteins. If your doctor looks for all possible mutations, regardless of whether there are drugs for these mutations, it is called comprehensive biomarker testing.



Biomarker test results can help determine which treatment might be best for you.

What is the difference between biomarkers and genes?

Your cancer has DNA that is different from the DNA in your healthy cells. Many cancer biomarkers that respond to treatment do so because of your tumor's unique genes and molecular structure, not your own genes. The mutations of lung cancers are usually not inherited and cannot be passed on to your children.

We all have DNA. Even your tumor.

Liquid Biopsies:

A liquid biopsy is a test done on a sample of blood to look for cancer cells or for pieces of DNA from tumor cells 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 plan treatment, find out how well treatment is working or if cancer has come back. Taking multiple samples of blood over time may also help doctors understand what kind of molecular changes are taking place in a tumor.

T790M Mutation:

Sometimes tumors can develop new mutations that cause targeted therapies to stop working (a process known as resistance). The most common mutation that causes resistance to EGFR-targeted drugs is called T790M. Your doctor might recommend another biopsy or a blood test to see if your tumor has the T790M mutation. If your tumor has an EGFR mutation and it is starting to grow despite being on a targeted therapy, you should talk to your doctor about whether your tumor should be biopsied to test for T790M.

How can my biomarker information help plan my treatment?

It's all about the targets. When a particular characteristic is found through comprehensive biomarker testing, specific treatment options may be considered for you. Testing will show if your tumor has certain types of changes to the cell structures. Some of these changes are known as **mutations**

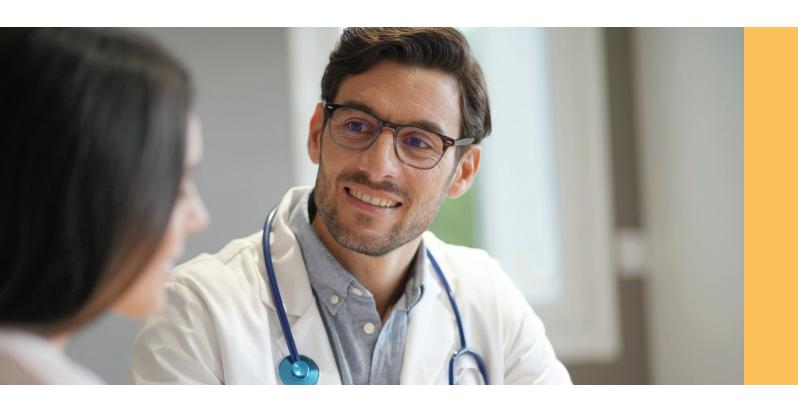
These mutations turn on processes that make cancer cells grow and divide uncontrollably. Research has been successful in creating treatments that directly target these specific traits and stop them from multiplying. These are called targetable mutations, and drugs that stop them are called targeted therapies.

Treatment that targets a specific biomarker may be recommended if you have an adenocarcinoma subtype of NSCLC that includes:

- Anaplastic Lymphoma Kinase (ALK) gene rearrangement
- BRAF V600E mutation
- Epidermal Growth Factor Receptor (EGFR) mutations
- KRAS mutation
- MET mutation
- NTRK gene rearrangement
- RET mutation
- ROS1 gene rearrangement



Knowing if your tumor has a unique trait, such as a targetable mutation, is important in helping you and your doctor make well-informed decisions about your treatment.



Besides targeted treatment, how else can comprehensive biomarker testing help me plan my treatment?

• **Immunotherapy:** Immunotherapy is proving to be a successful approach to treating lung cancer. Immunotherapies work by boosting your body's own natural defenses to fight cancer.

Cancer cells can use proteins called PD-1 to trick blood cells called T-lymphocytes, or T-cells. They trick the T-cells by using PD-1 to make them invisible. Common immunotherapies for lung cancer work hard to keep cancer cells from becoming invisible to your infection-fighting T-cells. Immunotherapy helps the T-cells recognize the cancer cells and destroy them.

PD-L1 testing looks at how much the biomarker PD-L1 is found in your tumor. Your doctor may feel immunotherapy is the best approach based on these test results.

- Clinical Trials: These studies are devoted to learning about how biomarkers can guide treatment decisions and further the success of personalized medicine. Clinical trials for personalized medicine are designed to ensure that the right treatment can get to the right patient, at the right dose, at the right time.
- Even if your tumor is negative for EGFR, ALK, ROS1, BRAF, NTRK, RET, KRAS, and MET mutations, it may still be tested for other biomarkers that may allow you to access additional treatment through a clinical trial.

Talk to your Health Care team about clinical trials or visit clinicaltrials.gov.



What if my test results don't qualify me for targeted treatment?

Even if your tumor does not have characteristics that can be matched to a targeted treatment that is available commercially or through a clinical trial, biomarker testing can still help you and your doctor decide on the right treatment option for you. In these cases, the very best systemic treatment (chemotherapy) will be given.

Will I need more than one biopsy?

Remember this—the tissue is the issue. If there is enough tissue from the original biopsy of your tumor, this tissue can be tested. If not, you may need a second biopsy to get enough tissue to test. As mentioned earlier, your doctor may recommend a liquid biopsy since there was not enough tissue.

You may need more than one because, in some cases, comprehensive biomarker testing was not conducted during the initial biopsy and a new provider wants it done. Some doctors may also want a second biopsy to see if you have developed a secondary mutation.

Where can I go to get my tumor tested?

Many major medical centers, offer biomarker testing for patients with lung cancer. Hospitals that treat lung cancer usually have a staff of pathologists on staff or they will have a contract with an outside lab service. If your medical center does not provide this testing, there are private companies that perform this service. Patient-led biomarker support groups are also a valuable resource for compassionate guidance on this issue.

What does tumor testing cost?

Most lung cancer tumor tests are covered by insurance. If you have concerns about whether your insurance will pay for biomarker testing, talk with your nurse, social worker, or insurance representative.

Questions to ask	How long will it take to get the results of this testing?
If you want to begin the discussion with your doctor, here are some questions to help guide the conversation:	
What type of biomarker testing should I ask for?	
	Can I still get comprehensive biomarker testing even though I have already begun treatment?
How could comprehensive biomarker testing affect my course of treatment?	
	If your doctor doesn't recommend biomarker testing for you, it is okay for you to ask, "why not?" There are cases where comprehensive biomarker testing will not
If I have a specific biomarker, does that mean I can only get treatment associated with that biomarker?	be useful to the patient's treatment plan. It is best for you to know as much as you can about your disease so you and your doctors can be full partners in your care. Remember that it is always okay to ask for a second opinion from another doctor about anything related to your treatment.
Is there enough biopsy tissue for this testing? Will I need another biopsy?	The more you know about your tumor, the more effectively you can treat it.
	Biomarker Collaborative can help you locate specific biomarker support communities and resources: biomarkercollaborative.org
How much does comprehensive biomarker testing cost? What is typically covered?	

This free resource provided with support from Bristol-Myers Squibb, Eisai Inc., Eli Lilly and Company, Genentech, Novartis, Pfizer, Takeda, Turning Point Therapeutics, and generous donations.

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