

## Advances in Lung Cancer Treatment

Treatment for lung cancer is changing rapidly. There are new therapies that target specific molecular changes that drive the growth and spread of the lung cancer. These therapies are called targeted therapies. This fact sheet explains how these new treatments work, possible side effects and what people facing lung cancer should know about access to these treatments.



SUPPORT FOR FINDING INFORMATION ABOUT LUNG CANCER

Cancer Support Community - 1-888-793-9355  
[www.cancersupportcommunity.org](http://www.cancersupportcommunity.org)

Free to Breathe - [www.freetobreathe.org](http://www.freetobreathe.org)

LUNGevery Foundation - [www.LUNGevery.org](http://www.LUNGevery.org)

Lung Cancer Alliance - 1-800-298-2436 - [www.lungcanceralliance.org](http://www.lungcanceralliance.org)

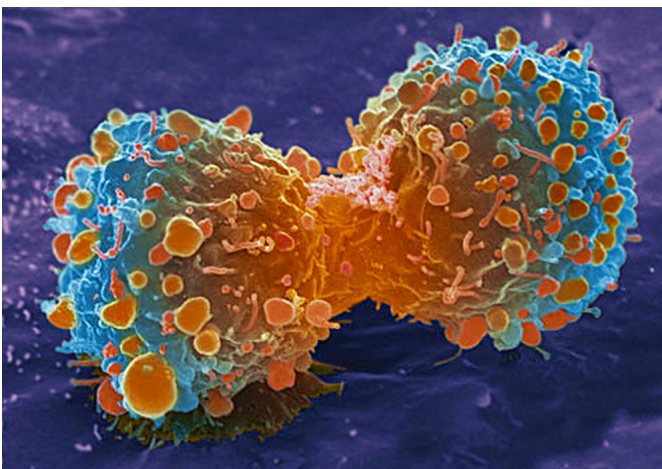
# Lung Cancer Today

In the United States, lung cancer is the second most common cancer in both men and women. The overall cure rates for lung cancer remain low, but have improved significantly in the past thirty years. Even among those who cannot be cured, many are living longer and better. Two major reasons for this progress are the discovery of new targeted therapies and immunotherapy. This fact sheet is about targeted therapies and the biomarkers used to determine when to use these treatments.

The two major types of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The targeted therapies described in this fact sheet are used to treat non-small cell lung cancers. While a great deal of research is being done to improve treatment for small cell lung cancers, at this time, there are no targeted therapies for this form of the disease.

## LUNG CANCER TREATMENT

Treatment for lung cancer is based on the type of cancer and its stage. For very early stage lung cancers, surgery and radiation therapy remain the primary treatments with the goal of removing the entire tumor and curing the person. Most people with lung cancer, however, have tumors that are more advanced at the time of diagnosis.



LUNG CANCER CELL DIVIDING

For lung cancers that have spread in the chest cavity or to nearby lymph nodes, called locally advanced tumors, treatment traditionally involves a combination of radiation, chemotherapy and sometimes surgery.

In the past, stage IV or advanced lung cancers were treated with chemotherapy and palliative radiation to try to stop the cancer's growth and reduce the symptoms of the disease. These treatments can sometimes control the cancer for a period of time, but the tumors almost always return or begin growing and spreading again. Yet, with the creation of targeted therapies, there are now more treatment options for people living with stage IV non-small cell lung cancer.

## CLINICAL TRIALS

*Many new drugs and agents are being tested in clinical trials. People with lung cancer should be aware of the importance of clinical trials and the potential benefits of participating in these studies. Clinical trials are the engine that moves cancer treatment forward. People who enter these studies receive state-of-the-art treatment and care for their cancers. Any person with advanced lung cancer should discuss the possibility of a clinical trial with their doctor.*

# How Does Targeted Therapy Work?

Cancers occur as a result of a series of changes or mutations in the cell. These changes affect the genes and molecular pathways that regulate cell growth, function and death. By studying both normal and cancerous cells, researchers have learned to identify changes or characteristics that can be targeted with drugs or other agents, which block the growth and spread of cancer cells.

There are a number of ways to destroy a cancer cell. A drug can:

- Interfere with the cell's ability to signal growth
- Interfere with the tumor's ability to form blood vessels (known as angiogenesis)
- Promote the death of cancer cells

It's important to know that only people with a specific genetic change will respond to the therapy targeted to that mutation or characteristic.

## A NEW APPROACH

Many people with stage IV or recurrent non-small cell lung cancer now receive targeted agents either alone or in combination with other treatments, including chemotherapy, radiation therapy, and more recently, immunotherapy.

If a person has a specific genetic mutation that can be targeted, the chances of responding to this therapy are very good. Many people, even those with very advanced disease, see their tumors shrink or even disappear. For some this means living for years rather than months with a good quality of life.

Yet even with targeted therapies, after a period of time, most lung cancers continue to change or mutate and become resistant to the initial therapy. This means the cancer begins to grow again. There is a great deal of research focused on learning how to prevent this resistance from occurring, either by using drugs that block multiple mutations or combining targeted therapies with other approaches.

## BIOMARKERS AND TARGETED THERAPIES

The goal of targeted therapy is to identify treatable molecular changes. The specific changes or indicators of the mutations or genetic alterations are called "biomarkers," which can be found when a tumor is tested.

One or more biomarkers are found in about 50% of people diagnosed with non-small cell lung cancer. These include:

■ **EGFR** is a protein found on the surface of cells. Its normal function is to help cells grow and divide. Some people with non-small cell lung cancer have too much EGFR. It is over-expressed so that cells grow faster and divide more often.

The EGFR mutation is found in about 15% of people with non-small cell lung cancer and 30% to 40% of those who never smoked. It is more common in younger people, women and people of Asian descent. There are now targeted therapies approved by the Food and Drug Administration (FDA) to block the signal from EGFR that tells NSCLC cells to grow; these include erlotinib

*"We are still very much in the infancy of understanding which pathways are activated when lung cancers occur and finding drugs to target them. In the next ten to fifteen years, this is going to be an area of explosive advances."* – Andrew Haas, MD, PhD

*“With targeted therapies, we are improving both the duration and the quality of life. In treating lung cancer, those two generally go hand in hand.” – Corey Langer, MD*

(Tarceva®) and afatinib (Gilotrif®). Clinical trials are also being done to find second line targeted therapies for lung cancers that have become resistant to the first line drugs. In addition, trials are being done to identify new agents that can be added to EGFR inhibitors to improve both response rates and survival.

■ **ALK** is a genetic change found in about 3 to 7% of people with non-small cell lung cancer—more frequently in people who have never smoked or have smoked very lightly. This biomarker results from the rearrangement of the ALK gene, which produces an abnormal protein that causes cells to grow and spread. There are two targeted therapies approved to treat ALK mutations in people with non-small cell lung cancer. They are crizotinib (Xalkori®) in the first line setting and ceritinib (Zykadia™) in those whose tumors have progressed on crizotinib. Several more drugs are being tested in clinical trials or under development. People with the ALK mutation often respond well to these therapies.

■ **KRAS** is a gene that is mutated in about 25% of non-small cell lung cases and occurs more often in people who have smoked or are currently smoking. It is a gene that is important in cell growth and tumor development. The search for a drug to inhibit KRAS met with failure for many years, but there are now several drugs in clinical trials that may work against this mutation.

## APPROVED TARGETED THERAPIES FOR ADVANCED NON-SMALL CELL LUNG CANCER:

- ERLOTINIB (TARCEVA®): EGFR MUTATION
- AFATINIB (GILOTRIF®): EGFR MUTATION
- CRIZOTINIB (XALKORI®): ALK AND ROS1 MUTATIONS
- CERITINIB (ZYKADIA™): ALK MUTATIONS

■ **BRAF, HER2, MET, MEK1, ROS, RET AND NRAS** are targetable molecular or genetic abnormalities. They help the cancer grow and spread, but only occur in 1% to 2% of people with non-small cell lung cancer. Although rare, their presence means that there are potentially effective treatments available for people with these biomarkers. There are many clinical trials underway now to test drugs that target these mutations. There are still many potential biomarkers for lung cancer that have not been identified or do not have agents that target them.

## OTHER TARGETED THERAPIES

All tumors form blood supplies to nourish themselves. Drugs that block this new blood vessel formation can, for some cancers, be an effective way of slowing or stopping the tumor's growth. The drug most commonly used to block blood vessel formation is bevacizumab (Avastin®). It is often given to people with non-small cell lung cancer in combination with chemotherapy.

In December 2014, the FDA approved ramucirumab (Cyramza™) in combination with docetaxel to treat metastatic NSCLC.

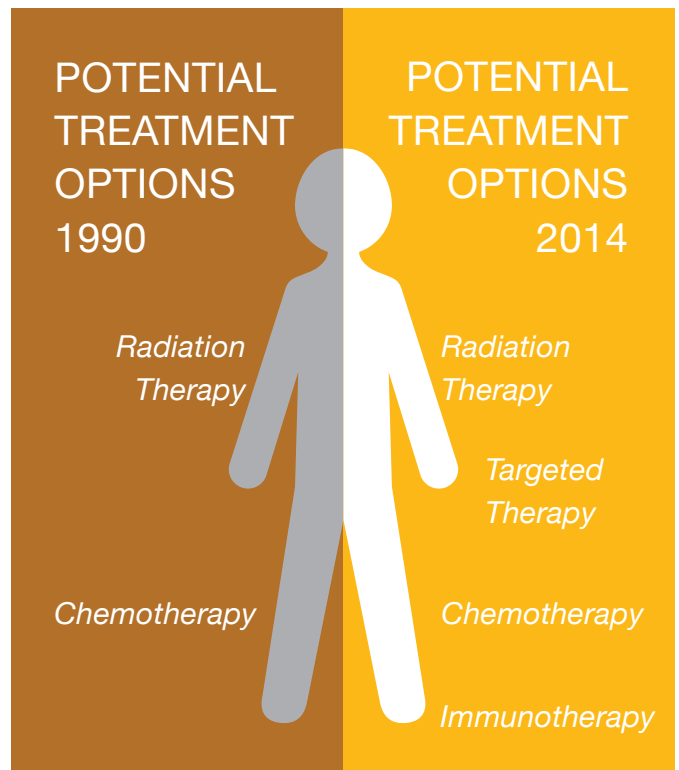
The therapeutic landscape in advanced NSCLC is rapidly changing and new treatments are continually emerging.

## GENETIC PROFILING

The only way to know if a person has a targetable mutation is to examine tissue from the tumor. The process of testing cancers for biomarkers is called genetic or genomic profiling. New technology has made it possible to test for over 80 biomarkers or genetic mutations and many cancer centers now use panels of multiple genes to profile tumors. The information obtained from identifying these mutations is critical to understanding how they work and developing new treatments.

Every person diagnosed with non-small cell lung cancer should either have genetic profiling or have enough tissue removed so that this test can be done when necessary. People with early stage lung cancers usually have surgery to remove their tumors—which assures that there will be adequate tissue for genetic profiling.

People with more advanced lung cancers do not always have surgery to remove the primary cancer. If the cancer has spread extensively, getting enough tissue can be difficult. This can also be true of people whose lung cancers are in hard-to-reach places. These are the people who are most likely to benefit from targeted therapies so it is very important to find a way to biopsy the cancer and obtain the tissue. New methods that



allow doctors to access and biopsy lung cancers are helping to overcome this problem.

Genetic profiling of lung cancer is critical because knowing the genetic profile provides essential information to deciding on the best treatment options. Those options can include standard therapies or clinical trials to test new agents.

*“The innovations in genomic testing and drug development have given doctors new ways to take advantage of the lung cancer’s ‘Achilles heels’ and have provided many people with treatments that specifically attack cancers and spare normal tissues. These advances bring us one step closer to the goal of delivering personalized care to all persons with lung cancers.” – Mark Kris, MD*



## Who Currently Benefits From Targeted Therapies?

The decision of how to treat any lung cancer must be individualized. It depends on the type of cancer, the stage of disease and the person's overall health.

Targeted therapies are most often used for people whose lung cancers have spread beyond the lung to other organs such as the liver, brain or bones. If a lung cancer cannot be surgically removed or treated with radiation or chemotherapy and radiation, targeted therapies can be very important in controlling the tumor. Increasingly, targeted therapies are given as first line treatment for people who have specific mutations, ahead of more "traditional" chemotherapy. However, there is no proven role yet in the curative setting. Studies testing targeted therapy in other treatment settings are still being done.

Only people with a specific biomarker will benefit from the therapy that targets that mutation—but not everyone with the biomarker responds to the targeted therapy. Generally, the response rates are much higher than those for chemotherapy, but some percentage of people with these biomarkers have lung cancers whose growth is controlled by other genes or pathways.

Those people who do respond to targeted therapies often have significant responses. Their tumors shrink or stop growing and their symptoms decrease. For some people, these benefits continue for months or years. In time, most lung cancers become resistant to the targeted therapy and begin to grow again.



*"I was devastated by my diagnosis of stage IV lung cancer. When I asked how long people with my condition lived, the answer was a year, maybe. I had the genetic testing done and it showed I had a mutation that could be treated.*

*That was four years ago and I'm still here." – Maria, diagnosed in 2010*

There is a tremendous amount of research being done today to understand why this happens and develop new drugs for second and third line use in people whose cancers recur after targeted therapy. Clinical trials are also underway to find the best ways to use the available drugs, including how and when to order them and how to combine them with other treatments. While drug resistance remains a serious problem, there is genuine hope that in the future, better understanding of how cancer cells work will lead to new approaches that will foster more lasting responses to targeted therapies

### **POSSIBLE SIDE EFFECTS**

One of the very positive aspects of targeted therapies is that they are generally easier to take and often have fewer side effects than standard chemotherapy. Many of the drugs are pills that people take by mouth at home.

The exact side effects depend on the drugs that a person takes and on the person themselves. Most people taking targeted therapies tolerate their treatments well, and your doctor can sometimes prevent or treat these problems before or when they occur.

Many people take targeted therapies for long periods of time, which means the side effects can last as long as the treatment does.

As targeted therapies are still relatively new, there is still more to be learned about the physical and emotional impact on the people who take them. For most people, however, the benefits of the targeted therapies outweigh the side effects.

The most common side effects of targeted agents are:

- Skin problems: Many targeted therapies can cause rashes or other skin changes including “acne-like” rash, dryness, a feeling of being “sunburned,” itching and red sore cuticles around the nails. These occur in over half of people taking these drugs. Rashes often appear about the 3rd or 4th week of treatment and can be uncomfortable. Your treatment team can help you take measures to prevent and control skin changes
- Changes in hair growth or hair color
- High blood pressure
- Diarrhea, nausea and vomiting
- Cough or shortness of breath
- Fatigue
- Headache

Not everyone has these side effects and not every drug causes all these problems. People who experience any side effect should always tell their doctors immediately what is happening. Side effects can and should be treated as early as possible.

## Real Progress...A Bright Future

The ability to match a cancer's specific genes or characteristics to a person's treatment is a major step forward in treating many forms of cancers, including lung cancer. Many targeted therapies are now available with many more being tested in clinical trials. These treatments are based on understanding what makes cancer cells different than normal cells, and how they change the environments in which they grow and spread. Targeted therapies represent a very real change in how cancer is treated, one which will continue to deepen and expand at a rapid pace.

# General Cancer Information, Survivorship & Support

Bonnie J. Addario Lung Cancer Foundation [www.lungcancerfoundation.org](http://www.lungcancerfoundation.org)

CancerCare 1-800-813-4673 [www.cancercare.org](http://www.cancercare.org)

Cancer.net 1-888-651-3038 [www.cancer.net](http://www.cancer.net)

Free to Breathe [www.freetobreathe.org](http://www.freetobreathe.org)

Lung Cancer Alliance 1-800-298-2436 [www.lungcanceralliance.org](http://www.lungcanceralliance.org)

LUNGeivity Foundation [www.LUNGeivity.org](http://www.LUNGeivity.org)

National Cancer Institute 1-800-422-6237 [www.cancer.gov](http://www.cancer.gov)

Patient Advocate Foundation 1-800-532-5274 [www.patientadvocate.org](http://www.patientadvocate.org)

## CANCER SUPPORT COMMUNITY RESOURCES

The Cancer Support Community's (CSC) resources and programs are available free of charge. To access any of these resources below call 1-888-793-9355 or visit [www.cancersupportcommunity.org](http://www.cancersupportcommunity.org).

## CANCER SUPPORT HELPLINE ®

Whether you are newly diagnosed with cancer, a longtime cancer survivor, caring for someone with cancer, or a health care professional looking for resources, CSC's toll-free Cancer Support Helpline (1-888-793-9355) is staffed by licensed CSC Helpline Counselors available to assist you Mon - Fri 9 am- 9pm ET.

## OPEN TO OPTIONS™

If you are facing a cancer treatment decision, Open to Options™ is a research-proven program that can help you prepare a list of questions to share with your doctor. In less than an hour, our Open to Options specialists can help you create a written list of specific questions about your concerns for your doctor.

## FRANKLY SPEAKING ABOUT CANCER ®

CSC's landmark cancer education series provides sound medical and psychological information for cancer patients and their loved ones. Information is available through books, online, and in-person programs.

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## AFFILIATE NETWORK SERVICES

Over 50 locations plus more than 100 satellites around the country offer on-site support groups, educational workshops, and healthy lifestyle programs specifically designed for people affected by cancer at no cost to the member.

## CANCER EXPERIENCE REGISTRY

The Cancer Experience Registry is a community of people touched by cancer. The primary focus of the Registry is on collecting, analyzing and sharing information about the experience and needs of patients and their families throughout the cancer journey. To join, go to [www.CancerExperienceRegistry.org](http://www.CancerExperienceRegistry.org)

## FRANKLY SPEAKING ABOUT CANCER: LUNG CANCER PROGRAM PARTNERS:

