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Cancer that begins in the lungs – lung cancer – is one of the most commonly diagnosed cancers in the United States. But lung cancer is not one disease.

**NON-SMALL CELL LUNG CANCER (NSCLC)**, the most common type. Two subtypes diagnosed most frequently are:

- Adenocarcinoma
- Squamous Cell Carcinoma

**SMALL CELL LUNG CANCER (SCLC)**

Knowing the type and subtype of your lung cancer is important. That information guides treatment options.
GENE CHANGES
THAT TRIGGER CANCER

There are many ways that normal cells in the lungs change into cancer. Research into how cancer develops has led to therapies that target cancer in some very specific ways. To understand targeted therapies, it helps to look at how cells work and how they can change into cancer.

A cell is the basic unit in our body that makes up all our organs and structures. Cells have different functions that are performed by parts inside the cell. Their nucleus or “brain” contains chromosomes, 23 from each parent. The chromosomes carry genes which are made up of material including DNA (deoxyribonucleic acid). These genes control how the cells work.

Over time, genes can change. The changes may happen over generations or over a lifetime in response to things we are exposed to or what we eat and drink. These changes may also happen by random chance. Some changes are helpful. Some do not make a difference one way or the other. But other changes can lead to the development of diseases, including abnormal growth of cells, such as cancer.

You will read and hear terms like mutations, fusions, alterations, translocations, deletions and rearrangements to describe various types of changes that happen inside cells that can trigger abnormal behavior of the cells.

GENES THAT CHANGE IN LUNG CANCER

It is helpful to know the gene where the change occurred to help match your tumor to a treatment. Genes are commonly called by the gene symbol which stands for a longer name.

<table>
<thead>
<tr>
<th>SYMBOL</th>
<th>NAME</th>
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<tbody>
<tr>
<td>EGFR</td>
<td>epidermal growth factor receptor</td>
</tr>
<tr>
<td>ALK</td>
<td>anaplastic lymphoma receptor tyrosine kinase</td>
</tr>
<tr>
<td>ROS1</td>
<td>ROS proto-oncogene 1 , receptor tyrosine kinase</td>
</tr>
<tr>
<td>BRAF</td>
<td>B-Raf proto-oncogene, serine/threonine kinase</td>
</tr>
<tr>
<td>KRAS</td>
<td>Kirsten rat sarcoma viral oncogene homolog</td>
</tr>
<tr>
<td>MET</td>
<td>MET proto-oncogene, receptor tyrosine kinase</td>
</tr>
<tr>
<td>ERBB2</td>
<td>erb-b2 receptor tyrosine kinase 2 (also known as human epidermal growth factor receptor 2)</td>
</tr>
<tr>
<td>RET</td>
<td>ret proto-oncogene</td>
</tr>
<tr>
<td>FGFR1</td>
<td>fibroblast growth factor receptor 1</td>
</tr>
<tr>
<td>PIK3CA</td>
<td>phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha</td>
</tr>
<tr>
<td>NTRK1,2,3</td>
<td>neurotrophic receptor tyrosine kinase</td>
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In order to know what kind of gene changes happened in the cancer, it must be tested. These tests may be done with samples collected at the time of the first biopsy (see page 9) to diagnose the cancer or on a new sample when another biopsy is done if the cancer grows or comes back. This testing may be called molecular profiling, molecular testing, biomarker testing, mutation testing or tumor testing. What all these tests have in common is that the goal is to find changes in the cancer that make it grow and spread. There are a lot of known changes that are common in each of the different types of lung cancer. If a specific change is found in the cancer, it is said to have tested “positive.”

Many of the gene changes that have been identified in lung cancer only occur in small percentages of people. Currently many more gene changes have been identified than there are approved therapies to treat but much research is ongoing to find treatments to target all of the known changes.

Testing your cancer is important to help determine your treatment options. Ask your treatment team if you have been tested and talk with them to make sure you understand the specific results of your tests.
A tissue biopsy, which involves removing tissue from the cancer to examine it under the microscope, is necessary to confirm a person has lung cancer and to tell what kind of lung cancer it is. Most molecular testing is done with tissue biopsy samples. To learn more about lung biopsies, see our brochure Understanding Lung Cancer Biopsies.

As lung cancer spreads, it can change. Understanding those changes may provide different treatment options. In the past, tissue biopsies were not often repeated. Today, biopsies for molecular testing may be done again later to help guide treatment decisions. Other new approaches are being used, including liquid biopsy, which uses blood or other fluids to study gene changes without the need for another tissue biopsy. These tests are starting to become available in some treatment centers to help guide treatment decisions.

Liquid biopsy is a new technology that can also be used for molecular testing. Liquid biopsy is when blood or other fluid is used to test the cancer. Small amounts of the cancer DNA can be found in your blood so sometimes this DNA can be used instead of DNA from the cancer tissue. Some liquid biopsy tests have been approved by the FDA and can be used to guide treatment choices. If there is not enough tumor tissue to do molecular testing or if a re-biopsy is not possible (or wanted), a liquid biopsy may be a good option.

We encourage all patients with lung cancer to ask their treatment team if they have had molecular testing and why or why not.

TESTING DURING DIAGNOSIS AND MONITORING

KNOW YOUR OPTIONS

New ways to understand and treat lung cancer are being tested and approved more quickly than ever before. Knowing your treatment options is important so you can be an informed and empowered member of your team.

If you have not had molecular testing, we can help you get it. Call our treatment and trial navigators at 1-800-298-2436 or visit www.lungmatch.org.

WHY TARGETED THERAPY?

Until the mid-2000's, treatment options were mostly limited to surgery, chemotherapy and radiation. Now, people diagnosed with lung cancer often have newer, more personalized treatment options.

The goal of targeted therapy is to accurately target your individual tumor, which hopefully leads to more effective treatments and less side effects. The purpose of this brochure is to help you understand targeted therapies and what they mean for you.

Targeted therapies work in similar ways in all cancers but certain drugs are more effective in certain subtypes of lung cancer.
Targeted therapies are aimed at a particular “target” in the tumor cell, with the goal of stopping the cancer from continuing to grow.

Targeting is meant to spare the rest of the body from side effects. This is different from chemotherapy which kills any fast growing cells in the body, including cancer cells. Targeted therapies are specific for the particular change in the cancer and therefore may have fewer side effects. Most targeted therapies for lung cancer are in pill form. Targeted therapies can also be given through a vein when they are monoclonal antibodies, man-made proteins targeted for a certain gene change.

Drugs typically have two names, a generic name and a brand name. An easy way to identify the difference between the two types of therapies (oral and infusion) is to look at the generic drug names.

**GENERIC DRUG NAMES**

| Oral Targeted Drugs | Ends in -ib  
| Example: Xalkori’s generic name is crizotinib |
| Monoclonal Antibodies | Ends in -mab  
| Example: Avastin’s generic name is bevacizumab |

The gene changes in non-small cell lung cancer that have targeted therapies approved by the Food and Drug Administration (FDA) are in EGFR, ALK, ROS and BRAF. The next section describes the FDA approved drugs for changes in each of these genes. Other types of cancer may have drugs approved to treat other gene changes. Your doctor may suggest using one of these if your lung cancer has that type of change.
DRUGS TARGETING EGFR

GILOTRIF (AFATINIB) | IRESSA (GEFITINIB) | TARCEVA (ERLOTINIB)

Gilotrif, Iressa and Tarceva are used to target multiple, different types of EGFR changes which typically happen in non-small cell lung cancer.

TAGRISSO (OSIMERTINIB)

Cancer often finds a way around targeted therapies and they stop working (see Drug Resistance information on page 16). Tagrisso is a different EGFR therapy that targets a specific change in EGFR called T790M. It may be an option if the cancer spreads after being treated with Gilotrif, Iressa or Tarceva. Tagrisso is also being tested as a first treatment for those who have EGFR mutations with promising results. It may receive FDA approval for first-line soon.

PORTRAZZA (NECITUMUMAB)

Another drug, Portrazza works by targeting EGFR and is approved in combination with chemotherapy only in squamous cell lung cancer.

DRUGS TARGETING ALK

ALECENSA (ALECTINIB) | ALUNBRIG (BRIGATINIB) | XALKORI (CRIZOTINIB) | ZYKADIA (CERITINIB)

All four of these drugs are ALK inhibitors that are used to treat non-small cell lung cancer that has spread to other parts of the body and has an ALK gene change (“ALK positive”). As of mid-2017, Xalkori and Zykadia are approved as a first treatment and all four are approved for later therapy after the cancer stops responding to the first treatment (see Drug Resistance on page 16). Alecensa is expected to be approved as a first treatment later this year. Importantly, some of these drugs work to treat cancer in the brain and central nervous system better and some drugs are better for specific gene changes in ALK. Talk to your treatment team about your testing results and your cancer to determine which is best for you.

DRUGS TARGETING ROS1

XALKORI (CRIZOTINIB)

Xalkori also targets changes in the ROS1 gene and is approved for treating advanced NSCLC with ROS1 gene changes.
A common example of this would be if you are positive for an EGFR mutation and taking Tarceva. You may initially respond very well to Tarceva, but after a while (months to years) the drug stops working. A second round of molecular testing shows that the tumor now has developed a specific change in EGFR called T790M. In this situation, Tagrisso can be prescribed for you.

Often targeted therapies work well for a period of time, but then stop working (the cancer develops “resistance”). This is more common with some drugs than others. When the cancer outsmarts the targeted therapy, it does so in different ways. Your treatment team may order additional biopsies and molecular testing to determine whether there are any new changes in the drug target or if there are other changes in the tumor. There may be drugs to treat the way the resistance happens.

A common example of this would be if you are positive for an EGFR mutation and taking Tarceva. You may initially respond very well to Tarceva, but after a while (months to years) the drug stops working. A second round of molecular testing shows that the tumor now has developed a specific change in EGFR called T790M. In this situation, Tagrisso may be prescribed for you.
While targeted therapies may have fewer overall side effects compared to chemotherapy, the most common side effects (rash and diarrhea) can be severe. Talk with your treatment team about how you might manage them. Other side effects may include vision disturbances, liver function abnormalities, fatigue, nausea, heart and lung problems.

Researchers are studying how to best give these drugs and are currently testing whether they should be combined with other types of treatments, such as chemotherapy or immunotherapy (a type of therapy used to stimulate or suppress the immune system to fight cancer). Combinations of multiple drugs may become more common in the future.

Targeted therapies cost more than most chemotherapy. The companies that make targeted drugs have programs to help you access their medications, so if you need help paying for them, do not hesitate to reach out. We can direct you to these assistance programs. Please call our HelpLine at 1-800-298-2436.

**IMPORTANT INFORMATION**

A doctor may also recommend a drug that is approved to target a gene change in a different type of cancer, if the lung cancer has that specific change. For targeted therapy, directing the drug at the correct gene change is more important than the site of the cancer. For example, if you have a mutation in HER2, a drug normally given for breast cancer might be an option for you. Similarly, drugs that are normally for thyroid cancer may be recommended if you have a mutation in RET.

**OFF-LABEL USE**

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KNOW YOUR OPTIONS

New ways to understand and treat lung cancer are being tested and approved more quickly than ever before. Knowing your treatment options, including clinical trials, is important so you can be an informed and empowered member of your team. Talk with your doctor to see if one of these new treatments is right for you.

CLINICAL TRIALS

Research in this area is moving quickly and there are many drugs in clinical trials targeting different gene changes. Having molecular testing may help your treatment team identify an appropriate clinical trial for you that is more precisely targeted to your cancer.

There are also new types of clinical trials including LUNG-MAP (for non-small cell lung cancer) and NCI-MATCH (for all cancers) where you will undergo molecular testing as part of the clinical trial to put you in a group testing a drug that is most likely to be effective for you.

Talk to your treatment team about whether a clinical trial is right for you. To see if you may qualify for a research study, call our clinical trial specialists at 1-800-298-2436 or visit www.lungmatch.org.
ABOUT

LUNG CANCER ALLIANCE

For more information about lung cancer, treatments and clinical trials, to discuss support options or for referral to other resources, please contact us.

HELPLINE
1-800-298-2436

MOLECULAR TESTING & CLINICAL TRIAL MATCHING
lungmatch.org

EMAIL
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lungcanceralliance.org

MAIL
1700 K Street NW, Suite 660
Washington, DC 20006

OUR MISSION

Saving lives and advancing research by empowering those living with and at risk for lung cancer.

WHAT WE DO

► Offer personalized support, information and referral services at no cost through a team of trained, dedicated staff members to help patients, their loved ones and those at risk.

► Advocate for increased lung cancer research funding and equitable access, coverage and reimbursement for screening, treatment, diagnostics and testing.

► Conduct nationwide education campaigns about the disease, risk and early detection.