

WHAT ARE TARGETED THERAPIES?

Researchers are learning more about what makes lung cancer cells grow and spread. Every cell in the body has the same library of genes that act as the blueprints for everything else that makes up a cell and makes it work. In cancer cells, damage to these genes (mutations) are responsible for the cells becoming cancerous and growing out of control. Some of these mutations create proteins in cells that act like a stuck gas pedal in your car to make it drive out of control. These mutant proteins in cancer cells are good "targets" for new drugs, because the targeted therapies can attack the cancer cells while sparing normal cells. **Erlotinib (ie: Tarceva)** is one example of a drug that targets the mutated proteins that are "stuck on" only in cancer cells.



WHY ARE TARGETED THERAPIES IMPORTANT AND WHAT MAKES THEM "PERSONALIZED"?

We call this "personalized" treatment because each patient's tumor can harbor different mutations. Patient A's tumor may have mutation X, while patient B's tumor may have mutation Y, and so on. This means that what works for one patient with lung cancer may not work for another. We are rapidly learning how to use this knowledge to match the best treatment for each individual patient.

Because targeted therapy and tumor testing for lung cancer is still a relatively new form of treatment, some doctors and oncologists may not be familiar with this new line of research. It is very acceptable and strongly advisable to get a second opinion, especially if your doctor is not familiar with tumor testing and targeted therapy. There are lung cancer experts all across the country at various medical centers and cancer centers that are available to offer second opinions.

FOR MORE INFORMATION ON TARGETED THERAPIES AND CLINICAL TRIALS

Vanderbilt-Ingram Cancer Center; My Cancer Genome

www.mycancergenome.com

ALK Inhibitors

alkinhibitors.com

The U.S. National Institutes of Health

www.clinicaltrials.gov

The National Cancer Institute

www.cancer.gov/clinicaltrials/search

Center Watch

www.centerwatch.com

Lung Cancer Foundation of America

www.LCFAmerica.org

If you would like to help support lung cancer research, please go to www.LCFAmerica.org and make a donation.



Now, let's cure it.

Lung Cancer Foundation of America

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TARGETING YOUR LUNG CANCER: PERSONALIZED MEDICINE AND TARGETED THERAPIES

Your Questions... with Answers from our Experts



Now, let's cure it.

WHAT TESTS and TARGETED THERAPIES ARE CURRENTLY AVAILABLE?

Many gene mutations have been identified in lung cancer-tumors, but not all mutations at the present time have effective targeted therapies developed for use in patients. The three genes that currently are most frequently tested for are **EGFR**, **KRAS**, and **ALK**. Usually, a positive result for one of these mutations means that the tumor will be negative for the other mutations.

EGFR (Epidermal Growth Factor Receptor)

There are several ways to identify the presence of EGFR in lung cancer tumors but mutational analysis is the best method to link potential therapy outcomes with anti-EGFR drugs like **Tarceva**.

- **EGFR “mutation positive”** tumors are likely to be highly sensitive to drugs like **Tarceva** (EGFR inhibitor) which is a pill taken by mouth. Side effects may include diarrhea and rash. In this situation, patients can actually receive Tarceva before receiving any chemotherapy. This treatment can cause the cancer to stay dormant or disappear for a long time.
- **EGFR “negative” or “wildtype”** tumors are likely to be less sensitive to drugs like **Tarceva**, although the drug may still inhibit cancer growth but is less likely to cause dramatic tumor shrinkage. In this case, the drug is usually used as a second or third line treatment after chemotherapy.

ALK (Anaplastic Lymphoma Kinase)

ALK mutations are found in a smaller number of non-small cell lung cancer patients than patients with the **EGFR** mutation. There are several ways to test for ALK mutations but the best method is to use test called by the acronym “FISH”.

- **ALK “positive”** tumors are likely to be highly sensitive to new drugs like **Crizotinib** (ALK inhibitor), a drug taken orally twice a day in a pill form. This drug is currently only available on clinical trials. It seems to have fairly mild side

effects and early clinical trial results are very promising. Drugs like **Tarceva** may not be effective against ALK positive tumors.

- **ALK “negative”** tumors are likely **not** to be sensitive to **Crizotinib**. Right now, it is difficult for patients to get Crizotinib if their tumors are negative for ALK fusions. Since Crizotinib also inhibits another receptor called “MET”, it is also possible to get this drug on a different clinical trial if your tumor over expresses MET.

KRAS (Kirsten-ras)

Mutational analysis is currently the only major way to test for KRAS mutations.

- **KRAS “mutation positive”** tumors are less likely to respond to drugs like **Tarceva**, but it may still slow their growth and is sometimes used. Importantly, KRAS mutation positive tumors are usually EGFR wildtype. There are currently no direct anti-mutant KRAS therapies; however there are multiple clinical trials testing whether a combination of new agents can be effective.
- **KRAS “mutation negative”** tumors may possibly be either ALK mutant or EGFR mutant positive.

If tumors are negative for mutations in all 3 genes (EGFR/KRAS/ALK), patients may be offered chemotherapy with or without **Avastin** or **Tarceva**, or a clinical trial for a new targeted therapy or stereotactic radiation.

HOW CAN I HAVE MY LUNG CANCER TESTED?

First, there needs to be enough tumor tissue available for testing. A “fine needle aspiration” or “FNA” biopsy may not provide enough tissue. A “core needle biopsy” usually does. If you had your tumor surgically removed, there likely will be enough tissue. In the future there may be a role for testing the blood for circulating cancer cells, but this is still under investigation.

Second, you need to be your own advocate and speak to your oncologist about being tested. You may be required to undergo another procedure to obtain enough tissue. Your doctor would be the one to order the tests; you need to make sure the doctor orders the right tests as discussed above.

WHAT SIZE TISSUE SAMPLE IS NEEDED FOR TESTING?

The more tissue the better. Tissue can be obtained thru bronchoscopy, lymph node biopsy, mediastinoscopy, CT guided CORE needle biopsy and via the VATS (video-assisted thoracoscopic surgery) procedure.

WHERE DO I GO TO HAVE MY TISSUE TESTED?

Many academic centers currently offer comprehensive tumor testing. Outside of academic centers, testing can be done through various “CLIA-certified” companies and laboratories in the US. In the latter case, your local oncologist can have these tests ordered. Once ordered, the local hospital pathology department is responsible for sending your tumor tissue to the appropriate facility.

HOW LONG DOES IT TAKE TO GET RESULTS?

Approximately 1 week to 1 month, depending on the availability of the tumor specimen for analysis and the amount and quality of the tumor in the biopsy. The tests themselves are relatively straightforward. The delay usually comes from the time it takes for the local hospital to locate your tumor specimen, to prepare the specimen for sending out to another facility, and then to actually send it. If your treatment is contingent on the test results, your doctor can request the test be expedited.

IF THERE IS LITTLE SAMPLE AVAILABLE, WHAT WOULD BE MOST IMPORTANT TO TEST?

Currently, because of the direct therapeutic implications, EGFR and ALK would be the priority.