Personalized Therapies for Lung Cancer

Questions & Answers

Lung Cancer Foundation of America
What are Personalized Therapies for lung cancer?

Like people, no two lung cancer tumors are the same. Personalized medicine (also known as precision medicine) is the idea of tailoring treatment to each patient. This takes into account both patient and specific tumor characteristics. Instead of using more general medical treatments that have been designed for the "average patient's tumor", personalized medicine seeks to identify unique characteristics of each patient's tumor in order to individualize care.

What are some examples of Personalized Therapies?

1. Targeted Therapies
   Targeted therapies are cancer treatments that specifically target certain known mutational changes in cancer cells. An oncologist will order biomarker testing of a patient’s lung cancer cells if they have a certain kind of lung cancer called adenocarcinoma, in order to identify the cell mutations unique to the lung cancer tumor. The list of mutations that are currently identified for testing continues to rapidly grow as more are discovered. Targeted therapies then work to shut down this mutation that would otherwise make the cancer cells grow and divide.

2. Immunotherapy
   Immunotherapy is the latest exciting research breakthrough for lung cancer. Immunotherapies are treatments that stimulate or use a person’s own immune system to attack cancer cells. By expressing certain proteins on their surface, cancer cells become hidden from the normal function of the immune system, which ordinarily serves to attack and kill “foreign” cancer cells. Immunotherapies function to wake up or restore the normal ability of the immune system. The Food and Drug Administration (FDA) approved immunotherapies for lung cancer are a group of medications called immune checkpoint inhibitors. Other immunotherapies are currently being investigated in clinical trials.

How do Personalized Therapies differ from chemotherapy and radiation?

Personalized therapies are unique treatments combining recently discovered therapies with more traditional therapies used in cancer, such as chemotherapy and radiation. Chemotherapy acts to stop the growth of all rapidly dividing cells in a patient’s body. Radiation is a therapy that works locally to destroy cancer cells with high-energy particles like X-Rays. Targeted therapies work selectively on those cells with a specific driver mutation, meaning they often don’t affect normal cells. Immunotherapies also work throughout the body to turn on the immune system to specifically attack cancer cells. Because of the different ways these treatments work, their potential side effects are also very different.

Right now, it is standard that some targeted therapies are used to treat advanced non-small cell lung cancer (NSCLC) with a treatable mutation before providing any chemotherapy. In certain instances, they may also be used later in treatment for patients with advanced NSCLC without any mutations. Immune checkpoint inhibitors, a specific type of immunotherapy, are currently being used to treat advanced or metastatic NSCLC patients. There are many new targeted therapies and immunotherapies in development. Whether available for use now or still under investigation, clinical trials are evaluating their effectiveness when used alone or in combination with different treatments (such as chemotherapy or radiation) for patients with a wide variety of lung cancer diagnoses. The goal of personalized therapy is to deliver the right treatment, to the right patient, at the right time.

How do I know what Personalized Therapies are available for my lung cancer?

The treatment of your lung cancer should be discussed with a lung cancer specialist, also known as a thoracic medical oncologist. When you are diagnosed, you should be told the stage of your lung cancer and the subtype of lung cancer you have. Based on this information, your lung cancer could then be tested for its unique mutations and proteins that would determine whether targeted therapies or immunotherapies might be the right treatment for you. These tests are sometimes repeated later on in your treatment in an effort to find other potential therapy options.

Targeted Therapies

What are the most commonly tested mutations and treatments in lung cancer?

1. EGFR (Epidermal Growth Factor Receptor)
   A patient’s tumor is referred to as “EGFR positive” if it has this mutation alteration in its cells. These mutations can make cancer cells sensitive to targeted therapies known as EGFR inhibitors. NOTE: There are some uncommon EGFR mutations that don’t respond to these medications, and you should talk with your oncologist about what your treatment options are in this case.

2. ALK/ROS-1
   Tumors found to have an “ALK positive” gene mutation or a ROS-1 gene rearrangement are likely to be highly sensitive to targeted therapies known as ALK inhibitors.

3. RET, MET & BRAF
   Recent findings that certain mutations found in other cancer types can also be found in lung cancer. This has led to studies showing that targeted therapies for these mutations are also active in lung cancer patients. While these medications are not yet FDA-approved for lung cancer patients, it is expected to happen soon based on recent encouraging clinical trial results.

What are other mutations/markers being tested or under investigation?

There are many other mutations that have been identified. These mutations are currently being studied as candidates for targeted therapy, with promising results pointing to a rapid increase in available new therapies. You should talk with your oncologist about the biomarker testing that is available, and consider having your cancer tested for a large panel of these gene mutations. You should also consider participating in clinical trials for which you are qualified based on these testing results, as all new drugs must go through this standard approval process.

Examples of other commonly tested mutations (in addition to EGFR, ALK and ROS-1):

- VEGFR2
- HER2
- HER3
- IGF-1R
- PIK3CA
- RET
- KRAS
- BRAF

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For which types of lung cancer are targeted therapies available?
Lung cancer is divided into NSCLC and small-cell lung cancer (SCLC). NSCLC in turn is broadly divided, based on the way cells look under the microscope, into squamous and non-squamous (example: adenocarcinoma) types. Most currently available personalized treatments discussed here are for the most common type of lung cancer, NSCLC, for patients with more advanced stages (IIIb or IV) where the cancer cannot be completely removed with surgery. The targeted mutations in this brochure are currently more common in non-squamous NSCLC. However, there is exciting research looking into these types of therapies for other types of lung cancer—squamous NSCLC and SCLC.

Using targeted therapies for early stage lung cancer (stages I to IIIA) is currently being investigated, so may only be available for use in clinical trials.

How can I have my lung cancer tumor tested for mutations?
1. Tumor Based Testing
Tumor based testing is the primary testing method at present. To test the tumor, there needs to be enough cancer cells (tissue) for testing; the more tissue there is, the more likely you will be able to have all of the required or recommended tests. The tests will depend on the type of lung cancer you have; you may need biomarker testing, and you may need to have your tumor tested for potential use of immune checkpoint inhibitors. Your oncologist will work with you to make sure that the lab has enough tumor cells to test.

2. Blood Tests
Blood tests for biomarker testing is a new, rapidly evolving area of discovery. The idea of being able to test for biomarkers or signs that immunotherapy may work for you as a blood test instead of requiring a piece of your cancer is an area of active study, with many exciting results expected soon.

What about tumors testing negative for treatable mutations?
If no treatable mutation is identified, a patient may be offered expanded biomarker testing or other types of standard therapy such as radiation, chemotherapy (with or without radiation), immunotherapy, and/or clinical trial enrollment (for an investigational treatment that isn’t yet a standard option).

THE GOAL OF PERSONALIZED THERAPY IS TO DELIVER THE RIGHT TREATMENT, TO THE RIGHT PATIENT, AT THE RIGHT TIME.
Immunotherapy

**What are immunotherapy treatments and how are they different from targeted therapies?**

Immunotherapy treatment enhances a patient’s own immune system response to stop the growth of cancer cells. Unlike targeted therapies, there are currently no mutations to identify candidates for immunotherapy. There are tests to identify tumor markers that may be required to start certain immunotherapies.

**How does immunotherapy work?**

Our immune systems work around the clock protecting our bodies from “foreign” substances such as bacteria and viruses. We know that this immune “surveillance” also protects us from cancer by recognizing a cell that has become cancerous as something foreign. When this surveillance system fails, cancers begin to grow. An everyday example of this process occurring naturally is in the case of pregnancy…this is the mechanism by which a fetus can grow in a woman’s body without being identified as foreign and hence being attacked.

**How do cancers evade our immune system?**

Spontaneous mutations in the genes of a cancer cell cause the cells to be altered in such a way that they can no longer be recognized by our bodies as something foreign. T-cells are the cells in our immune system that ordinarily fight cancer. A patient’s tumor can express molecules that trick their T-cells or other cells in the immune system preventing the T-cells from attacking the cancer cells.

The T-cells have receptors called PD-1 (PD stands for programmed death). A patient’s tumor can express molecules called PDL-1 (programmed death ligand). When the PD-1 on the T-cell bonds with the PDL-1 on the tumor, it prevents the T-cell from doing its job. This bond between PD-1 and PDL-1 is called a checkpoint. A CTLA-4 bond is also being explored.

Drugs known as “ANTI-PD-L1” or “checkpoint inhibitors” break that bond which then allows the tumor cells to be attacked by T-cells.

**What immunotherapies are available for lung cancer patients?**

The use of immunotherapy in lung cancer is rapidly changing. “Immune checkpoint inhibitors” are currently FDA-approved for the treatment of NSCLC. There are ongoing clinical trials investigating never-treated as well as previously-treated lung cancer patients with either early stage or advanced stage lung cancer. They are being looked at for use alone and in combination with a variety of other treatments (targeted therapies, radiation, chemotherapies and other immune checkpoint inhibitors). You should discuss with your oncologist whether you may qualify for immune checkpoint inhibitors or a clinical trial of any other form of immunotherapy.

A very important finding about immunotherapy is that when a patient responds to the treatment, the response can last longer than conventional chemotherapy... on the order of 1-2 years rather than 1-2 months. Scientists are studying why some patients’ cancers respond, as well as why other patients’ cancers do not. Combinations of these drugs with chemotherapy and/or other targeted therapies are also being investigated and appear extremely promising.

Ask your oncologist about the latest advancements in immunotherapy treatment for lung cancer.

**What does “treatment resistance” refer to?**

A tumor being treated with a targeted therapy can develop resistance to that drug after a period of time. Sometimes the drug stops working because the tumor cells develop new mutations that effectively “outsmart” the drug, allowing the cancer to grow. Depending upon the new mutation a tumor develops, the oncologist may have other targeted therapies specifically designed to overcome this drug resistance. Again, this is an area of active research with many available clinical trials looking at other treatment options.

**Should I be seeking a second opinion?**

Because a lung cancer diagnosis and lung cancer treatments are increasingly complex and continue to rapidly change, some oncologists may not be familiar with all of the most current research and available clinical trials. It is very acceptable and strongly advisable to get a second opinion. However, if your lung cancer is making you feel very sick, you may not want to delay treatment while trying to set up this appointment. There are many cancer centers nationwide with highly trained thoracic oncologists available to render second opinions. They will be able to talk with you about standard treatment options that you may be able to receive closer to home, as well as the more recent developments in the treatment of lung cancer including a review of available clinical trials.

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For more information on Personalized Therapies and clinical trials

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National Comprehensive Cancer Network
www.nccn.org/patients/guidelines/cancers.aspx

The National Cancer Institute - Comprehensive Cancer Centers:
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Revision: April, 2017