Immunotherapy and Lung Cancer

Immunotherapy is quickly developing as an important approach to treating many forms of cancer, including lung cancer. Immunotherapy uses the body’s own natural defenses to fight cancers. Understanding the interaction between the immune system and cancer is opening doors to new treatments that are changing the outlook for many people with advanced or metastatic lung cancer. Many studies are currently underway to test new drugs and agents. This fact sheet provides an overview of immunotherapy and how it is used to treat lung cancer.
About Lung Cancer

KEY TAKEAWAYS

■ NEW TREATMENTS ARE BRINGING HOPE TO PEOPLE WITH ADVANCED LUNG CANCER.

■ IMMUNOTHERAPY USES THE BODY’S OWN DEFENSE SYSTEM TO HELP FIGHT THE CANCER.

■ CANCERS OFTEN ELUDE THE IMMUNE SYSTEM. NEW APPROACHES TO IMMUNOTHERAPY BLOCK THE ESCAPE MECHANISMS OR BOOST THE IMMUNE RESPONSE.

■ MOST IMMUNOTHERAPY FOR LUNG CANCER IS DONE IN CLINICAL TRIALS, WHICH STUDY THE EFFECTIVENESS AND SAFETY OF THESE NEW AGENTS AND APPROACHES.

■ IMMUNOTHERAPY IS AN EXCITING AREA OF CANCER RESEARCH AND TREATMENT, WHICH IS SHOWING PROMISING RESULTS FOR PEOPLE WITH ADVANCED LUNG CANCERS.

According to the National Cancer Institute (NCI), this year in the United States, almost 225,000 people will be diagnosed with lung cancer. Only about 15% of these lung cancers will be early stage, meaning that the tumor has not spread to nearby lymph nodes or other parts of the body. Early stage lung cancers can be treated with surgery to remove the tumor, but once a tumor has spread, other approaches are needed to try to control the cancer and its symptoms for as long as possible.

For many years, chemotherapy and radiation therapy were the only options available for treating advanced lung cancers. More recently, researchers have discovered that some people have specific gene mutations that can be “targeted” with new drugs. These therapies are effective in extending survival and quality of life for many people with lung cancer. Not all people with lung cancer have these genetic changes, and only those who do have them benefit from targeted therapies. After a period of time, most lung cancers become resistant to the therapies and the cancers come back or begin to grow again. New studies are currently underway to find new ways to treat lung cancers that cannot be treated effectively with available therapies or have stopped responding to treatments that worked for months or even years.

The newest approach to treating lung cancer is called immunotherapy. It uses your body’s natural defenses to recognize and fight the cancer. For a more detailed description of how the immune system works and how it interacts with cancer cells, visit www.cancersupportcommunity.org. Researchers and people with lung cancer are excited about the possibilities of immunotherapy to treat lung cancer, but it is important to remember that these treatments are still very new and are being studied to determine if they are safe and effective, which patients will benefit and when to use them.
Researchers have known for some time that the immune system can recognize lung cancer cells as abnormal and mount a defense against them. There is evidence that:

- T cells, blood cells that are key components of the immune system, respond to lung cancer cells and attack them. They do this by identifying what are called “tumor specific antigens,” substances expressed by the cancer cells.
- Pathologists, who examine tissue from lung cancers, find evidence that the immune system has attempted to destroy the cancer.
- The presence of T cells in and around the tumor is associated with longer overall survival and longer disease free survival in people with lung cancer.

Understanding the relationship between the immune system and lung cancer provides a strong basis for developing ways of increasing the strength and duration of the immune response. There are currently several approaches to immunotherapy for lung cancer.

### Targeted Therapies

- **Most Often People with a Known Genetic Mutation Receive These Drugs**
- **Response Rates Are 60% or More in These Patients**
- **People Continue to Take the Drugs Indefinitely**
- **Most People Become Resistant to the Targeted Agents After a Period of Time and the Cancer Recurs**

### Immunotherapy - Checkpoint Inhibitors

- **Response Rates Are About 20-25%**
- **In People Who Respond, the Response Continues After They Stop Taking the Therapy**
- **The Immune System Appears to Reset Itself, Recognizing and Attacking the Lung Cancer**

**Top: Small Cell Lung Cancer Cells**

**Bottom: Non-Small Cell Lung Cancer Cells**
Types of Immunotherapy

If the immune system recognizes and attacks lung cancer cells, why do these abnormal cells often grow and spread so successfully? The answer is that it takes many years for any cancer cell to develop and during that time the cancer cells go through many changes. This ability to change and adapt allows the cancer cells to escape from the immune system or in some cases even use the body’s own defenses to help the tumor grow and spread. The key to successful immunotherapy lies in understanding exactly how that occurs.

There are three major approaches to immunotherapy:
- Immune Checkpoint Inhibitors
- Therapeutic Vaccines
- Adoptive T Cell Therapies

All of these approaches use different ways of stimulating the immune system to attack lung cancer cells.

Immune Checkpoint Inhibitors

One way that cancer cells escape the immune system is to fool the body into turning its own defenses off. The ability to turn off is a necessary checkpoint that protects normal tissue from being attacked by the immune system, much like the brakes in a car. Immune checkpoint inhibitors work either by preventing the tumor from putting on the brakes or stimulating the immune response.

There are several promising new treatments that use this approach.

CTLA-4 TARGETED MONOCLONAL ANTIBODIES. These drugs are man-made antibodies that act like the ones our bodies produce naturally. They work by activating T cells that can seek out and destroy cancer cells. Ipilimumab (Yervoy®) is approved to treat advanced melanoma, but is now being studied for a number of other tumors, including non-small cell lung cancer and small cell lung cancers. Tremelimumab is another monoclonal antibody being tested in the treatment of mesothelioma.

“In it’s really important for patients (or their caregivers or family members) to get in touch with their doctors to let them know what their side effects are.”
— Suzanne McGettigan, NP

In non-small lung cancer, ipilimumab is being studied in combination with chemotherapy. Studies have shown that some people with advanced lung cancer respond well to these drugs and have longer overall survival. It is important to remember that while these drugs can be effective, some people do not respond well to the drugs and those who do usually relapse after a period of time.

NOTE: These drugs have not been approved by the Food and Drug Administration (FDA) to treat lung cancer. This means that they are only available to people with lung cancer through clinical trials.

Side effects of ipilimumab and similar drugs include fever, rashes, diarrhea, itching, fatigue and problems with the thyroid or other glands. Most people are able to tolerate these side effects well or be supported through them, but in some, they are severe.

PD-1 INHIBITORS. These drugs target an immune checkpoint found on T cells. Cancer cells can use the PD-L1 pathway to deactivate T cells and escape from the immune system. In March 2015, the FDA approved the first PD-1 inhibitor, nivolumab (Opdivo®). It is used to treat people with metastatic squamous non-small cell lung cancer who no longer respond after chemotherapy. A number of new drugs are also being tested in clinical trials for lung cancer and a number of other cancer types. The results to date are promising.
Another source of excitement about PD-1 inhibitors is that the side effects of these drugs are usually relatively minor and most people are able to tolerate them well. They include fatigue, itching, diarrhea and skin rashes. There are also people who cannot take these drugs because they have certain medical conditions.

There is still a great deal to learn about these exciting new therapies. Some common questions are:

- Why do they work so well in some people and not at all in others?
- How can they be combined with other treatments?
- When is the best time to use them?

Once a drug is approved by the FDA, it can be used as standard therapy outside of a clinical trial. Many people with lung cancer will still get PD-1 inhibitors on clinical trials as researchers learn more about how these drugs work and which person will benefit. There are also several new drugs that work like PD-1 inhibitors that are available only in clinical trials.

People with lung cancer that is locally advanced or has spread to other sites who are interested in learning more about checkpoint inhibitors should talk to their doctors about the options available to them.

Lung Cancer Vaccines

There are several agents now being tested in clinical trials as vaccines to treat lung cancer. These drugs target tumor-specific antigens, characteristics expressed by the cancer cells that mark them as different or abnormal. There are currently trials to determine if these vaccines can delay or prevent recurrence in people with lung cancers that are high risk to return or spread, as well as trials to treat people with advanced disease.

Vaccines are being developed to target antigens expressed in lung cancers such as MAGE-3 and NY-ESO-1. These targets provide promising approaches for new lung cancer vaccines, but they are not the only one. There are a wide variety of potential targets, many of which are being tested today.
When a person living with cancer undergoes chemotherapy or radiation therapy, the results are usually evident fairly quickly. The tumor may shrink, remain the same size, or even grow. Doctors measure these responses within the first few weeks after treatment begins. Immunotherapy is proving to be different. The benefits of immunotherapy can take much longer to become apparent. Some cancers actually appear to get bigger before they shrink or disappear. It can take weeks before the positive results are seen. While the goal of treatment is to shrink tumors, there is also a benefit for many people in having their cancers remain stable, neither shrinking nor growing. This result is also seen more often in people who respond to immunotherapy—in some for long periods of time.

This delayed response is seen most often in people receiving ipilimumab. It can be challenging for these people to have to wait for a potentially extended period of time to learn whether the treatment is working or not. Many doctors recommend doing the first scan to measure results at twelve weeks instead of the more standard six to nine weeks. There are a number of possible explanations for these delayed responses, including a start-up period for the immune response, and the possibility that the immunotherapy produces an inflammatory response around the tumor that looks on a scan like tumor growth.

Immunotherapy is very new for treating lung cancer. There is a great deal to be learned about why some people respond and others do not, and about why the response in some people appears to last a long time, perhaps even being a cure, while others relapse after a period of time. Little is known at this time about the long-term effects of activating or boosting the immune system.

Today, virtually all people with lung cancer treated with immunotherapy have advanced cancers. The goal of treating these cancers is to control them for as long as possible with the highest quality of life. There is tremendous excitement about the potential of immunotherapy to improve both the length and quality of survival, but there is also a great deal of work to be done and much to be learned about how these treatments work.
If you have lung cancer and are interested in learning more about immunotherapy options, here are some important points to remember.

- Right now, almost all immunotherapy for lung cancer is available by participating in a clinical trial. There are many of these trials, but most are conducted in specialized cancer centers by doctors who are very experienced and expert in treating lung cancer and developing new treatments.

There are many different approaches to immunotherapy and a large number of new drugs and agents that are being tested. The only way to learn about these options and understand which ones are right for your case is to talk to your doctors and the doctors who are conducting the trials. Different drugs are used to treat the various types of lung cancer.

- Participating in a clinical trial assures that you will receive the best available standard of care for your lung cancer or a new approach that may offer improved outcomes. No one with high risk or advanced lung cancer receives a placebo or inactive treatment.

- Participating in a clinical trial means that you are giving yourself an opportunity to benefit from a new treatment, and helping advance research for other people who have or will be diagnosed with lung cancer.

- The primary goal of all cancer treatment is to extend survival, but today, doctors also care about assuring that every person has the best possible quality of life for their type and stage of cancer. Understanding and meeting your goals is an important part of the treatment plan.

The Cancer Support Community’s Clinical Trials Matching Service, powered by EmergingMed, can help you find clinical trial options that match your unique diagnosis and treatment history. Visit http://www.cancersupportcommunity.org/MainMenu/About-Cancer/Treatment/Clinical-Trials.html or call 1-800-814-8927 to learn about available trials.

An Exciting Future

Lung cancer is a serious disease. When lung cancer is advanced, it remains a difficult cancer to treat. New approaches to targeted therapy and, more recently, to immunotherapy are making a difference for people facing lung cancer. There is hope for longer survival and better quality of life. As researchers learn more about the ways in which the immune system interacts with lung cancers, there is genuine promise for changing the possibilities for people with lung cancer.

YET TO COME...

- CLINICAL TRIALS TO STUDY COMBINING TARGETED AND IMMUNOTHERAPIES
- MORE RESEARCH TO UNDERSTAND WHY SOME PEOPLE RESPOND TO IMMUNOTHERAPY AND OTHERS DO NOT
- MORE RESEARCH TO UNDERSTAND HOW THE IMMUNE SYSTEM “RESETS” ITSELF
- CLINICAL TRIALS FOR PEOPLE WITH LUNG CANCER WHO HAVE EARLY OR LESS EXTENSIVE DISEASE
General Cancer Information, Survivorship & Support

American Cancer Society 1-800-227-2345 www.cancer.org
Bonnie J. Addario Lung Cancer Foundation www.lungcancerfoundation.org
CancerCare 1-800-813-4673 www.cancercare.org
Cancer.net 1-888-651-3038 www.cancer.net
Free to Breathe www.freetobreathe.org
LUNGevity Foundation www.LUNGevity.org
National Cancer Institute 1-800-422-6237 www.cancer.gov
Patient Advocate Foundation 1-800-532-5274 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.

CANCER SUPPORT HELPLINE ®
Whether you are newly diagnosed with cancer, a long-time 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.

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A special thanks to our contributors and reviewers: Julie Brahmer, MD, John’s Hopkins University; Jennifer Maloney, NP, Memorial Sloan-Kettering Cancer Center; Ellen Levine, MSW, LCSW, OSW-C, Cancer Support Community Central New Jersey; Danielle Hicks, Bonnie J. Addario Lung Cancer Foundation; Annie Dutcher, Free to Breathe; Susan Mantel, LUNGevity Foundation.

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THIS PROGRAM WAS MADE POSSIBLE THROUGH A CHARITABLE GRANT FROM:
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