

TREATMENT UPDATE:

Lung Cancer

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Treatment Update: Lung Cancer

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There have been exciting developments in the treatment of lung cancer, with more options available than ever before.

Through genetic testing of tumor samples, doctors can identify specific types of lung tumors and prescribe treatments designed to target them. Immunotherapy has also emerged as a treatment option for certain types of lung cancers. These advances have made treatments more effective, often with fewer side effects.



Types of Lung Cancer

There are two major types of lung cancer: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

NSCLC accounts for about 85 percent of lung cancers and includes adenocarcinoma (the most common form of lung cancer in the United States), squamous cell carcinoma and large cell carcinoma. SCLC tumors account for the remaining 15 percent of lung cancers in the United States. They tend to grow more quickly than NSCLC tumors.

Tumors are classified by stage. Stages are based on whether the cancer is local (in the lung only), locally advanced (has spread to nearby lymph nodes in the lung area) or metastatic (has spread to other parts of the body).

Treatment Options

Surgery

Surgery, sometimes in combination with chemotherapy, is the most common treatment option for tumors confined to the lung. Advances in surgical techniques allow doctors to make much smaller incisions to remove tumors or sections of a lung affected by cancer. Using video-assisted thoracoscopic surgery (VATS), the surgeon inserts a tube called a thoracoscope into the chest. This device has a light and a tiny camera connected to a video monitor.

Radiation Therapy

In cases where surgery is not possible, radiation therapy is sometimes used, either alone or in combination with chemotherapy. Radiation may also be used before surgery to shrink the tumor or after surgery to help prevent the cancer from recurring (coming back).

“External beam” radiation is commonly used in treating lung cancer. Standard external beam radiation uses a machine that directs a beam (or multiple beams) of radiation to the tumor. The use of CT (computerized tomography), MRI (magnetic resonance imaging) and PET (positron emission tomography) scans allows radiation oncologists to accurately target tumors, shaping the radiation beams to the size and dimensions of the tumor to help spare healthy tissue.

A newer form of radiation called SBRT (stereotactic body radiation therapy) is sometimes used in the treatment of early-stage lung cancer or lung cancer that has spread to only one site (or a small number of sites). SBRT delivers higher doses of radiation to a small area over a shorter period of time, which kills more cancer cells and minimizes the impact on healthy tissue. For early-stage lung cancer, SBRT has been shown to be beneficial with survival rates that are close to those expected with surgery. Research is ongoing to determine which people with early-stage lung cancer could best benefit from this type of focused radiation as an alternative to surgery.

Another form of radiation therapy uses streams of protons (tiny positively-charged particles located at the center of atoms) to kill tumor cells. With proton beam radiation therapy, precise doses of protons can be delivered to the exact location of the tumor.

Recent research has shown that this type of radiation is a viable treatment option for people whose lung cancer has not spread outside of the lung area.

Enhanced technologies, such as image-guided radiation therapy (IGRT) and intensity modulated radiation therapy (IMRT), may be used to help radiation oncologists treat lung cancers with greater precision.

Chemotherapy

Chemotherapy has long been an effective treatment for lung cancer. It is extremely effective in treating SCLC, and is also used to treat many cases of NSCLC. Chemotherapy can also be helpful for people with early stage cancers that have been (or will be) removed by surgery, and in combination with radiation for locally advanced cancer. It is also an important part of treatment for most people with advanced stage lung cancer.

Chemotherapy drugs approved by the U.S. Food and Drug Administration (FDA) for the treatment of lung cancer include:

- **Cisplatin (Platinol) and carboplatin (Paraplatin).** These platinum-based drugs are the most common chemotherapies used in treating lung cancer. Most chemotherapy treatment approaches include either cisplatin or carboplatin in combination with another chemotherapy drug.
- **Pemetrexed (Alimta).** Pemetrexed is used in combination with cisplatin for the initial treatment of advanced non-squamous NSCLC. Pemetrexed is also approved for use alone to treat advanced non-squamous NSCLC after another chemotherapy has been given.

In January 2019, the FDA expanded the approval of pemetrexed to include its use with platinum-based chemotherapy and the immunotherapy pembrolizumab for the initial treatment of advanced non-squamous NSCLC that is not caused by a gene mutation.

- **Gemcitabine (Gemzar).** Gemcitabine is used to treat NSCLC, either in combination with cisplatin or carboplatin as an initial treatment or as a single drug after another chemotherapy has been given.
- **Paclitaxel (Taxol), nab-paclitaxel (Abraxane), docetaxel (Taxotere).** These drugs are forms of “taxane” chemotherapy and can be given in combination with cisplatin or carboplatin for all types of NSCLC. Docetaxel is frequently given alone or in combination with ramucirumab as a later line of therapy in advanced stage lung cancer. (See the section entitled “Cutting off the blood supply to tumors” for information on ramucirumab.)
- **Etoposide (Etopophos, Vepesid).** Etoposide is used in combination with other cancer medications for the treatment of SCLC.

Targeted Therapy

Targeted therapies are designed to target the specific cell mechanisms that are important for the growth and survival of tumor cells.

Researchers have discovered that mutations in a gene called epidermal growth factor receptor (EGFR) can cause the development, growth and spread of lung cancer. Approximately ten percent of people with lung cancer have EGFR mutations present in their tumors. EGFR inhibitors—targeted therapies given in pill form—are often used to treat this type of lung cancer. Today, five medications are approved treatment options in the United States for lung cancer that has this gene mutation:

- **Erlotinib (Tarceva).** In 2004, the FDA approved the use of erlotinib for the treatment of NSCLC. In 2013, the approval was expanded as an initial treatment for people with NSCLC that has spread to other parts of the body and has certain types of EGFR mutations, or has a piece missing (called a “deletion”) from the EGFR gene.
- **Afatinib (Gilotrif).** In 2013, the FDA approved afatinib for the initial treatment of metastatic NSCLC in people with the same EGFR gene mutations or deletions as those treated with erlotinib. In 2018, the FDA expanded its approval to include the treatment of lung cancers with less common EGFR mutations.
- **Gefitinib (Iressa).** In 2015, the FDA approved gefitinib for the initial treatment of people with NSCLC whose tumors harbor specific types of EGFR gene mutations, as detected by an FDA-approved test.
- **Osimertinib (Tagrisso).** In 2016, the FDA approved osimertinib for the treatment of people with NSCLC whose tumors have specific EGFR gene mutations and have started to regrow after treatment with erlotinib, afatinib or gefitinib. In 2018, the FDA approved the use of osimertinib as a first-line treatment for people with metastatic NSCLC that harbors common EGFR mutations.



- **Dacomitinib (Vizimpro).** After a priority review, the FDA approved dacomitinib in September 2018 as an initial treatment for NSCLC with certain EGFR gene mutations as detected by an FDA-approved test.

Another genetic change found in some lung cancers is referred to as ALK fusion or rearrangement. Five targeted therapies are approved by the FDA as treatment options for people whose cancer has this genetic change. These drugs are designed to block the rearranged ALK gene, stopping the growth of the tumor.

- **Crizotinib (Xalkori).** Crizotinib was approved by the FDA in 2013 for the treatment of metastatic NSCLC tumors with the ALK gene fusion. Additionally, crizotinib was approved in 2016 to treat people with metastatic NSCLC that has a fusion of the ROS-1 gene.
- **Ceritinib (Zykadia).** Ceritinib was approved in 2014 for the treatment of people with metastatic ALK-positive lung cancer who cannot tolerate crizotinib or whose cancer continued to grow while being treated with crizotinib. In 2017, it was approved for the treatment of newly-diagnosed ALK-positive lung cancer.
- **Alectinib (Alecensa).** Alectinib was approved in 2015 for people with ALK-positive lung cancer who had already been treated with crizotinib. In 2017 alectinib was approved to be given as a first-line treatment option.
- **Brigatinib (Alunbrig).** In 2017, brigatinib was approved for the treatment of ALK-positive lung cancer that was previously treated with crizotinib.
- **Lorlatinib (Lorbrena).** In November 2018, lorlatinib was approved for the treatment of ALK-positive metastatic NSCLC that progressed while being treated with crizotinib or another ALK inhibitor.

In 2017, the FDA approved the targeted therapies dabrafenib and trametinib, administered in combination, for people with NSCLC that has a mutation of the BRAF V600E gene as detected by an FDA-approved test.

There are other gene mutations seen in NSCLC for which targeted therapy options may be available. As most gene mutations tend to be more common in the adenocarcinoma type of NSCLC, it is important that people with adenocarcinoma discuss the value of genetic testing with their oncologist.

Because the genes of cancer cells can evolve, some tumors may become resistant to being treated with a targeted therapy. Medications to meet those challenges are being studied in clinical trials.

Immunotherapy

Our immune system is constantly working to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.



The following immunotherapies have been approved for the treatment of lung cancer in specific situations:

- **Nivolumab (Opdivo).** In 2015, the FDA approved nivolumab for the treatment of metastatic squamous NSCLC that was unsuccessfully treated with chemotherapy. In the same year, the indication was expanded to include treatment of non-squamous NSCLC after unsuccessful chemotherapy. Nivolumab, an immune checkpoint inhibitor, works by releasing a molecular “brake” known as PD-L1 that prevents the body’s immune system from attacking tumors.
- **Pembrolizumab (Keytruda).** Initially approved by the FDA in 2015 for PD-L1 positive metastatic NSCLC in the second-line setting, this drug belongs to the same category of drugs as nivolumab. After several expansions of its approval, as of April 2019 it is the only drug in this category approved for the first-line treatment of NSCLC, either alone for treatment of PD-L1 positive tumors, or in combination with chemotherapy regardless of PD-L1 status.
- **Atezolizumab (Tecentriq).** Approved by the FDA in 2016, atezolizumab is another immune checkpoint inhibitor for the treatment of metastatic NSCLC after failure of chemotherapy. In December 2018, the FDA expanded its approval, in combination with the chemotherapy regimen of bevacizumab, paclitaxel and carboplatin, for previously untreated SCLC that has spread beyond the lung.
- **Durvalumab (Imfinzi).** In February 2018, the FDA approved durvalumab for the treatment of locally advanced NSCLC after treatment with chemotherapy and radiation.

Cutting off the blood supply to tumors

Another approach to destroying cancer cells is cutting off the blood supply that tumors need to grow.

Blood vessels grow in several ways, but the process depends on the presence of a substance called vascular endothelial growth factor (VEGF) that can be produced both by both tumors and normal cells. This substance can stimulate blood vessels to penetrate tumors and supply them with the oxygen, minerals and other nutrients that feed their growth.

Bevacizumab (Avastin), a monoclonal antibody, works by stopping VEGF from stimulating the growth of new blood vessels. When combined with chemotherapy, bevacizumab has been shown to effectively shrink tumors in adenocarcinoma (the most common type of NSCLC).

Ramucirumab (Cyramza), also a monoclonal antibody, targets VEGF receptors to help stop the formation of new blood vessels. Ramucirumab is most often given with the chemotherapy docetaxel as a later line of therapy in the treatment of NSCLC, after another treatment stops working.



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy. The changes can include dryness, swelling, peeling, redness and blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful areas, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but it can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt an immune response. Because it can trigger an attack on healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, decreased appetite, and digestive tract symptoms.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals cold or at room temperature, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade, which provide electrolytes as well as liquid.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary and after having a discussion with a member of your health care team.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow).
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, granola bars, liquid nutritional supplements, nuts and canned tuna.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.



Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if he or she thinks any of these conditions may be contributing to your fatigue.

Managing Pain

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication, to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

CancerCare's Free Support Services and Programs

Receiving a diagnosis of lung cancer can be very difficult, and adjusting to the necessary changes in your life can be challenging.

CancerCare® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and provide information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, comprised of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.



MORE ABOUT LUNG CANCER

Frequently Asked Questions

Q: My breathing has been affected by surgery and chemotherapy. What can I do about this?

A: When surgery reduces the size of the lungs, you cannot take in as much air. Some medications also change lung function and lead to shortness of breath. Any time you have difficulty breathing, you should report it to your doctor. He or she can prescribe pulmonary (lung) rehabilitation therapy. To improve lung function, this therapy may include exercise training, energy-conserving techniques, breathing strategies and nutritional counseling.

Q: My lung cancer has an RET gene mutation. Are any drugs being studied for this type of tumor?

A: RET proteins send signals to cells, telling them to divide, mature and “specialize” (perform specific functions). When there is a mutation in the RET gene, this signal can get stuck, causing unchecked cell growth. In 2011, it was discovered that a mutation of the RET gene mutation was linked to lung cancer.

Three medications have been approved by the FDA for people with other types of cancer that have the RET mutation: cabozantinib (Cometriq) and vandetanib (Caprelsa) for people with thyroid cancer, and sunitinib (Sutent) for people with kidney cancer, pancreatic cancer or gastrointestinal stromal tumors (GISTs). Talk with your doctor about lung cancer clinical trials for people with the RET gene mutation.

Q: I had Stage 1A lung cancer surgically removed. My doctor says I don't need chemo or any other type of treatment. Should I get a second opinion?

A: If your cancer was truly Stage 1A (tumor of 3 centimeters or smaller that had not spread beyond the lung), treatment after successful surgery is generally not recommended. However, it's important to get a computerized tomography (CT) scan every six months for the first two years after surgery, to check for recurrence and any new cancer. After the first two years, your doctor will recommend how frequently you should get a CT scan.



Resources

CancerCare®

800-813-HOPE (800-813-4673)
www.cancercares.org

American Cancer Society

800-227-2345
www.cancer.org

Cancer.Net

Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute

800-422-6237
www.cancer.gov

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship

877-622-7937
www.canceradvocacy.org

CLINICAL TRIALS WEBSITES

EmergingMed

www.emergingmed.com

National Cancer Institute

www.cancer.gov

American Lung Association

800-586-4872
www.lung.org

Lung Cancer Alliance

800-298-2436
www.lungcanceralliance.org

LungCancer.org

A Program of CancerCare
800-813-HOPE (800-813-4673)
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