

TREATMENT UPDATE:

Lung Cancer

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Treatment Update: Lung Cancer

TABLE OF CONTENTS

Introduction.....	2
Types of Lung Cancer	2
Treatment Options.....	3
Treatment Side Effects.....	13
General Side Effects.....	14
Communicating With Your Health Care Team.....	17
CancerCare’s Free Support Services and Programs.....	19
Frequently Asked Questions.....	20
Resources.....	21

There have been many 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. In NSCLC, 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). In SCLC, a 2-stage system is typically used: limited stage and extensive stage.

Treatment Options

After your diagnosis, you and your health care team will discuss the best way to proceed with your treatment. Factors that influence the choice of treatment include the type of lung cancer, its stage and whether it has a genetic mutation.

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. When additional precision is needed, robotic surgery is sometimes an option for the removal of tumors in the lung.



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, called a linear accelerator, that directs multiple beams of radiation to the tumor. The use of CT (computerized tomography) 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 destroys more cancer cells and minimizes the impact on healthy tissue. Research is ongoing to determine those people with early-stage lung cancer who 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 with minimal doses delivered to nearby areas of the body. This type of radiation is especially useful for people whose tumor is close to a critical structure, such as the spinal cord, or who have previously received radiation.

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.

Prophylactic cranial irradiation (radiation to the head) helps lower the risk of SCLC spreading to the brain. It is mostly used in the treatment of limited stage SCLC, but it may also help some people with extensive stage SCLC.

Chemotherapy

Chemotherapy, the use of drugs to destroy cancer cells by stopping the ability of the cells to grow and divide, has long been a mainstay of lung cancer treatment. Chemotherapy is extremely effective in treating SCLC, and is also used to treat many cases of NSCLC. Chemotherapy can also be helpful for people whose tumors have (or will be) removed by surgery, and in combination with radiation (chemoradiation) for locally advanced cancer. It is also an important part of treatment for many 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, often etoposide.
- **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 and for 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) and docetaxel (Taxotere).** These drugs 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.
- **Etoposide (Etopophos, Vepesid).** Etoposide is used in combination with other cancer medications, including chemotherapy, for the treatment of SCLC.
- **Lurbinectedin (Zepzelca) and Topotecan (Hycamtin).** These chemotherapies are for the treatment of metastatic SCLC that has progressed after platinum-based chemotherapy.

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 NSCLC 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, six 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).** In 2018, the FDA approved dacomitinib as an initial treatment for NSCLC with certain EGFR gene mutations as detected by an FDA-approved test.
- **Amivantamab-vmjw (Rybrevant).** In May 2021, the FDA approved amivantamab-vmjw for the treatment of NSCLC with EGFR exon 20 insertion mutations.

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 NSCLC 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 NSCLC 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 NSCLC who were previously 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 NSCLC that was previously treated with crizotinib.
- **Lorlatinib (Lorbrena).** In 2018, lorlatinib was approved for the treatment of ALK-positive metastatic NSCLC that progressed while being treated with crizotinib or another ALK inhibitor. In March 2021, the approval was extended to the first-line treatment of NSCLC that has the ALK mutation.

There are other targeted therapies for the treatment of NSCLC that has other specific gene mutations:

- In 2017, the FDA approved dabrafenib and trametinib, administered in combination, for people whose NSCLC has a mutation of the BRAF V600E gene.
- In September 2020, the FDA granted approval to pralsetinib (Gavreto) for the treatment of metastatic RET fusion-positive NSCLC.
- In March 2021, the FDA approved tepotinib (Tepmetko) for the treatment of metastatic NSCLC that has the MET exon 14 skipping alteration.
- In June 2021, the FDA approved sotorasib (Lumakras) as a first-line treatment for NSCLC that has the KRAS G12C genetic mutation and that has been treated with at least one prior therapy.
- In September 2021, the FDA approved mobocertinib (Exkivity) for the treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations and which has progressed on or after platinum-based chemotherapy.
- In December 2022, the FDA granted accelerated approval to adagrasib (Krazati) for the treatment of KRAS G12C-mutated locally advanced or metastatic NSCLC.

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. In 2020, the FDA approved nivolumab in combination with ipilimumab (Yervoy) as first-line treatment for people with metastatic NSCLC whose tumors have the PD-L1 characteristic.
- **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. It was subsequently 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. In January 2023, the approval was expanded to include treatment, following surgery and platinum-based chemotherapy, of stage IB, II, or IIIA NSCLC.

- **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 2018, the FDA approved durvalumab for the treatment of locally advanced NSCLC after treatment with chemotherapy and radiation. In March 2020, the approval was extended to the first-line treatment of extensive stage SCLC, in combination with etoposide and either carboplatin or cisplatin.
- **Cemiplimab-rwlc (Libtayo).** In February 2021, the FDA approved cemiplimab-rwlc for the first-line treatment of NSCLC that has high PD-L1 expression and cannot be treated with surgery or chemoradiation.

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 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) 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) 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

Fatigue is the most common side effect of radiation. Additionally, changes to the skin can frequently occur. The changes can include dryness, swelling, peeling, redness and (rarely) 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 area, 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 that are chilled, 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. Electrolytes are body salts that must stay in balance for cells to work properly.
- 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. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- 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.

Managing 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). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- 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 Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

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 lung 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 (either on paper or in a digital format) 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 or have them be present during telehealth sessions. 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. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you. If you have a mobile device, ask if you can use it to take notes. Keeping notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your lung cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.



CancerCare's Free Support Services and Programs

It can be very difficult to receive a diagnosis of lung cancer, 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 offer 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 composed 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, or ask a friend who's a good listener to come over for a chat.

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, as there is pulmonary (lung) rehabilitation therapy that may be available to you. To improve lung function, this therapy may include exercise training, energy-conserving techniques, breathing strategies and nutritional counseling.

Q: I had Stage 1A NSCLC surgically removed. My doctor says I don't need chemotherapy 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.

Q: I have SCLC and recently read about trilaciclib and its impact on bone marrow. What is it?

A: Bone marrow is the spongy tissue inside bones where blood cells are made. Trilaciclib (Cosela) is designed to help protect bone marrow cells from damage caused by certain types of chemotherapy. Protecting bone marrow function may help make chemotherapy safer and allow people to complete their course of treatment as prescribed.

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**ClinicalTrials.gov**

www.clinicaltrials.gov

EmergingMed

www.emergingmed.com

American Lung Association

800-586-4872
www.lung.org

GO2 Foundation for Lung Cancer

800-298-2436
www.go2foundation.org

LungCAN

www.lungcan.org

LUNgevity Foundation

LUNgevity Lung Cancer Helpline:
844-360-LUNG (5864)
www.lungevity.org

Medicine Assistance Tool

www.medicineassistancetool.org

National Cancer Institute

www.cancer.gov

This booklet is supported by an educational grant from Daiichi Sankyo, Inc.



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