TREATMENT UPDATE:

Lung Cancer

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Treatment Update: Lung Cancer

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In recent years, there have been exciting developments in treating lung cancer.

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 among both men and women), 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 now 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, such as in many locally advanced cancers, radiation therapy is sometimes used, either alone or in combination with chemotherapy. These treatments may also be used before surgery to shrink the tumor or after surgery to help prevent the cancer from coming back (recurring).

"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 tissues.

A newer form of radiation called SBRT (stereotactic radiation) is sometimes used in the treatment of early-stage lung cancer instead of surgery. SBRT delivers higher doses of radiation over a shorter period of time; this approach minimizes the impact on healthy tissue.
In patients at high risk from surgery, SBRT has been shown to be curative at rates that are close to expected rates with surgery. Ongoing research is trying to determine which patients could benefit from this type of focused radiation instead of surgery.

Chemotherapy

Chemotherapy has long been an effective treatment for lung cancer, and continues to be one of the most important elements of treatment for many patients. Chemotherapy is extremely effective in treating SCLC, and is also used to treat most NSCLCs. Chemotherapy can be helpful for patients with early stage

cancers that have been or will be removed with surgery, and in combination with radiation for locally advanced cancer. It is also an important part of treatment for most patients 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 are the most common medications used in treating lung cancer. Most treatment approaches include either cisplatin or carboplatin in combination with another chemotherapy drug.
- **Pemetrexed (Alimta).** Pemetrexed is used in combination with the chemotherapy 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. Pemetrexed is only used for adenocarcinoma of the lung and is not active for squamous cell lung cancer or for small cell lung cancer.
- **Gemcitabine (Gemzar and others).** These drugs are used to treat NSCLC, either in combination with cisplatin or carboplatin as an initial treatment, or as a single drug after other chemotherapy has been given. This drug works for all types of NSCLC.
- **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 NSCLC. Docetaxel is frequently given alone as a later line of therapy in advanced stage lung cancer.
- **Etoposide (Etopophos, Vepesid).** Etoposide is used in combination with other cancer medications for the treatment of SCLC.

Targeted Therapy

To destroy cancer cells, targeted therapy focuses on specific cell mechanisms thought to be important for the growth and survival of tumors. These medications cause different, often less severe side effects than chemotherapy.

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 therapy given in pill form—are often used to treat this type of lung cancer. Today, four medications are approved treatment options in the United States for lung cancer patients with this gene mutation:

- **Erlotinib (Tarceva and others).** The FDA first approved the use of erlotinib for lung cancer in 2004. In 2013, erlotinib was approved as an initial treatment for patients 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 patients with the same EGFR gene mutations or deletions as those who can be treated successfully with erlotinib.
- **Gefitinib (Iressa).** In July 2015, the FDA approved gefitinib for the initial treatment of patients with NSCLC whose tumors harbor specific types of EGFR gene mutations, as detected by an FDA-approved test.
- **Osimertinib (Tagrisso).** In November 2016, the FDA approved osimertinib for the treatment of patients with NSCLC whose tumors have specific EGFR gene mutations and have started to regrow after treatment with erlotinib, afatinib, or gefitinib.

Another gene mutation found in some lung cancers is referred to as ALK. Four targeted treatments are FDA-approved options for people whose cancer has this mutation:

- **Crizotinib (Xalkori).** This treatment was approved by the FDA in 2013 for treating metastatic NSCLC tumors with the ALK gene mutation. Crizotinib blocks the mutated ALK gene, stopping the growth of the tumor. In clinical trials, it was found to be more effective than chemotherapy. Additionally, crizotinib was approved in 2016 to treat people with metastatic NSCLC tumors that have a mutation of the ROS-1 gene.
- **Ceritinib (Zykadia).** This medication was approved in 2014 for 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 newly diagnosed patients with ALK-positive lung cancer.
- **Alectinib (Alecensa).** Alectinib was approved in December 2015 for patients with lung cancer who had already been treated with crizotinib. As a result of a large clinical trial, in November 2017 alectinib was approved to be given as a first-line treatment choice (before any prior treatment).
- **Brigatinib (Alunbrig).** In April, 2017, brigatinib was approved for patients who had already been treated with crizotinib.

In June 2017, the FDA approved the targeted therapies dabrafenib and trametinib, administered in combination, for patients with NSCLC that has a mutation of the BRAF V600E gene as detected by 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 patients 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 a targeted therapy treatment. 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.

Cutting off the blood supply to tumors

One immunotherapy approach to destroying cancer cells is changing 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 oxygen, minerals, and other nutrients, which feeds 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 be more likely to shrink tumors and to help some patients with certain types of NSCLC—such as adenocarcinoma—to live longer.

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

PD-1 Inhibitors

In March 2015, the FDA approved the immunotherapy nivolumab (Opdivo) for the treatment of metastatic squamous NSCLC that was unsuccessfully treated with chemotherapy. Nivolumab works by interfering with a molecular "brake" known as PD-1 that prevents the body's immune system from attacking tumors.

Two additional drugs in the same category were approved in October 2016: atezolizumab (Tecentriq) and pembrolizumab (Keytruda). Pembrolizumab is the only drug in this category approved for the first-line (initial) treatment of lung cancer.

Recent Immunotherapy Approval

In February 2018, the FDA approved the immunotherapy durvalumab (Imfinzi) for the treatment of patients with stage III NSCLC whose tumors are unable to be surgically removed, and whose cancer has not progressed after treatment with chemotherapy and radiation.

Treatment Approaches Being Studied

The effectiveness of combining immunotherapies in the treatment of NSCLC is being studied in many clinical trials. One promising approach is pairing nivolumab with ipilimumab (Yervoy), an immunotherapy currently approved by the FDA for the treatment of metastatic melanoma.

Another area of ongoing research is the combination of immunotherapy with chemotherapy as a first-line treatment option. In 2017, the FDA approved the use of pembrolizumab in combination with chemotherapy as a first-line treatment for metastatic NSCLC.

Additionally, the effectiveness and potential side effects of adding radiation therapy to immunotherapy is currently being studied.

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 patients experience all side effects, and patients may experience side effects not listed here.

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:

- Fatigue (being more tired)
- 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 Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy; those 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 Targeted Therapy

Targeted therapy drugs don't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects. Some of the potential side effects of targeted therapy include rashes, diarrhea, liver problems (such as elevated liver enzymes), problems with blood clotting and wound healing, and high blood pressure.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt an immune response. Because it may attack healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, decreased appetite, and digestive tract symptoms. The management of these potential side effects is discussed in the next section of this booklet.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried, or highly seasoned food.
- 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.
- Many effective medications for nausea and vomiting have been developed in recent years; talk to your doctor about which ones may be right for you.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes as well as liquid. 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 foods that contain soluble fiber—for example beans, oat cereals, oranges, and flaxseeds. High-pectin foods such as peaches, apples, oranges, grapefruit, bananas, and apricots can also help to avoid diarrhea.

Loss of appetite

- To help maintain your weight, eat small meals throughout the day. That's an easy way to take in more protein and calories. 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 and focus on liquids that have nutritional value.
- 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 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.
- 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.

There are also prescription medications that may help, such as modafinil. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

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.

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, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

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

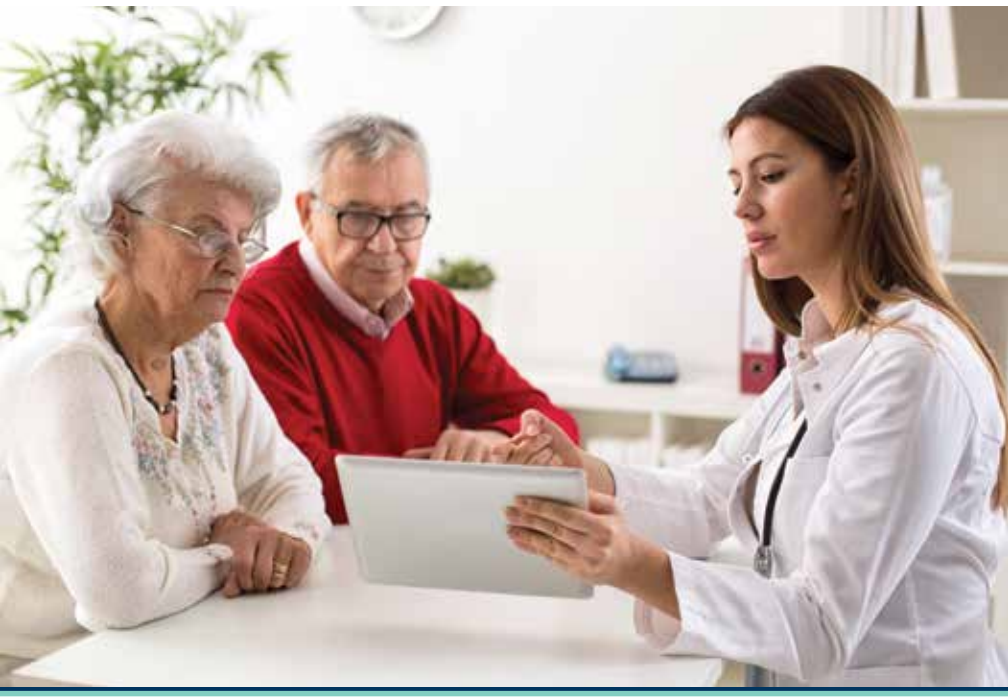
Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with symptoms related to your illness or treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific and brief 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. The person who accompanies you can serve as a second set of ears. 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.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice, and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, ask if you can use it to take notes. Writing notes will help you review the information later.

Remember, there is no such thing as over-communication.



Cancer*Care*'s Free Support Services and Programs

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

Cancer*Care* 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 Cancer*Care* 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.

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. This therapy may include exercise training, energy-conserving techniques, breathing strategies, and nutritional counseling to improve lung function.

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 those 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 and ask whether he or she recommends prescribing any of these medications to you "off label" (using a prescription drug legally to treat a cancer for which the drug has not been approved by the FDA).

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, treatment after surgery is not recommended. However, it's very important to get a 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 to get a CT scan.

Resources

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800-813-HOPE (800-813-4673)
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American Cancer Society
800-227-2345
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Cancer.Net
Patient information from the American Society of Clinical Oncology
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National Cancer Institute
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