Learning that you have cancer can be overwhelming. The goal of this book is to help you get the best cancer treatment. It explains which cancer tests and treatments are recommended by experts of non-small cell lung cancer.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 of the world’s leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat lung cancer. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of non-small cell lung cancer. Key points of the book are summarized in the related NCCN Quick Guide™. NCCN also offers patient resources on lung cancer screening as well as other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other patient and caregiver resources.
DANA REEVE HAD IT ALL. She was a beautiful woman, an actress who married “Superman” actor Christopher Reeve. They had a son, Will. Then, in 1995, Christopher Reeve suffered a catastrophic injury in a riding accident and was paralyzed from the neck down. Dana cared for him for almost 10 years, tirelessly crusading for research on paralysis and stem cells. Christopher Reeve died in 2004, but Dana pressed forward with her foundation and with raising their son, then an adolescent. Just a few months later, this vibrant, healthy, non-smoking young woman was diagnosed with stage IV lung cancer. She lived for just seven months.

Dana Reeve was my sister, and until Dana was diagnosed, I didn't understand how hard it can be for patients to find good information about their treatment options. I am a third-generation physician, pathologist, and an oncology researcher. After Dana's death, I began working with lung cancer advocacy groups to raise awareness of the needs of lung cancer patients. I began to realize that the overall understanding of lung cancer is very naive. People just don't understand the breadth and scope of the problem.

In 2009, I joined NCCN after being asked to participate in the Roundtable discussion that opened the NCCN Annual Conference that year. That first acquaintance with NCCN struck a strong chord in me. When I was asked to join the newly formed NCCN Foundation Board one year later, I gladly accepted. And when they decided to dedicate the NCCN Guidelines for Patients®: Lung Cancer in memory of my sister, I was thrilled.

NCCN plays a critical role in translating complicated treatment information into easily understandable patient resources. I use NCCN's clinical guidelines regularly, and know there is a tremendous need for patient-friendly versions. The more that this information gets into the hands of patients, the more patients can feed it back to their doctors and make informed decisions for themselves. NCCN Guidelines for Patients® are a powerful resource.

- Debora Morosini, MD
  Sister of Dana Reeve
  Member, NCCN Foundation Board of Directors
NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Guidelines for Patients®. Each book presents the best practice for a type of cancer. The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients.

Panels of experts create the NCCN Guidelines®. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors. For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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Supported by NCCN Foundation®

NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Lung Cancer
NON-SMALL CELL LUNG CANCER

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How to use this book

Who should read this book?

The information in this book is about cancer of the non-small cells of the lung. About 85 out of 100 patients with lung cancer have non-small cell lung cancer. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with doctors what care is best.

Does the whole book apply to me?

This book includes information for many situations. Your treatment team can help. They can point out what information applies to you. They can also give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

The recommendations in this book are based on science and the experience of NCCN experts. However, these recommendations may not be right for you. Your doctors may suggest other tests and treatments based on your health and other factors. If other recommendations are given, feel free to ask your treatment team questions.

Where should I start reading?

To understand your treatment options, it’s important to know how lung cancer grows and to where it spreads. Part 1 is a good starting point to learn about the parts of the lungs and what lung cancer is. Part 2 addresses the process of assessing a lung mass for cancer.

If you have lung cancer, your doctors will assess how far it’s grown and spread. This is called cancer staging. Treatment options in this book are based on cancer staging. Read Part 3 for detailed information. Knowing the stage of the cancer will help you use Parts 4, 6, and 7.

Part 4 lists the tests needed to plan treatment. Some tests are used to stage the cancer. Others reveal the features of the cancer and if you can have surgery.

Parts 5 through 8 address treatment. Part 5 briefly describes cancer treatments. Part 6 is a guide to treatment options for when there is one primary tumor, and Part 7 is for multiple primary tumors. Part 8 gives tips for anyone making treatment decisions.

Making sense of medical terms

In this book, many medical words are included. These are words that you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Don’t be shy to ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the Dictionary. Words in the Dictionary are underlined when first used on a page.

Acronyms are also defined when first used and in the Glossary. Acronyms are short words formed from the first letters of several words. One example is DNA for deoxyribonucleic acid.
Lung cancer basics
You’ve learned that you have lung cancer. It’s common to feel shocked and confused. Part 1 reviews some basics that may help you learn about lung cancer. These basics may also help you start planning for treatment.

Parts of the lungs

The lungs are the main organs of the respiratory system. They transfer oxygen—a gas that cells need to live—from the air into the blood. The blood then carries oxygen to all the cells in the body. The lungs also remove carbon dioxide—a gas made by cells—from the blood. Carbon dioxide is then exhaled from the lungs into the air. The transfer of these gases in and out of the body is called respiration.

When you inhale, air enters your mouth or nose and travels down your throat into your windpipe (trachea). See Figure 1. Air then enters your lungs through the bronchi. The bronchi branch off into each part (lobe) of your lung. Your right lung has three lobes and your left lung has only two lobes to make space for your heart.

Within the lobes, the bronchi divide into smaller airways called bronchioli. At the end of each bronchioli are bunches of alveoli wrapped in blood vessels. The transfer of gases in and out of the blood occurs in the alveoli.

Throughout your body—including in your lungs—is a clear fluid called lymph. Lymph gives cells food and water. It also contains germ-fighting blood cells. Lymph drains from tissue into vessels that transport lymph to the bloodstream. See Figure 2. As lymph travels, it passes through small, oval-shaped structures called lymph nodes. Lymph nodes remove germs from lymph.
Figure 1
The airways and lungs

Oxygen enters your body through a series of airways that include the windpipe (trachea), bronchi, and bronchioli. Inside your lungs, oxygen is transferred into the bloodstream in the alveoli. Carbon dioxide is transferred out of the bloodstream in the alveoli and exits your body through your airways.

Figure 2
Lymph vessels and nodes

Throughout your body, including your lungs, is a network of vessels that transport lymph to the bloodstream. Lymph is a clear fluid that contains germ-fighting blood cells. As lymph travels in vessels, it passes through lymph nodes, which remove germs from lymph.
Your lungs are protected by tissue called the pleura. Pleura covers each lung and helps the lungs safely rub against other organs. Pleura is made of two layers. The outer layer is known as the parietal pleura. The inner layer is called the visceral pleura. The space in between the two layers is called the pleural cavity. It is filled with a small amount of fluid called pleural fluid.

A disease of cells

Cancer is a disease of cells. Inside of cells are coded instructions for building new cells and controlling how cells behave. These instructions are called genes. Genes are a part of DNA (deoxyribonucleic acid), which is grouped together into bundles called chromosomes. See Figure 3. Abnormal changes (mutations) in genes cause normal cells to become cancer cells. Researchers are still trying to learn what causes genes to mutate and cause cancer.

Lung cancer starts in cells of the lung. Cancers of cells from elsewhere that spread to the lung are not lung cancers. Almost all lung cancers are carcinomas. Carcinomas are cancers of cells that line the inner or outer surfaces of the body. Lung carcinomas start in cells that line the airways of the lungs.

Lung carcinomas are divided into two groups based on how the cells look. One group is called small cell lung cancers and the other group is called non-small cell lung cancers. The second group is much more common and is the focus of this book.

Cancer’s threat

Cancer cells don’t behave like normal cells in three key ways. First, mutations in genes cause cells to grow more quickly and live longer. Normal cells grow and then divide to form new cells when needed. They also die when old or damaged as shown in Figure 4. In contrast, cancer cells make new cells that aren’t needed and don’t die quickly when old or damaged. Over time, lung cancer cells form a mass called the primary tumor.

The second way cancer cells differ from normal cells is that they can grow into nearby tissues. If not treated, the primary tumor can grow large and invade other tissue like a bronchus or pleura. Cancer cells can replace so many normal lung cells that it is hard to breathe.

Third, unlike normal cells, cancer cells can travel to other parts of the lung and body. This process is called metastasis. In this process, cancer cells break away from the tumor and merge with blood or lymph. Then, the cancer cells travel in blood or lymph through vessels to other sites. In other sites, the cancer cells may form secondary tumors, replace many normal cells, and cause major health problems. The sites to which lung cancer spreads are described in Part 3 Cancer staging.
Figure 3
Genetic material in cells

Most human cells contain the “blueprint of life”—the plan by which our bodies are made and work. The plan is found inside of chromosomes, which are long strands of DNA that are tightly wrapped around proteins. Genes are small pieces of DNA that contain instructions for building new cells and controlling how cells behave. Humans have about 24,000 genes.

Figure 4
Normal cell growth vs. cancer cell growth

Normal cells increase in number when they are needed and die when old or damaged. In contrast, cancer cells quickly make new cells and live longer because of abnormal changes in genes.
Review

• The lungs help the body get the air it needs to live.
• The lungs are made of many small airways and sacs.
• Lung cancer often starts in the cells that line the airways.
• Cancer cells form a tumor since they don’t grow and die as normal cells do.
• Cancer cells can spread to other body parts through lymph or blood.
Assessing lung nodules
Many people have small masses of tissue in their lungs. These small masses are called nodules. Nodules can be caused by cancer, infections, scar tissue, and other conditions. Most nodules are not cancer.

Part 2 discusses how doctors decide if a nodule is likely cancer. If you take part in a lung cancer screening program, read the NCCN Guidelines for Patients®: Lung Cancer Screening for related information. If you aren’t in a screening program, the information in Part 2 is for you.

Team work

It takes a team of experts to decide if a nodule is cancer. Your treatment team should include a pulmonologist, thoracic radiologist, and thoracic surgeon. A pulmonologist is a doctor who’s an expert of lung diseases. A thoracic radiologist is a doctor who’s an expert of imaging tests of the chest. A thoracic surgeon is a doctor who’s an expert in operations within the chest.

Your team will assess if a lung nodule is cancer by three or four methods. One method is to assess your risk for lung cancer. Another method is to review test results for signs of cancer. A third method is to repeat tests to see if there are changes that suggest cancer is present. When doctors suspect cancer, a fourth method is used. Tissue is removed from your body and tested to confirm if cancer is present.
Your cancer risk

**Guide 1** lists the risk factors that doctors use to assess if a nodule may be cancer. A risk factor is anything that increases your chance of lung cancer. Risk factors can be activities that people do, things in the environment, or personal traits like age and health history. If one or more risk factors applies to you, it doesn’t mean you have lung cancer. Likewise, lung cancer occurs in some people who have no known risk factors.

**Tobacco smoke**
Smoking tobacco is the biggest risk factor for lung cancer. There are more than 50 compounds in tobacco smoke known to cause cancer. Any smoking increases your risk for lung cancer, but the more you smoke, the higher your risk. If you quit smoking, your risk will decrease. However, the risk for lung cancer is higher for former smokers than for people who never smoked. Thus, current or past tobacco smoking is a risk factor for lung cancer.

In 1981, a link between second-hand smoke and lung cancer was first suggested. Since then, other studies have found the risk for lung cancer is greater for people exposed to second-hand smoke. However, the risk may depend on how much contact a person has had.

**Older age**
As you get older, you are more likely to get cancer, including lung cancer. Half of the people who were diagnosed with lung cancer in recent years were 70 years old or older. Only 12 out of 100 people with lung cancer were younger than age 55.

**Having had cancer**
Your risk for lung cancer may be increased if you’ve had cancer. Having had any type of lung cancer increases your risk for other types of lung cancer. Likewise, if you’ve had a smoking-related cancer, like head and neck cancer, your risk for lung cancer is increased.

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**Guide 1. Risk factors for lung cancer**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco smoke</td>
<td>Major contact with cancer-causing agents</td>
</tr>
<tr>
<td>Being older in age</td>
<td>Infectious lung diseases</td>
</tr>
<tr>
<td>Having had cancer</td>
<td>Other lung diseases</td>
</tr>
<tr>
<td>Parent, sibling, or child who has had lung cancer</td>
<td></td>
</tr>
</tbody>
</table>
Some cancer treatments also increase risk. The risk for lung cancer increases after receiving radiation therapy in the chest for other cancers, especially if you smoke. Treatment of Hodgkin’s lymphoma with an alkylating agent—a type of cancer drug—increases the risk for lung cancer too.

**Family who’ve had lung cancer**
If your parent, sibling, or child has had lung cancer, your risk for lung cancer is higher than a person with no family history. Your risk is even higher if your relative had cancer at a young age or if more than one relative has had lung cancer.

**Cancer-causing agents**
Uranium is a substance found in rocks and soil. As it decays, a gas called radon is made and gets into air and water. Miners of uranium have a high risk of developing lung cancer. Some studies of radon found in the home have linked radon to lung cancer, while other studies have not. The risk for lung cancer may depend on how much radon is in the home. For people who’ve had major contact with radon, such as uranium miners, the risk for lung cancer is higher for those who smoke than for those who don’t smoke.

Besides radon, there are 10 other agents known to cause lung cancer. Five are metallic metals: arsenic, beryllium, cadmium, chromium, and nickel. The others are asbestos, coal smoke, soot, silica, and diesel fumes. Among people who’ve had major contact with these agents, the risk for lung cancer is higher for those who’ve smoked than for those who’ve never smoked.

**Infectious lung diseases**
Some infectious lung diseases have been linked to lung cancer. Tuberculosis is an infection caused by bacteria. If you’ve had tuberculosis, you are more likely to get lung cancer than someone who’s never had tuberculosis. The same is true if you’ve had a fungal infection in the lungs.

**Other lung diseases**
Two lung diseases have been linked to lung cancer. A history of COPD (chronic obstructive pulmonary disease) increases your risk for lung cancer. COPD makes breathing hard because the lung tissue is damaged or there’s too much mucus. The second disease linked to lung cancer is pulmonary fibrosis. Pulmonary fibrosis is major scarring of lung tissue that makes it hard to breathe.
Signs of cancer

Imaging tests make pictures of the insides of the body. CT (computed tomography) and PET (positron emission tomography) are imaging tests used to see inside the lungs. A CT machine is shown in Figure 5.

You may have had one or both of these tests. Your doctors will review the results of these tests to help decide if a nodule may be cancer. Important test results are the features of the nodule, abnormal lung tissue, and PET hot spots.

Features of the nodule
Nodules caused by cancer have specific traits. First, they aren’t likely to have calcium buildup. Second, they often have rough edges and odd shapes. Third, they often grow faster and are larger in size than nodules without cancer. Thus, nodules that are large are more likely to be cancer than small nodules.

The density of the nodule is also assessed to decide if the nodule may be cancer. Non-solid nodules have low density. Solid nodules have high density. Part-solid nodules have both high and low areas of density. Part-solid nodules are found less often than solid nodules, but more of them are caused by cancer. On the other hand, solid nodules that are cancer grow faster than part-solid nodules that are cancer.

Abnormal lung tissue
Besides nodules, your doctors will look at your imaging results for other abnormal findings. The imaging tests may show tissue inflammation, tissue scarring, or both. The nodule is more likely to be cancer if there’s inflammation or scarring than if neither is present.

PET hot spots
PET shows how your cells are using a simple form of sugar. To create the pictures, a sugar radiotracer is put into your body. The radiotracer emits a small amount of energy that is detected by the imaging machine. Cancer appears brighter (“hotter”) in the pictures, because cancer cells use sugar more quickly than normal cells. Hot spots suggest that cancer is present.
Repeat testing

Often, the use of one imaging test detects a nodule but doesn’t clearly reveal whether the nodule is cancer. Thus, tests need to be repeated to look for increases in nodule size or density over time. Such changes are likely signs of cancer.

Guide 2 lists the recommended care after a nodule is found on an imaging test. Follow-up care is based on the size and type of nodule.

For small nodules that may be cancer, the screening guidelines recommended by NCCN should be followed. The NCCN Guidelines for Patients®: Lung Cancer Screening can be found on NCCN.org/patients. Tests repeated over time will help your doctors know if there’s cancer.

A medium-sized non-solid nodule should be tested again in 3 to 6 months with a spiral LDCT (low-dose computed tomography) of the chest. Spiral LDCT is also called also called helical LDCT. This test takes many pictures of the insides of your body from different angles using x-rays. The amount of radiation used is much lower than standard doses of a CT scan. Contrast dye should not be used. Getting an LDCT scan is much like getting the imaging test you’ve had before.

For a medium-sized solid or part-solid nodule, think about getting PET with CT instead of LDCT. When used together, they are called a PET/CT scan. A PET/CT scan may find if there’s cancer quicker than LDCTs repeated over a period of time. It may also show signs of cancer spreading in the body. PET/CT may be done with one or two machines depending on the cancer center.

Nodules that are large are likely cancer. In this case, you should see a surgeon. The surgeon can remove the nodule so it can be tested for cancer.

Guide 2. Care after first imaging test

<table>
<thead>
<tr>
<th>Imaging results</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small nodule*</td>
<td>➔ Follow NCCN screening guidelines</td>
</tr>
<tr>
<td>Medium-sized non-solid nodule*</td>
<td>➔ Get follow-up LDCT in 3–6 months</td>
</tr>
<tr>
<td>Medium-sized solid or part-solid nodule*</td>
<td>➔ Consider getting follow-up PET/CT now</td>
</tr>
<tr>
<td>Large nodule*</td>
<td>➔ See a surgeon</td>
</tr>
</tbody>
</table>

*There are multiple factors that determine the size of a lung cancer nodule. Ask your doctor what size the tumor is.
Guide 3 lists the recommended care after having an LDCT. Your doctor will look to see if the nodule has increased in size or density. If there’s no increase, one option is to have another LDCT. If cancer is present, the nodule will likely be larger or denser in 6 to 12 months.

Instead of waiting 6 to 12 months, you may have other options. You could have a biopsy now in order to test tissue samples for cancer. However, sometimes a biopsy is not possible. Also your doctor may think it’s better to wait.

A third option may be surgery to remove the whole nodule. Surgery to remove the whole nodule but not much else is called an excision. Surgery may be done if your doctor strongly thinks cancer is present.

If cancer isn’t found in the biopsy or surgical tissue, the screening guidelines recommended by NCCN should be followed. The NCCN Guidelines for Patients®: Lung Cancer Screening can be found on NCCN.org/patients. If cancer is found in the biopsy or surgical tissue, finish reading this book to learn about your treatment options.

The follow-up LDCT may have showed that the nodule increased in size or density. In this case, surgical excision is advised. The nodule is very likely cancer.

Guide 3. Care after follow-up LDCT

<table>
<thead>
<tr>
<th>LDCT results</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No increase</td>
<td>- LDCT in 6–12 months</td>
</tr>
<tr>
<td></td>
<td>- Biopsy</td>
</tr>
<tr>
<td></td>
<td>- Consider surgery</td>
</tr>
<tr>
<td>Increase</td>
<td>- Surgery</td>
</tr>
</tbody>
</table>

- If no lung cancer is found, follow NCCN screening guidelines
- If lung cancer is found, read Parts 3–8 of this book
Guide 4 lists the recommended care after having a PET/CT. If results suggest that the nodule is not likely cancer, an LDCT. When the PET/CT results suggest the nodule is cancer, a biopsy to remove tissue samples for cancer testing may be an option. Another option may be surgical excision.

If cancer isn’t found in the biopsy or surgical tissue, the screening guidelines recommended by NCCN should be followed. The *NCCN Guidelines for Patients*: Lung Cancer Screening can be found on NCCN.org/patients. If cancer is found in the biopsy or surgical tissue, finish reading this book to learn about your treatment options.

### Guide 4. Care after follow-up PET/CT

<table>
<thead>
<tr>
<th>PET/CT results</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not likely cancer</td>
<td>LDCT in 3 months</td>
</tr>
<tr>
<td>May be cancer</td>
<td>Biopsy</td>
</tr>
<tr>
<td></td>
<td>• If no lung cancer is found, follow NCCN screening guidelines</td>
</tr>
<tr>
<td></td>
<td>• If lung cancer is found, read Parts 3–8 of this book</td>
</tr>
</tbody>
</table>
Confirming cancer

Tissue or fluid must be removed from your body and be tested to confirm (diagnose) cancer. There is no single plan for diagnosis that is best for all people. Your plan will depend on the tumor’s size, where cancer might be in your body, your health, and the experience of your doctors.

Choice of method

For lung cancers, biopsy and surgery are two methods that doctors use to remove tissue or fluid. Some people have a choice between the two methods. When deciding between methods, doctors should think about 1) how strongly they think there’s cancer; 2) where the cancer is in your body; and 3) what method you prefer.

There is more than one type of biopsy and surgery to diagnose lung cancer. They are briefly described next by broad groups. Read Part 4 for more details. Which type you will have depends partly on where the cancer is.

- **External needle biopsies** involve inserting a needle through your chest wall. The needle is guided to the site with an imaging test like CT. These biopsies include TTNA (transthoracic needle aspiration) and thoracentesis.
- **Down-the-throat biopsies** involve guiding tools down the throat into the windpipe or esophagus. Samples may be removed by needle, brush, tongs, or liquid. These biopsies include bronchoscopy and EUS (endoscopic ultrasound)-guided biopsies.
- **Phlegm biopsy** requires that you cough up some mucus (phlegm). The phlegm will be tested for cancer cells. This may be the easiest way to test for cancer but you’ll likely have another biopsy or surgery. More tissue is needed for the cancer tests discussed in Part 4.
- **Portal surgeries** involve cutting small holes (ports) into your chest. Small tools are inserted through the ports to remove tissue. Compared to open surgery, this technique is “minimally invasive.” These surgeries include thoracoscopy and mediastinoscopy.
- **Open surgery** involves making a large cut between your ribs to spread them farther apart. The whole nodule is removed by your doctor with a surgical knife. You may have open surgery when other methods won’t work or a larger piece of tissue is needed.

Choice of timing

Another choice you may have is when to confirm whether there’s cancer. Diagnosis may occur before or at the time of surgical treatment. There may be no need to have a biopsy before treatment if your doctors strongly think a nodule is cancer. A biopsy done beforehand would increase health risks, time spent, and costs. If confirmed at the time of surgery, tissue can be removed by biopsy or excision. More lung tissue may be removed if cancer is present.

A biopsy before treatment may be done if diagnosis during surgery would be hard or risky. Likewise, FNA (fine-needle aspiration) or core needle biopsy before treatment may be done if the cancer may not be lung cancer. An FNA removes a small group of cells with a thin needle and a core needle biopsy removes a solid tissue sample with a needle. A biopsy before treatment is also needed if you will receive treatment other than surgery.
Review

- It takes a team of experts to assess lung nodules for cancer.
- Tobacco smoking is the biggest risk factor for lung cancer.
- Signs of cancer can be found with imaging tests. For lung cancer, doctors assess a nodule’s features, the condition of the lung tissue, and for PET hot spots.
- Doctors assess changes in a nodule’s size and density with repeat testing. Nodules that increase fast in size or density are likely cancer.
- Testing of tissue that is removed by biopsy or surgery is needed for diagnosis.
Cancer staging
Cancer staging is a rating by your doctors of how far the cancer has grown and spread. Doctors plan additional tests and treatment based on how much the cancer has grown. In Part 3, the scoring system used for cancer staging is explained.

Staging plan

Staging is very important for treatment planning. Like diagnosis, there is no single plan for staging that is best for all people. Your plan will depend on the cancer site, your health, and the experience of your doctors.

Lung cancer is often staged twice. The first staging is done before treatment and is called the clinical stage. Imaging tests, like CT and PET/CT, may show where the cancer has grown and spread. Blood tests should also be done. Read Part 4 for more information on tests.

Your doctors may try to diagnose and stage the cancer at the same time. This can be done by testing the furthest site from the nodule that likely has cancer. Examples of such sites are lymph nodes and adrenal glands. By doing this, you’ll likely have fewer procedures.

Some cancers may not be correctly staged until after surgical treatment. For example, all the lymph nodes with cancer might not be found until surgery. This second staging is called the pathologic stage. For some people, lung cancer is diagnosed, staged, and treated during one operation.
TNM scores

The AJCC (American Joint Committee on Cancer) staging system is used to stage lung cancer. In this system, the letters T, N, and M describe different areas of cancer growth. Your doctors will assign a score to each letter. These scores will be combined to assign the cancer a stage.

T = Tumor

The T score tells how large or where the primary tumor has grown. Figure 6 shows some areas of tumor growth. In medicine, tumors are measured in cm (centimeters). About 0.4 inch equals 1 cm. T scores for lung cancer include:

- **TX** tumors are too small for testing or can't be found with tests.
- **Tis** means there are abnormal cells in the bronchi that haven't invaded tissue.
- **T1** tumors are in the lungs only and are not larger than 3 cm.
  - **T1a** tumors are 2 cm or smaller.
  - **T1b** tumors are more than 2 cm but not larger than 3 cm.

Figure 6. Areas to which lung tumors grow

Lung cancer may spread beyond the lobe in which it started to other parts of the lung and nearby organs.
• **T2** tumors: a) are larger than 3 cm but not larger than 7 cm; b) have grown into the bronchus but not closer than 2 cm to the carina; c) have grown into the visceral pleura; or d) have caused a partial lung collapse (atelectasis) or swelling (pneumonitis) in part of the lung.
  - **T2a** tumors are larger than 3 cm but not larger than 5 cm with or without other features, or are smaller in size with other features.
  - **T2b** tumors are larger than 5 cm but not larger than 7 cm with or without other features.

• **T3** tumors: a) are larger than 7 cm; b) have grown into the bronchus within 2 cm of the carina; c) have grown into the parietal pleura, chest wall, diaphragm, phrenic nerve, mediastinal pleura, or outer pericardium; d) have caused atelectasis or pneumonitis in the whole lung; or e) there are secondary tumors in the lobe with the primary tumor.

• **T4** tumors are scored based on invasion or the presence of secondary tumors. They: a) have grown into the mediastinum, heart or its major blood vessels, trachea, recurrent laryngeal nerve, carina, esophagus, or spine; or b) there are secondary tumors in the lung that has the primary tumor but in a different lobe.

---

**N = Nodes**

Cancer cells can spread throughout the body by traveling in lymph. Lymph in lung tissue first travels to the intrapulmonary and peribronchial lymph nodes inside the lungs. See Figure 7. From these nodes, lymph then travels to the hilar lymph nodes. Hilar lymph nodes are found right outside the lungs where the bronchi attach.

From the hilar lymph nodes, lymph travels to nodes in the mediastinum. The mediastinum is the center of the chest where the heart is. Subcarinal lymph nodes are located right below the windpipe. Lymph also travels above the collarbone to the supraclavicular lymph nodes and to the scalene lymph nodes within the neck.

The N score reflects how far lung cancer has spread within the described lymph nodes. N scores for lung cancer include:

- **N0** means that there is no cancer in nearby lymph nodes.
- **N1** means that the cancer has spread to the peribronchial nodes and/or to the hilar and intrapulmonary nodes of the lung with the primary tumor.
- **N2** means that the cancer has spread to mediastinal lymph nodes, which include subcarinal nodes, near the lung with the primary tumor.
- **N3** means that the cancer has spread to the mediastinal or hilar nodes near the lung without the primary tumor, or to any supraclavicular or scalene lymph nodes.
Figure 7. Lymph nodes in or near the lungs

Lung cancer can spread to lymph nodes inside the lung then to nodes in between the lungs and to nodes in the neck and collarbone area.
M = Metastasis

The M score tells you if there are metastases to distant sites. Lung cancer tends to spread to the brain, adrenal gland, and to the lung without the primary tumor. M scores for lung cancer include:

- **M0** means the cancer hasn’t spread to distant sites.
- **M1** means the cancer has spread to distant sites.
  - **M1a** means the cancer has spread:
    a) from one lung into the other lung;
    b) into the lung's lining (pleura) and has formed secondary tumors; or
    c) into the fluid around the lungs or the heart.
  - **M1b** means the cancer has spread to areas outside the chest area.

The 5 stages

**Chart 1** shows the five cancer stages labeled by Roman numerals 0–IV. Occult carcinoma is also included. Occult carcinoma is the finding of cancer cells in the absence of a tumor.

The five stages are defined by TNM scores. The stages group tumors together that have a similar prognosis. A prognosis is the outlook (prediction) of the pattern and outcome of a disease.

In general, earlier cancer stages have better outcomes. However, doctors define cancer stages with information from thousands of patients, so a cancer stage gives an average outcome. It may not tell the outcome for one person. Some people will do better than expected. Others will do worse. Other factors not used for staging cancer are also very important. Such factors include your general health and the type of lung cancer.
## Chart 1. Lung cancer stages

<table>
<thead>
<tr>
<th>Anatomic stage / Prognostic groups</th>
<th>TX</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occult carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IA</td>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IB</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T2b</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T4</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>Any T</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Review

- Lung cancer is grouped into stages to help plan treatment.
- The timing of and methods used for staging are not the same for everyone.
- Doctors rate the extent of cancer with T, N, and M scores.
- There are five cancer stages for lung cancer. Earlier cancers often have better outcomes.
Treatment planning
Doctors plan treatment with many sources of information. These sources include tests of your health and the cancer. Part 4 describes who should receive which tests before treatment. Some are used to confirm the clinical stage of the cancer. Others are used to know which treatments would work best.

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Medical history

Your medical history includes any health events and medicines you’ve taken in your life. Doctors should collect a medical history for every person with lung cancer. Your doctor will ask about symptoms that may be related to lung cancer. Such symptoms include cough, trouble breathing, chest pain, and weight loss. Knowing which symptoms you have can help your doctors stage the cancer. Since some health problems run in families, your doctor may also ask about the medical history of your blood relatives.
Physical exam

Doctors often perform a physical exam along with taking a medical history. A physical exam is a study of your body for signs of disease. During this exam, your doctor will listen to your lungs, heart, and gut. Your doctor will also look at and feel parts of your body. This is done to see if organs are of normal size, are soft or hard, or cause pain when touched. Cancer and other health conditions can cause organs to become enlarged and hard.

Your doctor will also rate your performance status. Performance status is your ability to do daily activities. It is used by doctors to assess if you can undergo certain treatments. Read Part 6 for more information.

Blood tests

Blood tests are used to look for signs of disease. For a blood test, a needle will be inserted into your vein to remove a sample of blood. The needle may bruise your skin and you may feel dizzy from the blood draw. Your blood sample will then be sent to a lab where a pathologist will test it.

Complete blood count
A CBC (complete blood count) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Cancer and other health problems can cause low or high counts.

Chemistry profile
Another blood test is a chemistry profile. Chemicals in your blood come from your liver, bone, and other organs. A blood chemistry test assesses if the chemicals in your blood are too low or high. Abnormal levels can be caused by spread of cancer or by other health problems.
Imaging tests

Imaging tests make pictures (images) of the insides of your body. They can show which sites have cancer. This information helps your doctors stage the cancer and plan treatment.

Your treatment team will tell you how to prepare for these tests. You may need to stop taking some medicines and stop eating and drinking for a few hours before the scan. Tell your doctors if you get nervous when in small spaces. You may be given a sedative to help you relax.

Diagnostic CT
Diagnostic CT of your chest and belly area (upper abdomen) is needed for clinical staging. Higher doses of radiation are used than for LDCT. As a result, the images show more details. Imaging of your chest and upper abdomen may show if the cancer has spread to your lymph nodes, adrenal glands, liver, or other sites.

CT should be one of the first tests done in the treatment planning process. Your doctors will be better able to plan which sites to biopsy and which treatment is best. The CT scan used to assess if you can have surgery should not be older than 60 days.

PET/CT
If you haven’t had PET/CT, it is advised for clinical stages I, II, and III. It’s best to have this test before a biopsy site is chosen if your doctors think the cancer is quickly spreading. PET/CT may detect cancer in the lymph nodes or other sites that wasn’t found by CT. Thus, PET/CT results may change the clinical stage of the cancer and your treatment options. The PET/CT scan used to assess if you can have surgery should not be older than 60 days.

Stage IV cancer is often found with a CT scan and has often spread to more than one site. In these cases, PET/CT isn’t needed. PET/CT may be helpful only if metastases are in one site, such as the brain or adrenal gland.

Cancer detected by PET/CT needs to be confirmed. A biopsy can be done and in some cases, another imaging test. For example, MRI (magnetic resonance imaging), described next, of your bones may help. A biopsy of the most distant site may help with diagnosis and correctly staging the cancer.

Brain MRI
MRI is an imaging test that uses a magnetic field and radio waves to make pictures. It may show small tumors in the brain that aren’t causing symptoms. It is advised for clinical stages IB, II, and III. If you have stage IV cancer, you may receive a brain MRI only if you have symptoms suggesting the cancer has spread to the brain. Such symptoms include unusual headaches or weakness in a specific part of your body.

For brain MRI, a device will be placed around your head that sends and receives radio waves. You may also be given a contrast dye to make the pictures clearer. It’s important to lie still during the test, so straps may be used to help you stay in place. You may be given a sedative beforehand if you feel nervous.

During MRI, you will be inside the MRI machine. The machine makes loud noises but you can wear earplugs. After MRI, you will be able to resume your activities right away unless you took a sedative. A brain MRI may cause your head to feel a bit warm.

MRI of spine and thoracic inlet
Some stage IIB and III lung cancers are superior sulcus tumors. This type of tumor starts at the top of the lung and easily grows into the chest wall. If this tumor has grown next to your spine or nearby blood vessels, MRI of your spine and thoracic inlet is advised. The thoracic inlet is the center of a ring of bones at the top of the ribcage.
Airway tests

To assess your airways, your doctors will perform a bronchoscopy. It is very important for diagnosis and cancer staging. A tool, called a bronchoscope, will be used to see inside your lungs and collect samples. Common types of bronchoscopy are described below.

Bronchoscopy is advised for clinical stages I, II, and IIIA before treatment is started. A bronchoscopy is very rarely done if there is stage IIIIB or IV disease. If your doctors strongly think a nodule is cancer, you might not need a bronchoscopy until the day of your surgery. It should be done right before the surgery as one procedure. Doing so reduces health risks and saves time and money.

**Standard bronchoscopy**

To perform this test, part of the bronchoscope will be inserted into your body. This part looks like a thin, long tube about as thick as a pencil. It has a light, camera, and open channel. The light and camera allow your doctor to guide the tube down your nose or mouth and into your lungs. A small brush, needle, or tongs can be inserted into the open channel to collect samples. Also, liquid may be sprayed into the airway and then sucked back up.

There are two types of standard bronchoscopes. A rigid bronchoscope is straight and doesn’t bend. A flexible bronchoscope is thinner and longer and can bend. It can reach the smaller airways of the lung. **General anesthesia** is needed for a rigid bronchoscopy. **Local anesthesia** is used for a flexible bronchoscopy. After the biopsy, you may feel some swelling and sound hoarse.

**Radial EBUS bronchoscopy**

**Radial EBUS** (endobronchial ultrasound) bronchoscopy uses a flexible bronchoscope that is fitted with an ultrasound device. Ultrasound uses high-frequency sound waves to make pictures of the insides of the body. Your doctor will move the device back and forth to see a 360-degree view of the area on a screen. The ultrasound device will then be removed so that the sampling tool can be inserted.

**Navigational bronchoscopy**

The airways of the lungs get smaller as they extend toward the sides of the body. Flexible bronchoscopes are often too large to travel through these small airways. A navigational bronchoscopy uses a flexible bronchoscope that is fitted with a second open channel that is thinner and longer.

For this test, your doctor will first plan how to reach the cancer site using CT. Your doctor will then guide the bronchoscope to the site with a sensor that will be inserted through an open channel. When the site is in reach, the sensor will be removed and the sampling tool will be inserted.
Cancer spread tests

Most people with lung cancer will have a biopsy of their lymph nodes or other distant sites. The clinical stage, based on prior tests, will be used to decide which sites to biopsy. Biopsy results may change the clinical stage.

The area between your two lungs is called the mediastinum. This area has lymph nodes. Lung cancer is more likely to have spread to these nodes when the tumor is larger and closer to this spot. As such, testing of mediastinal lymph nodes may not be needed for stage IA. These nodes should be tested if the cancer is clinical stage IB, II, or IIIA.

In stage IIIB, the cancer has spread to the mediastinal lymph nodes (N2) or to hilar, supraclavicular, or scalene lymph nodes (N3 disease). In this case, a mediastinal biopsy may be the best test to get. For others, a test of your supraclavicular or scalene lymph nodes might be better to confirm N3 disease.

For clinical stage I and II cancers, you might not need a mediastinal biopsy until the day of your surgery. It should be done right before the surgery as one procedure. Doing so saves money and time, and reduces health risks. On the other hand, a mediastinal biopsy may be done before the day of surgery if there’s a strong chance of N2 or N3 disease (stage III). It may also be done beforehand if tissue can’t be tested for cancer during the operation.

If imaging or other tests suggest stage IV, the presence of cancer needs to be confirmed before treatment. A mediastinal test is very rarely done for stage IV cancers. A needle biopsy of your adrenal gland may be done to check for cancer. Some lung cancers spread into the fluid around the lungs or heart. If this has likely happened, a biopsy of the fluid should be done.

There are many ways to biopsy lymph nodes and other sites. Navigational bronchoscopy, described in the prior section, is one way to access mediastinal nodes. Other common types of biopsies are described next.

**TTNA**

TTNA (transthoracic needle aspiration) can be used to biopsy certain lung nodules and also some lymph nodes. This test is also called a percutaneous needle biopsy. A very thin needle will be inserted through your chest wall to get a tissue sample.

Before inserting the needle, your skin will be cleaned and numbed with local anesthesia. Next, a small cut will be made into your skin. The needle will be inserted through the cut and into the nodule by your doctor. An imaging test should be used to help guide the needle to the right spot.

During the biopsy, you may be asked to stay still and hold your breath at times. After the biopsy, the cut will be bandaged and you will be given a chest x-ray to check the results. After TTNA, you may feel sore and have some redness at the needle site.

**Mediastinoscopy**

This biopsy accesses lymph nodes in the middle of the chest with a mediastinoscope. A mediastinoscope is very much like a bronchoscope. A cut right above your breastbone will be made to insert the mediastinoscope into your body. When a cut alongside the breastbone is made, the biopsy is called a Chamberlain mediastinoscopy. This method allows access to lymph nodes on the left side of your chest. General anesthesia will be used for these biopsies. You may have some pain and swelling and a small scar afterward.

**EBUS-TBNA**

EBUS-TBNA (endobronchial ultrasound-guided transbronchial needle aspiration) can access
mediastinal lymph nodes. A flexible bronchoscope fitted with an ultrasound device will be guided down your trachea. For this biopsy, the device doesn’t need to be removed in order to insert the sampling tool. Once the bronchoscope is in place, a needle will be inserted through the bronchus and into a lymph node to obtain a sample. EBUS-TBNA requires local anesthesia.

**EUS-FNA**
Food passes from the throat into the stomach through the esophagus. The esophagus extends lower into the body than the bronchi. Thus, lymph nodes below the bronchi can be accessed through the esophagus. For **EUS-FNA** (endoscopic ultrasound-guided fine-needle aspiration), a bronchoscope will be guided down your esophagus. Ultrasound is used to help find the right spot. A needle will then be inserted through your esophagus and into a lymph node to obtain a sample. Local anesthesia is used to prevent pain.

**Thoracentesis**
When cancer spreads into the fluid around the lungs, it can cause a buildup of fluid. This excess fluid is called pleural effusion. Fluid samples can be removed with thoracentesis. First, anesthesia will be injected into your skin. Then, a needle will be inserted between your ribs and into your chest cavity to remove fluid. The fluid will be assessed with a microscope to see if there are cancer cells. If cancer isn’t found by thoracentesis, a thoracoscopy may be done.

**Pericardiocentesis**
Pericardiocentesis is much like thoracentesis. Like the lungs, there is fluid around the heart. Excess fluid may build up if cancer invades it. This excess fluid is called pericardial effusion. Pericardiocentesis removes the excess fluid with a needle inserted through your chest wall. You will receive local anesthesia beforehand.

**Thoracoscopy**
This procedure can obtain samples of N2 and N3 lymph nodes as well as fluid from around the lungs and heart. It requires general anesthesia. A thoracoscope will be inserted through a cut between your ribs. Thoracoscopes work much like bronchoscopes allowing doctors to see any abnormal tissue. Samples can be collected with different types of tools. This surgery may cause some pain and swelling and will leave a small scar. This test is also called a VATS (video-assisted thoracic surgery).
Cancer lab tests

Samples from the biopsy or surgery will be sent to a pathologist. A pathologist is a doctor who’s an expert in testing cells to find disease. He or she will examine the samples using a microscope. All lab results are recorded in a pathology report. It’s a good idea to get a copy of your pathology report. It’s used to plan treatment.

**Histologic typing**
The pathologist will study the parts of the cancer cells to classify the disease. This is called histologic typing. The pathology report will state if the cancer started in the lung or elsewhere. If the cancer started in the lung, the report will also list the type of lung cancer.

Histologic subtypes of non-small cell lung cancer include squamous cell carcinoma, adenocarcinoma, large-cell lung carcinoma, and other rare types. Squamous cells are thin and flat and line the airways of the lung. Adenocarcinoma is a cancer of epithelial cells that make fluids to keep the lungs moist. Large-cell lung carcinomas lack features to classify them as any other carcinoma.

The pathologist will also help with assessing how far the cancer has grown and spread. He or she will measure the size of the primary tumor. Lymph nodes and other removed tissue will be studied for cancer cells. If the cancer appears to have spread to a distant site, the pathologist will assess if the tumor cells from the distant site are from your lung.

**Biomarker testing**
Another task of pathologists is to do biomarker (or molecular) testing. Biomarker testing includes tests of genes or their products (proteins). It is done because not all lung cancers are alike. Lung cancer can differ between people by which genes are present. Biomarker testing is used to plan treatment for metastatic lung cancers.
Overactive **EGFR** mutations

**EGFR** (epidermal growth factor receptor) is a surface receptor. A surface receptor is a protein in the outer membrane of cells that starts changes within a cell when turned on. See Figure 7. **Mutations** in the gene that controls EGFR cause the receptors to be overactive. EGFR overactivity causes new cancer cells to form quickly.

*EGFR* mutation testing is advised for people with widespread adenocarcinomas, large-cell lung carcinomas, and unknown subtypes. Very few squamous cell carcinomas have overactive *EGFR* mutations. Thus, *EGFR* mutation testing for widespread squamous cell carcinomas may be considered, especially for people who never smoked and for mixed histology. Testing for *EGFR* is now approved both from a tissue sample or blood sample.

**ALK** gene rearrangement

For some lung cancers, the growth of the cancer cells is caused in part by an **ALK** (anaplastic lymphoma kinase) **gene rearrangement**. A gene rearrangement is the fusion of one gene with another gene to create a new gene. In some lung cancers, **ALK** fuses with **EML4**. The **ALK-EML4** fusion gene makes an overactive **ALK** surface receptor that helps lung cancer cells grow.

**ALK** testing is advised for people with widespread adenocarcinomas, large-cell lung carcinomas, and unknown subtypes. Very few squamous cell carcinomas have an **ALK** gene rearrangement. Thus, **ALK** testing for widespread squamous cell carcinomas may be considered, especially for people who never smoked and for mixed histology.

**ROS1** gene rearrangement

About 2 out of every 100 lung cancers (2%) consist of cells with a **ROS1** gene rearrangement. Several genes have been found to fuse with **ROS1**. Like **ALK**, the **ROS1** fusion gene makes an overactive **ROS1** surface receptor that helps lung cancer cells grow. **ROS1** testing may be considered for people with normal or unknown **EGFR** or **ALK** status.

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**Figure 7. Surface receptors**

Some lung cancers consist of cells with abnormal surface receptors. A surface receptor is a protein in the outer membrane of cells that starts changes within a cell when turned on. Receptors that may be abnormal and help lung cancer grow include **EGFR**, **ALK**, and **ROS1**.
**PD-L1 expression**

T-cells are part of your body’s disease-fighting (immune) system. One job of T-cells is to attack cancer cells. Some lung cancers consist of cells that make (express) molecules called PD-L1. PD-L1 attaches to PD-1 on T-cells and stops them from attacking cancer cells. **See Figure 8.**

Testing for PD-L1 expression may be needed for widespread lung cancers. Pembrolizumab and nivolumab are medicines for lung cancer that block PD-L1 from attaching to T-cells. They may be used if chemotherapy didn’t work. Testing for lung cancer cells with PD-L1 expression is needed before use of pembrolizumab.

**Other biomarkers**

There are other known biomarkers linked with non-small cell lung cancer. However, they are rare and related treatments are still being tested in clinical trials. Testing for these biomarkers should be done along with EGFR and ALK testing. There may be treatments available or a clinical trial you could join. Read Part 5 for more information on clinical trials. Other gene changes linked with lung cancer include:

- **BRAF V600E** mutation,
- High-level **MET** amplification,
- **MET** exon 14 skipping mutation,
- **RET** gene rearrangements, and
- **HER2** mutations.

Proteomic testing can assess for patterns of proteins related to lung cancer. This testing may be done when first-line treatment doesn’t work for widespread adenocarcinomas, large-cell lung carcinomas, and unknown subtypes that have a normal or unknown EGFR status. Test results help doctors plan what treatment will be best for you. Read Part 6 for more information on when proteomic testing may be done.

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**Figure 8. PD-L1 expression**

Some lung cancers consist of cells with PD-L1. PD-L1 attaches to a receptor on a T-cell called PD-1. When attached, PD-L1 stops the T-cell from attacking the cancer cell.
Lung function tests

Surgery and radiation therapy are treatment options for stage I and II, and some stage III and IV tumors. To assess if you can have these treatments, your doctors will need to know how well your lungs work. There are three lung tests that are called pulmonary function tests. A common side effect of these tests is shortness of breath.

- **Spirometry** involves blowing into a tube to measure how much air and how fast you breathe.
- A **gas diffusion** test involves breathing in a harmless gas and measuring how much you breathe out. It tells how much oxygen travels from your lungs into your blood.
- **Body plethysmograph** involves sitting in a small room and breathing into a tube. This test measures how much air your lungs can hold and how much air is left in your lungs after you exhale.
Review

• A medical history is a report of all health events in your lifetime.

• Your doctor will examine your body for signs of disease. He or she will touch parts of your body to see if anything feels abnormal.

• Blood tests may be done to look for signs of cancer.

• High-quality CT shows more details in pictures than LDCT and may show where the cancer has spread in your body. PET/CT may detect cancer that CT did not.

• MRI can be used to see if the cancer has spread to your brain. You may also have an MRI of your spine and thoracic inlet if you have a superior sulcus tumor.

• A bronchoscopy involves a tool that is guided into your airways to find and collect samples for cancer testing.

• There are many ways to biopsy lymph nodes and other sites to which lung cancer might have spread. Which biopsy you will receive partly depends on where the imaging tests show the cancer to be.

• Pathologists are doctors who conduct lab tests on body tissue or fluid to find disease. Lab tests can reveal if you have cancer, the type of cancer, and the cancer stage. Pathologists also do biomarker testing. These tests look for cancer-related changes in genes for which there may be treatment.

• Pulmonary function tests help doctors assess if surgery or radiation therapy is a treatment option.
Overview of cancer treatments
In Part 5, the main treatment types for lung cancer are briefly described. Knowing what a treatment is will help you understand your treatment options listed in Parts 6 and 7. There is more than one treatment for lung cancer. Not every person will receive every treatment described in this chapter.

**Surgery**

Removal of the tumor by surgery is the time-honored way to try to cure lung cancer. It is preferred over other local treatments. It is commonly used to treat stages I, II, and some III cancers, and rarely used for stage IV. If you will have surgery, a board-certified thoracic surgeon who treats lung cancer often should be on your treatment team.

**Lung tumor surgery**

As shown in Figure 9, how much lung tissue is removed during surgery can differ. Some surgeries for lung cancer remove only part of, rather than the whole lung. Names of common lung surgeries are:

- **Wedge resection** – Removal of a small part of a lobe.
- **Segmentectomy** – Removal of a large part of a lobe.
- **Lobectomy** – Removal of an entire lobe.
- **Sleeve lobectomy** – Removal of an entire lobe and part of the bronchus, and
- **Pneumonectomy** – Removal of the entire lung.
The goal of surgery is to remove all the cancer from the body. To do so, the tumor is removed, along with some normal-looking tissue around its rim, called the surgical margin. Thus, which surgery you will have depends on where the tumor has grown and how well your lungs work.

The preferred surgery for most lung cancers is a pneumonectomy or lobectomy. If a sleeve lobectomy and pneumonectomy are options, a sleeve lobectomy is preferred because it saves most of the lung. You may qualify for a segmentectomy and wedge resection if a lobectomy would seriously threaten your health or if you have a very small tumor that hasn’t likely spread. If you can have either surgery, a segmentectomy is the preferred choice.

**Classic and newer methods**

Removal of a lung tumor can sometimes be done with one of two methods. The classic method is thoracotomy. Thoracoscopy, also called VATS, is a newer method. VATS can be done with or without help from a robot (robotic VATS versus conventional VATS). It is also used to do biopsies as described in Part 4. Not enough research has been done to know if the classic or newer methods are better than the other.

Before either surgery, you will be asked to stop eating, drinking, and taking some medicines for a short period of time. If you smoke, it is important to stop. General anesthesia is used for both surgeries.

With thoracotomy, a large cut is made from the front of the chest to the back passing under the armpit and shoulder blade. The cut is made between the ribs and through the chest wall. The ribs are spread apart with retractors to allow the surgeon to work. Sometimes, a part of the rib is removed. During surgery, the lung with the tumor is deflated and a breathing tube is inserted down the throat to assist the other lung. After surgery, the cut is sewn closed, but chest tubes are left in place for a few days to drain fluid and air. The surgery can take between 2 and 6 hours to complete. You may stay in the hospital for a few days to recover.
Overview of cancer treatments

Surgery

With thoracoscopy, three or four small cuts are made between the ribs on the side of the chest. A small camera and surgical tools are inserted through the cuts. Video from the camera is shown on a screen so that the surgeon can clearly see your organs. Tissue is removed through the small cuts rather than a large opening as done for thoracotomy.

During surgery, the lung with the tumor is deflated and a breathing tube is inserted down your throat to assist the other lung. After surgery, the cuts are sewn closed, but chest tubes are left in place for a few days to drain fluid and air. The surgery can take between 2 and 3 hours to complete. You may stay in the hospital for a few days to recover.

Lymph node surgery
During the surgery to remove the tumor, lymph nodes with cancer and those that may have cancer are removed. Lymph nodes may be removed by systematic lymph node sampling or lymph node dissection.

For sampling, some nodes in the lung and some mediastinal lymph nodes are removed. A lymph node dissection removes as many nodes as possible from the lung and mediastinum. To remove nodes, some organs may need to be moved or cut.

If the cancer stage is N0 or N1, either type of surgery is an option. Lymph node dissection of the mediastinal nodes is advised for stage IIIA cancers with N2 lymph nodes that are treated with surgery.

Side effects of surgery
Side effects are unhealthy or unpleasant physical or emotional responses to treatment. You may experience side effects from the general anesthesia, lung tumor surgery, or the lymph node surgery. Side effects of general anesthesia include a sore throat from the breathing tube, nausea with vomiting, confusion, muscle aches, and itching.

Supportive care

Supportive care doesn’t aim to treat cancer but aims to improve quality of life. However, supportive care given with cancer treatment has been shown not only to improve quality of life and mood but also to extend life among people newly diagnosed with stage IV lung cancer.

Supportive care is also called palliative care. It can address many needs. One example is treatment for physical and emotional symptoms. As such, you may receive denosumab or zoledronic acid to strengthen bones. Mesna may be given to protect against the side effects of chemotherapy. Ask your treatment team for other ways to treat symptoms.

Supportive care can also help with treatment decisions as you may have more than one option. It can also help with coordination of care between health providers. Talk with your treatment team to plan the best supportive care for you.
Common side effects of any surgery are pain, swelling, and scars. Pain can be intense after lung surgery. Pain and swelling often fade away in the weeks after surgery. Numbness near the surgical area may be long-lasting. There is a chance of infection, which may cause pneumonia. There’s also a chance of a collapsed lung (pneumothorax).

Not all side effects of surgery are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

**Ablation**

Ablation destroys small tumors with little harm to nearby tissue. It isn’t used often for lung cancer. It may be used for small tumors. Radiofrequency ablation kills cancer cells using heat from electrodes that are passed through a bronchoscope. This treatment is done by an interventional radiologist.

**Complementary and alternative medicine**

CAM (complementary and alternative medicine) is a group of treatments that aren’t often given by doctors. There is much interest today in CAM for cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are treatments given along with usual medical treatments. While CAMs aren’t known to kill cancer cells, they may improve your comfort and well-being. Two examples are acupuncture for pain management and yoga for relaxation.

Alternative medicine is used in place of usual medicine. Some alternative medicines are sold as cures even though they haven’t been proven to work. If there was good proof that CAMs or other treatments cured cancer, they would be included in this book.

It is important to tell your treatment team if you are using any CAMs. They can tell you which CAMs may be helpful and which CAMs may limit how well medical treatments work.
Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy rays. The rays damage DNA. This either kills the cancer cells or stops new cancer cells from being made. Radiation can also harm normal cells. As a result, new methods keep being made that target the tumor more precisely.

The current standard of radiation therapy is described next. Radiation can be used to treat or control lung cancer. A board-certified radiation oncologist who treats lung cancer often should be on your treatment team if you may have radiation therapy.

External radiation
Most often, EBRT (external beam radiation therapy) is the method used to treat lung cancer. This method delivers radiation from outside your body using a large machine. See Figure 10. The radiation passes through your skin and other tissue to reach the tumor.

Simulation
Treatment planning with a simulation session is needed. During simulation, pictures of the tumor will be taken with an imaging test. Pictures are taken after your body is moved into the position needed for treatment.

CT scans are advised for simulation. However, 4D-CT (four-dimensional computed tomography) is ideal to account for tumor movement from breathing. Contrast can improve scans of tumors in the inner two-thirds of the lung or of lymph nodes with cancer.

A PET/CT scan can help to aim radiation beams when the lung has collapsed or contrast can't be used. PET/CT scans within 4 weeks of treatment are advised. If your breathing causes large movements, motion control methods during the scans may be used.

Using the pictures, your treatment team will plan the best radiation dose, number and shape of radiation beams, and number of treatment sessions. Beams are shaped with computer software and hardware added to the radiation machine. Radiation beams are aimed at the tumor with help from ink marks on the skin or marker seeds in the tumor.

Figure 10. External beam radiation therapy
Radiation therapy is often delivered from a large machine. The rays pass through skin and travel to the tumor. Healthy tissue is protected using modern types of treatment.
Conformal techniques

EBRT should be given with a technique called conformal radiation therapy. This technique molds the radiation beams to the shape of the tumor so healthy tissue around the tumor is spared. However, some healthy tissue still gets radiated. The types of conformal radiation include:

- **3D-CRT** (three-dimensional conformal radiation therapy) uses a photon beam that matches the shape of the tumor. Treatment is completed in about 6 weeks.
- **IMRT** (intensity-modulated radiation therapy) is a more precise form of 3D-CRT. The radiation beam is divided into smaller beams, and the strength of each beam can vary. Treatment is completed in about 6 weeks. IMRT should be used only for a second treatment with radiation or for cancer in an uncommon site.
- **Proton therapy** treats cancer with proton beams that deliver radiation mostly within the tumor. Treatment is completed in about 6 weeks.
- **SABR** (stereotactic ablative radiotherapy) treats cancer with very precise, high-dose photon beams. Receiving SABR is much like other conformal techniques except treatment is finished in about 1 to 2 weeks.
- **SRS** (stereotactic radiosurgery) treats cancer in the brain with precise, high-dose photon beams. Treatment is completed in 1 to 2 weeks.
- **WBRT** (whole brain radiation therapy) uses small amounts of radiation to treat the entire brain. Treatment is completed in 2 weeks.

A lung tumor is harder to target than some other tumors in the body. This is because breathing causes the tumor to move. IGRT (image-guided radiation therapy) can improve how well the radiation beam targets the tumor. IGRT uses a machine that delivers radiation and also takes pictures of the tumor. Pictures can be taken right before or during treatment. These pictures are compared to the ones taken during simulation. If needed, changes will be made to your body position or the radiation beams.

During treatment, you will lie on a table in the same position as done for simulation. Devices may be used to keep you from moving so that the radiation targets the tumor. You will be alone while the technician operates the machine from a nearby room. He or she will be able to see, hear, and speak with you. As treatment is given, you may hear noises. One session can take less than 10 minutes.

Internal radiation

The other method is internal radiation therapy. This method is also called brachytherapy. Internal radiation therapy involves placing a radioactive object in or near the tumor. For lung cancer, internal radiation can shrink a tumor blocking an airway. Radiation is given through a plastic tube that is inserted into the airway. The tube is removed after the treatment session.

Side effects of radiation

The most common side effects of radiation therapy are changes in skin. Your skin in the treated area will look and feel as if it has been sunburned. It will likely become red and may also become dry, sore, and feel painful when touched. You may also have hair loss where treatment was received. Other side effects of radiation include swelling of the lungs or esophagus, extreme tiredness despite sleep (fatigue), and loss of appetite.

Not all side effects of radiation are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.
Chemotherapy

Chemotherapy, or “chemo,” includes drugs that disrupt the life cycle of cancer cells. Some chemotherapy drugs kill cancer cells by damaging their DNA or by disrupting the making of DNA. Other drugs interfere with cell parts that are needed for making new cells. Thus, no new cells are made to replace dying cells. Chemotherapy can affect both cancer and normal cells.

As shown in Figure 11, some chemotherapy drugs work when cells are in an active growth phase. During the active growth phase, cells grow and divide to form a new cell. Chemotherapy drugs that disrupt the growth phase work well for cancer cells that are growing and dividing quickly. Other chemotherapy drugs work in any growth or resting phase.

Chemotherapy regimens used for lung cancer are listed in Guide 5. Sometimes, only one drug is used. Other times, more than one drug is used because drugs differ in the way they work. A combination regimen is the use of two or more chemotherapy drugs. Often, cisplatin or carboplatin—drugs made with platinum—is used with another drug. These regimens are called platinum-doublet chemotherapy.

Figure 11. Chemotherapy and the cell cycle

A cell goes through many changes to divide into two cells. Science has grouped these changes into 7 main phases. There may be another phase of rest, too. Some chemotherapy drugs work in any phase. Other chemotherapy drugs work in one or two growth phases.
Most chemotherapy drugs for lung cancer are liquids that are slowly injected into a vein. Some are a pill that is swallowed. By any method, the drugs travel in your bloodstream to treat cancer throughout your body. Doctors use the term “systemic” when talking about a cancer treatment for the whole body.

Chemotherapy is given in cycles of treatment days followed by days of rest. The cycles vary in length depending on which drugs are used. Common cycles are 14, 21, or 28 days long. Giving chemotherapy in cycles gives your body a chance to recover after receiving chemotherapy. If you will have chemotherapy, ask your doctor how many cycles and days of treatment there are within a cycle.

Part 6 is a guide that explains who should receive which treatments. You will learn if chemotherapy may be part of your treatment. The drugs which are used with surgery and radiation therapy are listed next.

You may receive chemotherapy before or after surgery. In this case, cisplatin is most often used along with another drug. The other drug may be vinorelbine, etoposide, vinblastine, gemcitabine, docetaxel, or pemetrexed. If these regimens make you too sick, paclitaxel with carboplatin is an option.

Chemotherapy is sometimes given with radiation therapy. When given at the same time, cisplatin with either etoposide or vinblastine are options.

### Guide 5. Chemotherapy for lung cancer

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Pemetrexed with either cisplatin or carboplatin may be used for lung cancers that aren’t squamous cell carcinomas. When chemotherapy is followed by radiation therapy, cisplatin with vinblastine or paclitaxel with carboplatin is used.

Chemotherapy may be given during and after radiation therapy. In this case, paclitaxel with carboplatin is used. Another option is cisplatin with etoposide.

**Side effects of chemotherapy**

Side effects of chemotherapy depend on many factors. These factors include the drug type, amount taken, length of treatment, and the person. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious. Most side effects appear shortly after treatment starts and will stop after treatment. However, other side effects are long-term or may appear years later.

In general, most side effects are caused by the death of fast-growing cells. These cells are found in the blood, gut, hair follicles, and mouth. Thus, common side effects of chemotherapy include low blood cell counts, not feeling hungry, nausea, vomiting, diarrhea, hair loss, and mouth sores.

Not all side effects of chemotherapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

**Targeted therapy**

Targeted therapy is a class of drugs that stops the action of molecules that help cancer cells grow. It is less likely to harm normal cells than chemotherapy. Targeted therapies for lung cancer are listed in Guide 6.

These treatments are briefly described next. Some side effects are listed. Ask your treatment team for a full list of common and rare side effects. In Parts 6 and 7, information on who should receive these drugs is provided.

**VEGF pathway**

Cancer cells need the food and oxygen in blood to grow. Cancer cells get blood from blood vessels that have grown into the tumor. VEGF (vascular endothelial growth factor) is one of the molecules that triggers the growth of these blood vessels.

VEGF is made by cancer cells. It travels from cancer cells to endothelial cells. Endothelial cells form blood vessels.

VEGF attaches to surface receptors on the outside of endothelial cells. Attachment of VEGF to surface receptors triggers growth signals. There are two medicines used to treat lung cancer that stop VEGF from triggering growth signals within endothelial cells.
## Guide 6. Targeted therapy for lung cancer

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**Bevacizumab**
Bevacizumab attaches to VEGF before it attaches to receptors on endothelial cells. See Figure 12. As a result, VEGF can’t attach to receptors. No growth signals caused by VEGF are started.

Bevacizumab is given by infusion. It takes about 90 minutes to get the first dose and 30 minutes for later doses. Bevacizumab is always first given with chemotherapy and after 4 to 6 treatments, may be given alone to maintain good results. It is given every two or three weeks depending on the chemotherapy.

Common side effects of bevacizumab are high blood pressure, diarrhea, and feeling tired and weak. You might also have nosebleeds, shortness of breath, and abnormal levels of protein in your urine (proteinuria). Rare but serious side effects include heart attack, stroke, kidney damage, holes in the intestine, and bleeding within the body.

**Ramucirumab**
Ramucirumab attaches to VEGF receptors on the outside of endothelial cells. This blocks VEGF from attaching. No growth signals caused by VEGF are started.

Ramucirumab is given by infusion. It takes 60 minutes to receive the full dose. Ramucirumab is always given with chemotherapy. It is given every two weeks on the first day of chemotherapy.

Common side effects of ramucirumab are high blood pressure and diarrhea. Serious side effects include bleeding, blood clots, holes in the gut, abnormal passage between body parts, and slow wound healing.

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**Figure 12. VEGF targeted therapy**
Cancer cells need blood to grow. They send VEGF to endothelial cells to start the growth of blood vessels. Ramucirumab blocks VEGF from attaching to receptors. Bevacizumab disables VEGF from attaching to receptors.
**EGFR pathway**

Cell growth is started by growth signals. EGFR is one of the surface receptors in lung cancer cells that can trigger growth signals within the cell. Some people with lung cancer have certain gene mutations that cause EGFR to be overactive. With overactive EGFRs, new cancer cells form quickly. There are five medicines used to stop EGFRs from triggering growth signals. See Figure 13.

**Erlotinib**

Erlotinib attaches to a part of EGFR that is within cells. This part of EGFR is a docking site for a chemical called phosphate as it is moved from one molecule to another. Erlotinib blocks phosphate and stops EGFRs from completing their job. Thus, growth signals aren’t triggered by EGFRs.

Erlotinib is made as a pill. It should be taken on an empty stomach. The dose given differs among people. Your doctor will decide the dose you need.

Common side effects of erlotinib are rash; diarrhea; nausea; vomiting; not feeling hungry; feeling tired despite sleep; trouble breathing; and cough. You may have severe eye, skin, lung, kidney, or liver problems, but these are rare. Other rare events include holes in your gut, bleeding, and blood clots.

**Gefitinib**

Gefitinib is the same type of drug as erlotinib. Gefitinib is made as a pill. It can be taken with or without food. It is usually taken once a day.

The most common side effects of gefitinib are skin reactions and diarrhea. Less common side effects include nausea, vomiting, not feeling hungry,
weakness, and sore mouth. Very rare side effects include severe lung and liver problems.

**Afatinib**
Afatinib is the same type of drug as erlotinib. However, it also stops another surface receptor called HER2 (human epidermal growth factor receptor 2) from triggering growth signals. Unlike erlotinib and gefitinib, afatinib doesn’t detach from EGFR and HER2. Its effect on cells doesn’t stop.

Afatinib is made as a pill. It should be taken on an empty stomach. The dose given differs among people. Your doctor will decide the dose you need.

Common side effects of afatinib include diarrhea, skin rash or dryness, acne, nail infection, mouth sores, itching, and not feeling hungry. Diarrhea and skin problems may be severe. Likewise, you may also have lung, liver, heart, and eye problems.

**Osimertinib**
Osimertinib is the same type of drug as erlotinib. It works when EGFR mutations are present and is approved by the U.S. FDA (Food and Drug Administration) for when a specific mutation in EGFRs, called T790M, is present. This mutation appears after taking erlotinib, gefitinib, or afatinib and causes these medicines not to work. At that point of time, osimertinib is an option.

Osimertinib is made as a pill. It can be taken with or without food. The dose given differs among people. Your doctor will decide the dose you need.

The most common side effects of osimertinib are diarrhea, skin rash, dry skin, and nail changes. Nail changes include redness, swelling, pain, and nails breaking and detaching from the finger. Osimertinib may also cause severe lung or heart problems, but these problems are rare.

**Cetuximab**
Cetuximab attaches to the ends of EGFRs that are outside of the cell. Thus, molecules (ligands) are blocked from attaching to and turning on EGFRs. No growth signals are started. Cetuximab also attracts immune cells that help to kill the cancer cells.

Cetuximab may be given with afatinib if the cancer grows or spreads while you were taking another medicine for overactive EGFR mutations. Cetuximab is given by infusion, usually once a week or every other week. It may take 2 hours to receive the first dose, but later doses will take only 1 hour.

Some people have an infusion reaction to cetuximab. Symptoms of a reaction include chills and fever. If you have a reaction, you will be given cetuximab more slowly.

Besides a reaction, common side effects of cetuximab include an acne-like rash, infections, mouth sores, and feeling tired and weak. Other possible side effects are nausea, diarrhea, trouble sleeping, and swelling of feet. Rare but serious side effects include heart, lung, eye, or kidney damage.
ALK pathway

ALK is another surface receptor in lung cancer cells that can trigger growth signals within the cell. In lung cancers with an ALK gene rearrangement, ALK is overactive. With overactive ALK, new cancer cells form quickly. ALK rearrangements almost never occur with EGFR mutations. There are three medicines used to stop ALK from triggering growth signals.

Crizotinib

Crizotinib attaches to a part of ALK that is within cells. This part of ALK is a docking site for a chemical called phosphate as it is moved from one molecule to another. Crizotinib blocks phosphate and stops ALK signaling.

Crizotinib also stops growth signals from ROS1. It stops growth signals from ROS1 in the same way as it does for ALK. Cancer cells that have overactive ROS1 do not have overactive EGFR or ALK.

Crizotinib is first used to treat lung cancers with an ALK gene rearrangement. It is made as a pill and is taken twice a day. It can be taken with or without food.

Common side effects of crizotinib include vision problems; nausea; stomach problems (vomiting, diarrhea, constipation); fluid buildup; and feeling tired despite sleep. Severe problems may include lung, liver, and heart problems.

Ceritinib

Ceritinib is the same type of drug as crizotinib and ceritinib. It a treatment option when crizotinib stops working. The structure of ceritinib differs from crizotinib. Thus, it is able to block phosphate when crizotinib can’t.

Ceritinib is made as a pill. It is taken twice a day with food. Common side effects of ceritinib are tiredness, constipation, swelling, and muscle pain. Other side effects include diarrhea, headache, rash, and dizziness. It rarely causes severe lung, heart, and liver problems.

Alectinib

Alectinib is the same type of drug as crizotinib and ceritinib. It is a treatment option when crizotinib stops working. The structure of alectinib differs from crizotinib. Thus, it is able to block phosphate when crizotinib can’t.

Alectinib is made as a pill. It is taken twice a day with food. Common side effects of alectinib are tiredness, constipation, swelling, and muscle pain. Other side effects include diarrhea, headache, rash, and dizziness. It rarely causes severe lung, heart, and liver problems.

Other targets

Although rare, there are other biomarkers of lung cancer for which there are treatments. These treatments are approved for lung or other cancers but still need more research. Such treatments include afatinib and trastuzumab for HER2. Cabozantinib targets RET. In addition to targeting ALK and ROS1, crizotinib targets MET. Dabrafenib, dabrafenib with trametinib, and vemurafenib target BRAF.
Immunotherapy

The immune system is the body’s natural defense against infection and disease. The immune system includes many chemicals and proteins. These chemicals and proteins are made naturally in your body. Immunotherapy increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells.

Nivolumab

Nivolumab is an immunotherapy used for lung cancer. It is sold as Opdivo®. Some lung cancers consist of cells that have PD-L1 on their surface. PD-L1 can stop T-cells from attacking cancer cells. Nivolumab attaches to a surface receptor on T-cells called PD-1 and blocks PD-L1 on cancer cells from attaching. Thus, T-cells are able to attack cancer cells. See Figure 14.

Nivolumab is given by infusion. It is given every two weeks. It takes about 60 minutes to receive the full dose.

Common side effects of nivolumab are feeling tired despite sleep; trouble breathing; muscle, bone, and joint pain; not feeling hungry; cough; nausea; and constipation. Severe problems with your lungs, gut, liver, kidney, and hormones may occur.

Pembrolizumab

Pembrolizumab is the same type of drug as nivolumab. It is sold as Keytruda®. It has a different structure than nivolumab and attaches to PD-1 in a different way.

Pembrolizumab is given by infusion. It is given every three weeks. It takes about 30 minutes to receive the full dose. Common side effects of pembrolizumab are tiredness, not feeling hungry, trouble breathing, and cough.

Figure 14. Immunotherapy

Some lung cancers consist of cells that have PD-L1 on their surface. PD-L1 can attach to T-cells and stop them from attacking cancer cells. Immunotherapy for lung cancer attaches to a surface receptor on T-cells called PD-1 and blocks PD-L1 from attaching. As a result, T-cells are able to attack cancer cells.
Clinical trials

New tests and treatments aren’t offered to the public as soon as they’re made. They first need to be studied. A clinical trial is a type of research that studies a test or treatment.

Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow’s standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with lung cancer. Future tests and treatments that may have better results than today’s treatments will depend on clinical trials.

New tests and treatments go through a series of clinical trials to make sure they’re safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Some examples of the four phases for treatment are:

- Phase I trials – aim to find the best dose of a new drug with the fewest side effects.
- Phase II trials – assess if a drug works for a specific type of cancer.
- Phase III trials – compare a new drug to the standard treatment.
- Phase IV trials – test new drugs approved by the U.S. FDA in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients.

To join, you’ll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study’s risks and benefits should be described and may include others than those described above.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you’re getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8.
Review

- Lung surgery removes the tumor with some normal tissue around its edge. Lymph node surgery removes nodes with cancer and nodes that may have cancer.

- Radiofrequency ablation kills cancer cells using heat.

- Radiation kills cancer cells or stops new cancer cells from being made.

- Chemotherapy stops cancer cells from completing their life cycle so they can’t increase in number.

- Targeted therapy drugs stop cancer cells from getting food or signals to grow.

- Immunotherapy activates your body’s disease-fighting system to destroy cancer cells.

- Clinical trials give people access to new tests and treatments that otherwise can’t usually be received. These new tests and treatments may in time be approved by the FDA.
Treatment guide:
One primary tumor
6 Treatment guide: One primary tumor

62 Cancer stage I

This section is a guide to treatment for stage I lung cancer. In stage IA, the lung tumor is 3 cm or smaller. A stage IB tumor can be as large as 5 cm or may have grown into the main airway or tissue lining of the lung.

66 Cancer stage II

This section is a guide to treatment for stage II lung cancer. A stage IIA tumor is 3 cm or smaller with cancer in the lung’s lymph nodes. Larger stage IIA tumors are between 5.1 and 7 cm but the cancer hasn’t spread to any nodes. Stage IIA tumors have not invaded nearby tissue.

A stage IIB tumor can also be as large as 7 cm but the lung’s nodes have cancer. Stage IIB tumors also include those larger than 7 cm without cancer in the lymph nodes, those that have invaded the chest wall or bronchi, or those with secondary tumors in the same lobe.

72 Cancer stage III

This section is a guide to treatment for stage III lung cancer. Stage IIIA is often defined by cancer spread to mediastinal nodes, presence of secondary tumors, or tumor growth into the mediastinum, neck, or spine. Stage IIIB is often defined by cancer that has spread to lymph nodes in or near the other lung or above the collarbone.

82 Cancer stage IV

This section is a guide to treatment for stage IV lung cancer. Stage IV cancer has spread to distant sites within the chest or to sites outside the chest. Distant sites within the chest include the other lung, the pleura, and the fluid around the lungs or heart. The options listed in this section also apply to lung cancer that was stage I, II or III but has reappeared in distant sites after a cancer-free period.

92 Review
Part 6 is a guide to the treatment options for people with one primary non-small cell lung tumor. You may also have secondary tumors. The aim is to cure or control the cancer. Receiving supportive care is also important.

This information is taken from the treatment guidelines written by NCCN experts for lung cancer doctors. Your doctors may suggest other treatments than those listed in Part 6 based on your health and personal wishes.

Primary tumors
A primary tumor is the first mass of cancer cells. Cancer cells may break away from the primary tumor and form other tumors. These are called secondary tumors.

Some people have more than one primary tumor. Treatment options for multiple primary tumors are listed in Part 7. If you're unsure, ask your doctor if you have one or more primary tumors.

Treatment options
Treatment options in Part 6 are listed by cancer stage. Cancer is staged based on tests given before treatment. This is called the clinical stage. To learn your options for initial treatment, read the part that is a match to the clinical stage. For example, if the cancer is stage II, read the section called Cancer stage II.

You may have surgery for initial treatment. During surgery, your doctors may find more cancer than first thought. This may change the stage of the cancer. The cancer stage based on surgery results is called the pathologic stage. If the cancer is upstaged, read the part that is a match to the pathologic stage. For example, if the cancer was upstaged from stage II to stage III, read the section Cancer stage III to learn your options for adjuvant treatment after surgery.
Cancer stage I

Guide 7. Initial treatment

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Guide 8. Adjuvant treatment

After surgery

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After radiation therapy

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</tbody>
</table>
Guide 7 lists the options for initial treatment of stage I lung cancer. Which initial treatment you will have depends on if you are able to have surgery. If lung surgery is an option, removal of the tumor and lymph nodes is advised. The goal of surgery is to cure the cancer.

If you are unable or refuse to have surgery, you may be treated with radiation therapy. The goal of radiation therapy is to cure the cancer. You may receive conventional radiation therapy. Conventional radiation therapy gives radiation in small doses for weeks and targets both the tumor and some normal tissue. One example is 3D-CRT. A newer type of radiation therapy—SABR—is also advised. Ablation may be another option for some stage IA tumors in the outer third of the lung.

Guide 8 lists options for adjuvant treatment. Adjuvant treatment is given to reduce the chances of the cancer returning. Options are based on whether your initial treatment was surgery or radiation therapy.

After surgery
Treatment options after surgery are based on whether the cancer is stage IA or IB. Cancer in the surgical margins also affects treatment options.

Cancer-free surgical margins are often a sign that all the cancer was removed. In this case, you may start your survivorship care plan. However, the chance of cancer cells still being in your body is higher for some stage IB cancers. Signs that cancer cells may remain include tumors larger than 4 cm, having a wedge resection, or if the cancer cells barely look like normal cells. In these cases, chemotherapy may be received.

When cancer is found in the surgical margins, a second surgery is the option preferred by NCCN experts. Radiation therapy is another option. If you have stage IB cancer, chemotherapy may be added to surgery or radiation therapy.

After radiation therapy
Treatment options after radiation therapy are based on whether the cancer is stage IA or IB. For stage IA, no more treatment is needed. You may start your survivorship care plan.

The chance of remaining cancer cells is higher for some stage IB cancers. Signs that cancer cells may remain include tumors larger than 4 cm and if the cancer cells barely look like normal cells. In these cases, chemotherapy may be received.
Guide 9. Survivorship care plan

<table>
<thead>
<tr>
<th>Type of care</th>
<th>Schedule of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history and physical exam</td>
<td>• Every 6–12 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>◦ If normal results, then repeat every year</td>
</tr>
<tr>
<td>Chest CT ± contrast</td>
<td>• Every 6–12 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>◦ If normal results, then LDCT without contrast every year</td>
</tr>
<tr>
<td>General health tests (eg, bone density)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Prevent other diseases (eg, cancer screening)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Healthy lifestyle (eg, healthy diet, no smoking)</td>
<td>• As needed</td>
</tr>
</tbody>
</table>
Guide 9 lists the health care that is advised for a survivorship care plan. These plans start when treatment is done and tests show no signs of cancer. The plan should address your whole health and well-being. Talk with your doctor about making a plan together.

Follow-up cancer tests are given to find any new lung tumors early. A medical history, physical exam, and chest CT scan with or without contrast should be received every 6 to 12 months for 2 years. If results are normal, it is suggested that you have these tests once a year. The yearly scan should be an LDCT given without contrast. You may need CT more often if you were treated with chemotherapy with or without radiation therapy and some test results are abnormal.

Besides follow-up tests, tests of your general health are advised. After going through treatment for cancer, it may be hard to think about taking care of “less important” issues. However, your general health can have a big impact on your well-being. Have your blood pressure, cholesterol, and glucose checked on a regular basis. Some people also need bone density testing.

Likewise, take steps to prevent other diseases. Such steps can include getting immunization shots for the flu, herpes, and other diseases. Dental cleaning and exams on a regular basis can prevent disease, too. Screening tests for other cancers are also very important.

The last recommendation is to start or keep a healthy lifestyle. There is proof that healthy behaviors can improve your treatment results. Limiting your use of alcohol, protecting yourself from the sun, and being at a healthy weight are important.

Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. However, you may have special food needs during and after treatment. A nutritionist—an expert in creating a healthy diet—can help.

Many patients benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.

Being hooked on nicotine is one of the hardest addictions to stop. The stress of lung cancer may make it harder or easier to quit. Quitting is important since smoking can limit how well cancer treatment works. Talk with your treatment team about ways to quit.
Cancer stage II

No invasion by tumor

Guide 10. Initial treatment

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>Cancer stage</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>Any stage II</td>
<td>• Lung tumor and lymph node surgery</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>Stage II with N0 disease</td>
<td>• Radiation therapy (including SABR)</td>
</tr>
<tr>
<td></td>
<td>Stage II with N1 disease</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

Guide 11. Adjuvant treatment

After surgery

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>Margin status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IIA with scores of: T2b, N0, M0</td>
<td>No cancer in the margins</td>
<td>• Start survivorship care plan, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemotherapy if cancer may still be in your body</td>
</tr>
<tr>
<td></td>
<td>Cancer in the margins</td>
<td>• Another surgery (preferred) ± chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td>Stage IIA or IIB with scores of: T1a, N1, M0 T1b, N1, M0 T2a, N1, M0 T2b, N1, M0 T3, N0, M0</td>
<td>No cancer in the margins</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is only seen with a microscope</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is seen with the naked eye</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

After radiation therapy

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II with N0 disease</td>
<td>• Consider chemotherapy if cancer may still be in your body</td>
</tr>
</tbody>
</table>
In this section, options for stage II cancers are grouped into four sections. The first section, No invasion by tumor, lists treatment options for tumors that have not grown into the chest wall or bronchi. Among stage II cancers, only those scored T3, N0, M0 may have invaded these sites. Treatment options for invasive T3 tumors are listed in Superior sulcus tumors and Other invasive tumors. For all stage II cancers, health care after cancer treatment is addressed in the section Survivorship care plan.

No invasion by tumor

Guide 10 lists options for initial treatment. Which initial treatment you will have depends on if you are able to have surgery. If lung surgery is an option, removal of the tumor and lymph nodes is advised. The goal of surgery is to cure the cancer. If you are likely to have chemotherapy after surgery, another option is to have it before surgery to shrink the tumor.

If you are unable or refuse to have surgery, options depend on if the cancer has spread to your lymph nodes. If not (N0), you may be treated with radiation therapy to try to cure the cancer. You may receive conventional radiation therapy. Conventional radiation therapy gives radiation in small doses for weeks and targets both the tumor and some normal tissue. One example is 3D-CRT. A newer type of radiation therapy—SABR—is also advised.

Tests may have found cancer in your intrapulmonary, peribronchial, or hilar lymph nodes. This is scored as N1 disease. For N1 disease, you may receive chemoradiation. The two types of treatment should be received at the same time.

Guide 11 lists options for adjuvant treatment. Adjuvant treatment is given to reduce the chances of the cancer returning. Options are based on whether your initial treatment was surgery or radiation therapy.

After surgery

Treatment options after surgery are based on cancer stages. Cancer in the surgical margins also affects treatment options.

For tumors scored T2b, N0, M0, cancer-free margins is often a sign that all the cancer was removed. In this case, you may start your survivorship care plan. However, the chance of remaining cancer cells is higher for some of these cancers. Signs that cancer cells may remain include tumors larger than 4 cm, having a wedge resection, or if the cancer cells barely look like normal cells. In these cases, chemotherapy may be received.

Some T2b, N0, M0 tumors will be removed with cancer in the margins. In these cases, a second surgery with or without chemotherapy is the option preferred by NCCN experts. However, chemoradiation is a second option. These two types of treatment may be given at the same time or back-to-back.

For all other stage II cancers, chemotherapy is advised when the margins are cancer-free. When the margins have cancer, options are based on if the cancer can be seen only with a microscope or with the naked eye. In either case, a second surgery followed by chemotherapy is an option. The second option for microscopic cancer is chemoradiation. These two types of treatment may be given at the same time or back-to-back. Chemoradiation may also be used to treat cancer seen with the naked eye. In this case, chemotherapy and radiation therapy should be received at the same time.

After radiation therapy

The chance of remaining cancer cells is higher for some stage II cancers. Signs that cancer cells may remain include tumors larger than 4 cm and if the cancer cells barely look like normal cells. In these cases, chemotherapy may be received.
### Superior sulcus tumors

**Guide 12. Treatment**

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Preoperative chemoradiation (at the same time),</td>
</tr>
<tr>
<td></td>
<td>• Surgery, and</td>
</tr>
<tr>
<td></td>
<td>• Adjuvant chemotherapy</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

### Other invasive tumors

**Guide 13. Initial treatment**

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Surgery (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Preoperative chemoradiation (at the same time) + surgery,</td>
</tr>
<tr>
<td></td>
<td>• Preoperative chemotherapy + surgery</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>Margin status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative treatment</td>
<td>No cancer in the margins</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is only seen with a microscope</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is seen with the naked eye</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (at the same time)</td>
</tr>
<tr>
<td>Preoperative treatment</td>
<td>No cancer in the margins</td>
<td>• Start survivorship care plan</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins</td>
<td>• Another surgery</td>
</tr>
</tbody>
</table>

---

NCCN Guidelines for Patients®
Superior sulcus tumors

A superior sulcus tumor starts at the top of the lung and easily grows into the chest wall. It is an invasive cancer. This section is about stage II superior sulcus tumors.

Guide 12 lists treatment options based on if you can have surgery. If surgery is an option, preoperative treatment is advised. Chemoradiation may shrink the tumor and make surgery easier. After surgery, adjuvant chemotherapy is advised. Adjuvant treatment reduces the chances of the cancer returning.

If you are unable or refuse to have surgery, chemoradiation is an option. These two types of treatment should be received at the same time. The goal is to try to cure the cancer.

Other invasive tumors

Other stage IIB tumors can be invasive like superior sulcus tumors. These tumors have grown into the chest wall or bronchi, but the cancer hasn’t spread to lymph nodes.

Guide 13 lists options for initial treatment. Surgery alone is the option preferred by NCCN experts. Other options are chemoradiation or chemotherapy to shrink the cancer before surgery. If you are unable or refuse to have surgery, chemoradiation is an option. These two types of treatment should be received at the same time.

Guide 14 lists the options for adjuvant treatment after surgery. Adjuvant treatment is given to reduce the chances of the cancer returning. Treatment options differ by if you had preoperative treatment. Cancer in the surgical margins also affects treatment options.

No preoperative treatment
Chemotherapy is advised when the surgical margins are cancer-free. When the margins have cancer, a second surgery followed by chemotherapy is an option. Chemoradiation is a second option. These two types of treatment may be given at the same time or back-to-back if the cancer in the margins can only been seen with a microscope. If seen with the naked eye, these two treatment types should occur at the same time.

Preoperative treatment
You may start your survivorship care plan if the margins are cancer-free. Otherwise, a second surgery to remove the cancer is advised.
## Survivorship care plan

### Guide 15. Health care after cancer treatment

<table>
<thead>
<tr>
<th>Type of care</th>
<th>Schedule of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history and physical exam</td>
<td>• Every 6–12 months for 2 years&lt;br&gt;◦ If normal results, then repeat every year</td>
</tr>
<tr>
<td>Chest CT ± contrast</td>
<td>• Every 6–12 months for 2 years&lt;br&gt;◦ If normal results, then LDCT without contrast every year</td>
</tr>
<tr>
<td>General health tests (eg, bone density)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Prevent other diseases (eg, cancer screening)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Healthy lifestyle (eg, healthy diet, no smoking)</td>
<td>• As needed</td>
</tr>
</tbody>
</table>
Survivorship care plan

Guide 15 lists the health care that is advised for a survivorship care plan. These plans start when treatment is done and tests show no signs of cancer. The plan should address your whole health and well-being. Talk with your doctor about making a plan together.

Follow-up cancer tests are given to find any new lung tumors early. A medical history, physical exam, and chest CT scan with or without contrast should be received every 6 to 12 months for 2 years. If results are normal, it is suggested that you have these tests once a year. The yearly scan should be an LDCT given without contrast. You may need CT scans more often if you were treated with chemotherapy with or without radiation therapy and some test results are abnormal.

Besides follow-up tests, tests of your general health are advised. After going through treatment for cancer, it may be hard to think about taking care of “less important” issues. However, your general health can have a big impact on your well-being. Have your blood pressure, cholesterol, and glucose checked on a regular basis. Some people also need bone density testing.

Likewise, take steps to prevent other diseases. Such steps can include getting immunization shots for the flu, herpes, and other diseases. Dental cleaning and exams on a regular basis can prevent disease, too. Screening tests for other cancers are also very important.

The last recommendation is to start or keep a healthy lifestyle. There is proof that healthy behaviors can improve your treatment results. Limiting your use of alcohol, protecting yourself from the sun, and being at a healthy weight are important.

Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. However, you may have special food needs during and after treatment. A nutritionist—an expert in creating a healthy diet—can help.

Many patients benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.

Being hooked on nicotine is one of the hardest addictions to stop. The stress of lung cancer may make it harder or easier to quit. Quitting is important since smoking can limit how well cancer treatment works. Talk with your treatment team about ways to quit.
## Cancer stage III

**No invasion by tumor – N0 or N1 disease**

### Guide 16. Initial treatment

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Lung tumor and lymph node surgery</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

### Guide 17. Adjuvant treatment after surgery

<table>
<thead>
<tr>
<th>Margin status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cancer in the margins</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>Cancer in margins that is only seen with a microscope</td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td>Cancer in margins that is seen with the naked eye</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>
In this section, options for stage III cancers are grouped into four main sections. The first section, No invasion by tumor, lists treatment options for tumors that have not grown into the chest wall, bronchi, or mediastinum. Within the first section, options are further grouped by N0 or N1 disease and N2 or N3 disease. Treatment options for tumors that have invaded chest wall, bronchi, or mediastinum sites are listed in Superior sulcus tumors and Other invasive tumors. For all stage III cancers, health care after cancer treatment is addressed in the section Survivorship care plan.

No invasion by tumor – N0 or N1 disease

Guide 16 lists options for initial treatment. N0 means that no cancer has been found in lymph nodes. N1 means that cancer has been found in peribronchial, intrapulmonary, or hilar lymph nodes of the lung with the primary tumor.

Which initial treatment you will have depends on if you are able to have surgery. If lung surgery is an option, removal of the tumor and lymph nodes is advised. The goal of surgery is to cure the cancer. If you are likely to have chemotherapy after surgery, another option is to have it before surgery to shrink the tumor. If you are unable or refuse to have surgery, you may receive chemoradiation. These two types of treatment should be given at the same time.

Guide 17 lists the options for adjuvant treatment after surgery. Treatment options are based on if there’s cancer in the surgical margins. If the margins are cancer-free, chemotherapy is an option.

If there’s cancer in the margins, chemoradiation may be received. These two treatment types may be given at the same time or back-to-back if the cancer in the margins can only been seen with a microscope. If seen with the naked eye, both treatment types should occur at the same time.
No invasion by tumor – N2 or N3 disease

Guide 18. Initial treatment

<table>
<thead>
<tr>
<th>Cancer stage</th>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IIIA (N2)</td>
<td>You’re not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
<tr>
<td></td>
<td>You may be approved for surgery</td>
<td>• Induction chemotherapy ± radiation therapy</td>
</tr>
<tr>
<td>Stage IIIB (N2 or N3)</td>
<td>You’re not approved for surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

Guide 19. Adjuvant treatment

After induction treatment for N2 disease

<table>
<thead>
<tr>
<th>Treatment results</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cancer growth</td>
<td>• Surgery followed by</td>
</tr>
<tr>
<td></td>
<td>• Radiation therapy (if not received before) ± chemotherapy</td>
</tr>
<tr>
<td>Local growth only</td>
<td>• Radiation therapy (if not received before) ± chemotherapy</td>
</tr>
</tbody>
</table>

After surgery for upstaged N2 disease

<table>
<thead>
<tr>
<th>Pathologic stage</th>
<th>Margin status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before surgery, the cancer was rated N0 or N1 but N2 disease was found during surgery</td>
<td>No cancer in the margins</td>
<td>• Chemoradiation (back-to-back)</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is only seen with a microscope</td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is seen with the naked eye</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>
No invasion by tumor – N2 or N3 disease

This section lists treatments for stage III (N2 or N3) tumors without invasion. N2 means that the cancer has spread to the mediastinal lymph nodes. Cancer that has spread to the lymph nodes near the lung without the primary tumor or to the supraclavicular or scalene lymph nodes is scored N3.

Guide 18 lists options for initial treatment of N2 or N3 disease found at diagnosis. Options for initial treatment slightly differ on whether the cancer is stage IIIA or IIIB.

Chemoradiation is an option for all stage III cancers. These two types of treatment should occur at the same time.

Some stage IIIA cancers may be able to be removed by surgery. In these cases, induction treatment may be given. Induction treatment should consist of chemotherapy with or without radiation therapy.

Guide 19 lists the options for adjuvant treatment. Options are grouped by whether you had induction treatment for N2 disease found at diagnosis or if N2 disease was only found after surgery.

After induction treatment for N2 disease

If induction treatment stopped the growth of the cancer, surgery can be done. After surgery, radiation therapy is advised if you didn’t have it before. You may receive chemotherapy before radiation therapy.

During induction treatment, the cancer may have grown in or near to the lung. In this case, radiation therapy is advised if you didn’t have it before. You may receive chemotherapy before radiation therapy.

After surgery for upstaged N2 disease

Sometimes N2 disease is found only after surgical treatment. In this case, options are based on if there’s cancer in the surgical margins. If there’s no cancer, chemoradiation is an option.

If there is cancer in the margins, chemoradiation may be received. These two types of treatments may be given at the same time or back-to-back if the cancer in the margins can only been seen with a microscope. If seen with the naked eye, both treatment types should occur at the same time.
## Superior sulcus tumors

### Guide 20. Initial treatment

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
<tr>
<td>You may be approved for surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

### Guide 21. Treatment after chemoradiation

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Surgery followed by</td>
</tr>
<tr>
<td></td>
<td>• More chemotherapy</td>
</tr>
<tr>
<td>You are still not approved for surgery because the</td>
<td>• Complete radiation therapy followed by</td>
</tr>
<tr>
<td>tumor is too big</td>
<td>• More chemotherapy</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Start survivorship care plan</td>
</tr>
</tbody>
</table>
Superior sulcus tumors

A superior sulcus tumor starts at the top of the lung and easily grows into the chest wall. It is an invasive cancer. This section is about stage III superior sulcus tumors.

Guide 20 lists options for initial treatment. Surgery is a likely treatment option for superior sulcus tumors with a T3 score. Tumors with T4 scores may or may not be able to be treated with surgery. Chemoradiation will be used to either shrink the tumor before surgery or to try to cure the cancer. These two types of treatment should be received at the same time.

Guide 21 lists treatment options after chemoradiation. You may have surgery followed by chemotherapy if the tumor is now small enough. If the tumor is still too big, radiation therapy to try to cure the cancer should be completed and more chemotherapy should follow. If you aren’t able or refuse to have surgery, you may start your survivorship care plan.
Other invasive tumors

Guide 22. Initial treatment

<table>
<thead>
<tr>
<th>Surgery status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>You are approved and agree to surgery</td>
<td>• Surgery (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Preoperative chemoradiation (at the same time) + surgery, or</td>
</tr>
<tr>
<td></td>
<td>• Preoperative chemotherapy + surgery</td>
</tr>
<tr>
<td>You are not approved or decline surgery</td>
<td>• Chemoradiation (at the same time)</td>
</tr>
</tbody>
</table>

Guide 23. Adjuvant treatment after surgery

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>Margin status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No preoperative treatment</td>
<td>No cancer in the margins</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is only seen with a microscope</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (same time or back-to-back)</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins that is seen with the naked eye</td>
<td>• Another surgery + chemotherapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chemoradiation (at the same time)</td>
</tr>
<tr>
<td>Preoperative treatment</td>
<td>No cancer in the margins</td>
<td>• Start survivorship care plan</td>
</tr>
<tr>
<td></td>
<td>Cancer in margins</td>
<td>• Another surgery</td>
</tr>
</tbody>
</table>
Other invasive tumors

Other stage III tumors can be invasive like superior sulcus tumors. These other tumors have grown into the chest wall, bronchi, or mediastinum. The cancer may or may not have spread to lymph nodes.

Guide 22 lists options for initial treatment. If you are able to have surgery, surgery alone is the preferred option of NCCN experts. Other options are chemoradiation or chemotherapy to shrink the cancer before surgery. If you are unable or refuse to have surgery, chemoradiation is an option. These two types of treatment should be received at the same time.

Guide 23 lists the options for adjuvant treatment after surgery. Adjuvant treatment is given to reduce the chances of the cancer returning. Treatment options differ by if you had preoperative treatment. Cancer in the surgical margins also affects treatment options.

No preoperative treatment
Chemotherapy is advised when the surgical margins are cancer-free. When the margins have cancer, a second surgery followed by chemotherapy is an option. Chemoradiation is a second option. These two types of treatment may be given at the same time or back-to-back if the cancer in the margins can only been seen with a microscope. If seen with the naked eye, these two treatment types should occur at the same time.

Preoperative treatment
You may start your survivorship care plan if the margins are cancer-free. Otherwise, a second surgery to remove the cancer is advised.
### Survivorship care plan

#### Guide 24. Health care after cancer treatment

<table>
<thead>
<tr>
<th>Type of care</th>
<th>Schedule of care</th>
</tr>
</thead>
</table>
| Medical history and physical exam               | • Every 6–12 months for 2 years  
  ◦ If normal results, then repeat every year |
| Chest CT ± contrast                             | • Every 6–12 months for 2 years  
  ◦ If normal results, then LDCT without contrast every year |
| General health tests (eg, bone density)         | • As needed                                                                      |
| Prevent other diseases (eg, cancer screening)   | • As needed                                                                      |
| Healthy lifestyle (eg, healthy diet, no smoking)| • As needed                                                                      |
Survivorship care plan

Guide 24 lists the health care that is advised for a survivorship care plan. These plans start when treatment is done and tests show no signs of cancer. The plan should address your whole health and well-being. Talk with your doctor about making a plan together.

Follow-up cancer tests are given to find any new lung tumors early. A medical history, physical exam, and chest CT scan with or without contrast should be received every 6 to 12 months for 2 years. If results are normal, it is suggested that you have these tests once a year. The yearly scan should be an LDCT given without contrast. You may need CT scans more often if you were treated with chemotherapy with or without radiation therapy and some test results are abnormal.

Besides follow-up tests, tests of your general health are advised. After going through treatment for cancer, it may be hard to think about taking care of “less important” issues. However, your general health can have a big impact on your well-being. Have your blood pressure, cholesterol, and glucose checked on a regular basis. Some people also need bone density testing.

Likewise, take steps to prevent other diseases. Such steps can include getting immunization shots for the flu, herpes, and other diseases. Dental cleaning and exams on a regular basis can prevent disease, too. Screening tests for other cancers are also very important.

The last recommendation is to start or keep a healthy lifestyle. There is proof that healthy behaviors can improve your treatment results. Limiting your use of alcohol, protecting yourself from the sun, and being at a healthy weight are important.

Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. However, you may have special food needs during and after treatment. A nutritionist—an expert in creating a healthy diet—can help.

Many patients benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.

Being hooked on nicotine is one of the hardest addictions to stop. The stress of lung cancer may make it harder or easier to quit. Quitting is important since smoking can limit how well cancer treatment works. Talk with your treatment team about ways to quit.
Cancer stage IV

Overactive EGFR mutation

Guide 25. First-line treatment

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>• Erlotinib</td>
</tr>
<tr>
<td></td>
<td>• Afatinib</td>
</tr>
<tr>
<td></td>
<td>• Gefitinib</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stay on first-line targeted therapy ± local treatment,</td>
</tr>
<tr>
<td>• Switch to osimertinib, or</td>
</tr>
<tr>
<td>• Start treatment for histologic type</td>
</tr>
<tr>
<td>◦ Adenocarcinoma, large cell, unknown</td>
</tr>
<tr>
<td>◦ Squamous cell carcinoma</td>
</tr>
</tbody>
</table>

Introduction

Stage IV includes cancers that are scored as M1a or M1b. If you have stage IV cancer, talk with your treatment team about starting supportive care early. Supportive care has been shown to extend and enhance life.

For M1a disease, the cancer has spread from one lung to the other, into the pleura, or into the fluid around the lung or heart. Some of these cancers may be able to be treated with surgery, radiation therapy, or both.

For M1b disease, the lung cancer has spread to sites beyond the chest area. Very rarely, lung cancer spreads to only one site beyond the chest. Examples of such sites are the adrenal gland or brain. In these cases, it may be possible to treat the lung tumor and the distant metastasis with surgery, radiation therapy, or both. However, these treatments aren’t suggested if there is N2 or N3 disease.

This section covers stage IV cancers that can’t be treated with surgery or radiation therapy. These cancers include those that have spread to more than one site within and beyond the chest. In these cases, treatment depends on the histologic...
subtype and biomarker test results. Thus, treatment options are presented in three sections: Overactive EGFR mutation, ALK gene rearrangement, and Unknown or no EGFR, ALK, or ROS1 biomarkers. The last section is further divided by type of non-small cell lung cancer.

There has been recent research on the ROS1 gene rearrangement. If the EGFR and ALK biomarkers are absent, you may be tested for a ROS1 gene rearrangement. If present, treatment with crizotinib may be received. More research on treatment for a ROS1 gene rearrangement is likely to be completed soon.

Chemotherapy is often used for stage IV disease. It can cause severe side effects. As such, it is only given if your health hasn’t seriously limited your activities. The ECOG (Eastern Cooperative Oncology Group) Performance Scale is used by doctors to decide who can have chemotherapy. The definition of each performance score is:

- A score of 0 means you are fully active.
- A score of 1 means you are able to do all self-care activities but are unable to do hard physical work.
- A score of 2 means you are able to do all self-care activities and spend most of waking time out of bed but are unable to do any work.
- A score of 3 means you are unable to do all self-care activities and any work and spend most of waking time in bed.
- A score of 4 means you are fully disabled.

Talk with your doctor about chemotherapy. Discuss which drugs will have greatest chance of treating the cancer. Also, talk about side effects. Let your doctor know which side effects you are willing to have.

**Overactive EGFR mutation**

**Guide 25** lists first-line treatments. First-line treatment isn’t based on performance status. Instead, any cancer with an overactive EGFR mutation should be treated with erlotinib, afatinib, or gefitinib. These drugs are targeted therapies.

Overactive EGFR mutations may be found while you are on first-line chemotherapy. In this case, you may stop chemotherapy early and start targeted therapy. Otherwise, you may start targeted therapy as a maintenance treatment after completing chemotherapy.

**Guide 26** lists the next options for cancer that grows or spreads while on first-line treatment. If the cancer doesn’t worsen much, one option may be to stay on your first-line treatment.

Local treatment may be added to first-line treatment if the cancer is causing symptoms. It is sometimes used when the metastasis is within a confined area, such as the brain or adrenal gland. Local treatment options depend on the metastatic site and may include SRS, SABR, and WBRT.

If you need to switch treatment, you should be tested for the T790M mutation. If it is present, osimertinib may be received. More research is needed to learn if osimertinib treats lung cancer that has spread to the brain.

If the cancer worsens while on EGFR-targeted therapy, platinum-based chemotherapy is another option. It is often used if there are multiple metastatic tumors that are causing symptoms. Read pages 86 to 89 to learn more options for Adenocarcinoma, large cell, and unknown types. Read pages 90 to 91 to learn more options for Squamous cell carcinoma.
**ALK gene rearrangement**

**Guide 27. First-line treatment**

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>• Crizotinib</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stay on crizotinib ± local treatment,</td>
</tr>
<tr>
<td>• Switch to ceritinib or alectinib ± local treatment, or</td>
</tr>
<tr>
<td>• Start treatment for histologic type</td>
</tr>
<tr>
<td>◦ Adenocarcinoma, large cell, unknown</td>
</tr>
<tr>
<td>◦ Squamous cell carcinoma</td>
</tr>
</tbody>
</table>
**ALK gene rearrangement**

**Guide 27** lists the first-line treatments. First-line treatment isn’t based on performance status. Instead, any cancer with an ALK gene rearrangement should be first treated with crizotinib. Crizotinib is a targeted therapy.

The ALK mutation may be found while you are on first-line chemotherapy. In this case, you may stop chemotherapy early and start crizotinib. Otherwise, you may start targeted therapy as a maintenance treatment after completing chemotherapy.

**Guide 28** lists treatment options for cancer that grows or spreads while on crizotinib. If the cancer doesn’t worsen much, one option may be to stay on crizotinib. If you need to switch treatment, ceritinib or alectinib may be options. Ceritinib and alectinib are also targeted therapies.

Local treatment may be added to ALK-targeted therapy if the cancer is causing symptoms. It is sometimes used when the metastasis is within a confined area, such as the brain or adrenal gland. Local treatment options depend on the metastatic site and may include SRS, SABR, and WBRT.

If the cancer worsens while on ALK-targeted therapy, platinum-based chemotherapy is another option. It is often used if there are multiple metastatic tumors that are causing symptoms. Read pages 86 to 89 to learn more options for Adenocarcinoma, large cell, and unknown types. Read pages 90 to 91 to learn more options for Squamous cell carcinoma.
Unknown or no EGFR, ALK, and ROS1 biomarkers – Adenocarcinoma, large cell, unknown types

Guide 29. First-line treatment

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
</table>
| 0 or 1             | • Doublet chemotherapy, or  
|                    | • Bevacizumab + chemotherapy |
| 2                  | • Chemotherapy        |
| 3 or 4             | • Supportive care     |

Guide 30. Maintenance treatment

<table>
<thead>
<tr>
<th>Maintenance type</th>
<th>What are my options?</th>
</tr>
</thead>
</table>
| Continuation      | • Bevacizumab,  
|                   | • Pemetrexed,  
|                   | • Bevacizumab + pemetrexed, or  
|                   | • Gemcitabine       |
| Switch            | • Erlotinib, or  
|                   | • Pemetrexed        |
| Either type       | • Observation       |
Unknown or no EGFR, ALK, and ROS1 biomarkers – Adenocarcinoma, large cell, unknown types

Guide 29 lists first-line treatments for adenocarcinomas, large cell carcinomas, and unknown types. These treatments may be used as first-line care for lung cancers without EGFR, ALK, or ROS1 biomarkers or unknown biomarker status. They also may be used as second- and third-line treatment for some widespread lung cancers with EGFR, ALK, or ROS1 biomarkers.

Treatment is based on performance status. You may be treated with chemotherapy if your performance score is between 0 and 2. Your doctor will choose a regimen based on how well it will stop cancer growth compared to how harmful it could be.

The use of two drugs is called doublet chemotherapy. It is an option if your performance score is 0 or 1. Another option is bevacizumab used with chemotherapy. To receive this treatment, you should not have a recent history of coughing up blood (hemoptysis).

After 1 or 2 cycles of chemotherapy, the cancer’s response to treatment will be tested. It will be tested again every 2 to 4 cycles. If there’s no cancer growth, a total of 4 to 6 chemotherapy cycles are advised.

A performance score of 3 or 4 suggests that chemotherapy will be too harmful. Therefore, the best supportive care is advised. Supportive care aims to treat the symptoms caused by the cancer.

Guide 30 lists treatment options for cancer that doesn’t grow during chemotherapy. You may stay on some of your first-line treatments. This is called continuation maintenance. Another option is changing to a medicine that you didn’t take as a first-line treatment. This is called switch maintenance. A third option is to start close observation. Observation is a period of testing to watch for cancer growth.
**Unknown or no EGFR, ALK, and ROS1 biomarkers – Adenocarcinoma, large cell, unknown types**

**Guide 31. Second-line treatment**

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0, 1, or 2</td>
<td>• Nivolumab (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Pembrolizumab (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Docetaxel,</td>
</tr>
<tr>
<td></td>
<td>• Pemetrexed,</td>
</tr>
<tr>
<td></td>
<td>• Erlotinib,</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine, or</td>
</tr>
<tr>
<td></td>
<td>• Ramucirumab + docetaxel</td>
</tr>
<tr>
<td>3 or 4</td>
<td>• Erlotinib,</td>
</tr>
<tr>
<td></td>
<td>• Afatinib,</td>
</tr>
<tr>
<td></td>
<td>• Gefitinib,</td>
</tr>
<tr>
<td></td>
<td>• Crizotinib, or</td>
</tr>
<tr>
<td></td>
<td>• Supportive care</td>
</tr>
</tbody>
</table>
Unknown or no EGFR, ALK, and ROS1 biomarkers – Adenocarcinoma, large cell, unknown types

Chart 31 lists treatment for cancers that grow during or after first-line treatment. Treatment is based on performance status. If your performance scale is 0, 1, or 2, nivolumab or pembrolizumab are preferred by NCCN experts over other options. Pembrolizumab is approved for lung cancers with PD-L1.

Other options include regimens with chemotherapy, targeted therapy, or both. Do not take the chemotherapy drugs listed if you’ve had them before. Proteomic testing can assess for patterns of proteins related to lung cancer. This test may be done if the EFGR status is normal or unknown. Results are used to decide if erlotinib might help treat the cancer.

If your performance score is 3 or 4, most drugs for lung cancer are likely to seriously harm your health. Thus, best supportive care is advised. Erlotinib, afatinib, and gefitinib can only be taken if an overactive EGFR mutation is present. Likewise, crizotinib may only be taken if an ALK gene rearrangement is present.

Joining a clinical trial is always an option for lung cancer treatment. Ask your treatment team if there is a clinical trial you can join. Also ask about the pros and cons of the trial.
### Unknown or no EGFR, ALK, and ROS1 biomarkers – Squamous cell carcinoma

#### Guide 32. First-line treatment

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or 1 or 2</td>
<td>• Chemotherapy</td>
</tr>
<tr>
<td>3 or 4</td>
<td>• Supportive care</td>
</tr>
</tbody>
</table>

#### Guide 33. Maintenance treatment

<table>
<thead>
<tr>
<th>Maintenance type</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuation</td>
<td>• Gemcitabine</td>
</tr>
<tr>
<td>Switch</td>
<td>• Docetaxel</td>
</tr>
<tr>
<td>Either type</td>
<td>• Observation</td>
</tr>
</tbody>
</table>

#### Guide 34. Second-line treatment

<table>
<thead>
<tr>
<th>Performance status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 or 1 or 2</td>
<td>• Nivolumab (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Pembrolizumab (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Docetaxel,</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine, or</td>
</tr>
<tr>
<td></td>
<td>• Ramucirumab + docetaxel</td>
</tr>
<tr>
<td>3 or 4</td>
<td>• Supportive care</td>
</tr>
</tbody>
</table>
Unknown or no EGFR, ALK, and ROS1 biomarkers – Squamous cell carcinoma

Guide 32 lists treatments for squamous cell carcinomas. These treatments may be used as first-line care for lung cancers without EGFR, ALK, or ROS1 biomarkers or unknown biomarker status. They also may be used as second- and third-line treatment for some widespread lung cancers with EGFR, ALK, or ROS1 biomarkers. Consider having tests for other mutations if only EGFR and ALK testing was done.

Treatment is based on performance status. You may be treated with chemotherapy if your performance score is between 0 and 2. Your doctor will choose a regimen based on how well it will stop cancer growth compared to how harmful it could be.

A performance score of 3 or 4 suggests that chemotherapy will be too harmful. Therefore, the best supportive care is advised. Supportive care aims to treat the symptoms caused by the cancer.

Guide 33 lists treatment options for cancer that doesn’t grow during chemotherapy. You may stay on some of your first-line treatments. This is called continuation maintenance. Another option is changing to a medicine that you didn’t take as a first-line treatment. This is called switch maintenance. A third option is to start close observation. Observation is a period of testing to watch for cancer growth.

Chart 34 lists treatment for cancers that grow during or after first-line treatment. Treatment is based on performance status.

If your performance scale is 0, 1, or 2, nivolumab or pembrolizumab are preferred by NCCN experts over other options. Pembrolizumab is approved for lung cancers with PD-L1 expression. Other options include regimens with chemotherapy, targeted therapy, or both. Do not take the chemotherapy drugs listed if you’ve had them before.

If your performance score is 3 or 4, most drugs for lung cancer are likely to seriously harm your health. Thus, best supportive care is advised.

Joining a clinical trial is always an option for lung cancer treatment. Ask your treatment team if there is a clinical trial you can join. Also ask about the pros and cons of the trial.
Review

• To try to cure stage I lung cancers, surgery or radiation therapy is given. If these treatments are not a cure, more treatment can be received. Once treatment is done, follow a survivorship care plan.

• Stage II tumors without invasion may be cured with surgery. More treatment is often given after surgery. If surgery isn’t an option, radiation therapy to cure is used for N0 disease, and chemoradiation is used for N1 disease. Once treatment is done, follow a survivorship care plan.

• Stage II tumors with invasion may be cured with surgery. You may receive chemotherapy or chemoradiation beforehand and more treatment afterward. If surgery isn’t an option, chemoradiation is used to cure. Once treatment is done, follow a survivorship care plan.

• For stage III tumors without invasion, N0 or N1 disease may be cured with surgery or chemoradiation. Surgery is less often used for N2 and N3 disease that was found before treatment was started. Chemotherapy, radiation therapy, or both is given after surgery. Once treatment is done, follow a survivorship care plan.

• Stage III tumors with invasion may be cured with surgery or chemoradiation. You may receive chemotherapy or chemoradiation before surgery. More treatment is often given afterward. Once treatment is done, follow a survivorship care plan.

• For stage IV cancers, supportive care may enhance and extend life. Ask your treatment team for a supportive care plan.

• Widespread metastatic disease with overactive EGFR mutations is first treated with erlotinib, afatinib, or gefitinib. Osimertinib may be an option if the cancer keeps growing. For ALK gene rearrangements, start with crizotinib and switch to ceritinib or alectinib if needed.

• If you are healthy enough, widespread metastatic disease with no known mutations is first treated with chemotherapy. Bevacizumab may be added for adenocarcinoma, large cell, and unknown subtypes. If the cancer grows, nivolumab and pembrolizumab are preferred treatment options. If you are unhealthy, supportive care is an option. Clinical trials are an option for all metastatic disease.
7

Treatment guide:
Multiple primary tumors
7 Treatment guide: Multiple primary tumors

96 Without symptoms
Treatment for multiple tumors that aren’t causing symptoms.

98 With symptoms
Treatment for multiple tumors that are causing symptoms.

100 Survivorship care plan
A guide to health care after cancer treatment has ended.

102 Review
Part 7 is a guide to the treatment options for people with multiple primary non-small cell lung tumors. You may also have secondary tumors. The aim is to cure or control the cancer. Receiving supportive care is also important.

This information is taken from the treatment guidelines written by NCCN experts for lung cancer doctors. Your doctors may suggest other treatments than those listed in Part 7 based on your health and personal wishes.

**Multiple primary tumors**

A primary tumor is the first mass of cancer cells. Cancer cells may break away from the primary tumor and form other tumors. These tumors are called secondary tumors.

A person can have more than one primary tumor. Multiple primary tumors may occur at the same time. They may occur in the same lung but different lobes or occur in both lungs. Multiple tumors may occur at different times. You may have been treated for one primary tumor and now have a second primary tumor. Multiple primary tumors may be the same or a different histologic subtype of lung cancer.

Multiple primary tumors that have spread to N2 or N3 lymph nodes or have spread outside the chest area are treated the same as metastatic disease. Read Part 6 Cancer stage IV on page 82 for treatment options. For N0 or N1 disease, read Part 7 to learn about treatment options.
## Without symptoms

### Guide 35. Initial treatment for co-occurring tumors

<table>
<thead>
<tr>
<th>Symptom onset</th>
<th>Treatment status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms won’t likely start soon</td>
<td>Any</td>
<td>• Start survivorship care plan</td>
</tr>
<tr>
<td>Symptoms likely to start soon</td>
<td>Local treatments may cure</td>
<td>• Surgery (preferred),</td>
</tr>
<tr>
<td></td>
<td>Local treatments won’t cure</td>
<td>• Radiation therapy, or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ablation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider chemotherapy with or without local treatment to prevent symptoms</td>
</tr>
</tbody>
</table>

### Guide 36. Initial treatment for back-to-back tumors

<table>
<thead>
<tr>
<th>Treatment status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local treatments may cure</td>
<td>• Surgery (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Radiation therapy, or</td>
</tr>
<tr>
<td></td>
<td>• Ablation</td>
</tr>
<tr>
<td>Local treatments won’t cure</td>
<td>• Consider chemotherapy with or without local treatment to prevent symptoms</td>
</tr>
</tbody>
</table>
Guide 35 lists treatment options for multiple tumors that appeared at the same time. Cancers that won’t likely cause symptoms soon don’t need treatment at this time. These tumors are either slow growing or are in a place that won’t cause severe symptoms.

If symptoms are likely in the near future, the cancer should be treated. If local treatments can be received, surgery that spares as much of the lung as possible is preferred by NCCN experts. Otherwise, radiation therapy or ablation is an option.

If local treatment isn’t possible, chemotherapy with or without local treatments for symptom relief may be given. Read Part 6 Cancer Stage IV on page 82 to learn options for chemotherapy.

Guide 36 lists treatment options for multiple tumors that appeared one after the other. If local treatment can be received, surgery that spares as much as the lung as possible is preferred. Otherwise, radiation therapy or ablation is suggested. If local treatment isn’t possible, chemotherapy or local treatments for symptom relief may be given. Read Part 6 Cancer Stage IV on page 82 to learn options for chemotherapy.
Guide 37. Initial treatment

<table>
<thead>
<tr>
<th>Treatment status</th>
<th>What are my options?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local treatments may cure</td>
<td>• Surgery (preferred),</td>
</tr>
<tr>
<td></td>
<td>• Radiation therapy, or</td>
</tr>
<tr>
<td></td>
<td>• Ablation</td>
</tr>
<tr>
<td>Local treatments won’t cure</td>
<td>• Consider chemotherapy with or without local treatment to prevent symptoms</td>
</tr>
</tbody>
</table>
Guide 37 lists treatment options for multiple tumors that are causing symptoms. Cancer symptoms are a sign of advanced cancer growth, so treatment is advised. If local treatment can be received, surgery that spares as much of the lung as possible is preferred by NCCN experts. Otherwise, radiation therapy or ablation is advised. If local treatment isn’t possible, chemotherapy or local treatments for symptom relief may be given. Read Part 6 Cancer Stage IV on page 82 to learn options for chemotherapy.
Survivorship care plan

Guide 38. Health care after cancer treatment

<table>
<thead>
<tr>
<th>Type of care</th>
<th>Schedule of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical history and physical exam</td>
<td>• Every 6–12 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>◦ If normal results, then repeat every year</td>
</tr>
<tr>
<td>Chest CT ± contrast</td>
<td>• Every 6–12 months for 2 years</td>
</tr>
<tr>
<td></td>
<td>◦ If normal results, then LDCT without contrast every year</td>
</tr>
<tr>
<td>General health tests (eg, bone density)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Prevent other diseases (eg, cancer screening)</td>
<td>• As needed</td>
</tr>
<tr>
<td>Healthy lifestyle (eg, healthy diet, no smoking)</td>
<td>• As needed</td>
</tr>
</tbody>
</table>
Guide 38 lists the health care that is advised for a survivorship care plan. These plans start when treatment is done and tests show no signs of cancer. The plan should address your whole health and well-being. Talk with your doctor about making a plan together.

Follow-up cancer tests are given to find any new lung tumors early. A medical history, physical exam, and chest CT scan with or without contrast should be received every 6 to 12 months for 2 years. If results are normal, it is suggested that you have these tests once a year. The yearly scan should be an LDCT given without contrast. You may need CT scans more often if you were treated with chemotherapy with or without radiation therapy and some test results are abnormal.

Besides follow-up tests, tests of your general health are advised. After going through treatment for cancer, it may be hard to think about taking care of “less important” issues. However, your general health can have a big impact on your well-being. Have your blood pressure, cholesterol, and glucose checked on a regular basis. Some people also need bone density testing.

Likewise, take steps to prevent other diseases. Such steps can include getting immunization shots for the flu, herpes, and other diseases. Dental cleaning and exams on a regular basis can prevent disease, too. Screening tests for other cancers are also very important.

The last recommendation is to start or keep a healthy lifestyle. There is proof that healthy behaviors can improve your treatment results. Limiting your use of alcohol, protecting yourself from the sun, and being at a healthy weight are important.

Healthy eating includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. However, you may have special food needs during and after treatment. A nutritionist—an expert in creating a healthy diet—can help.

Many patients benefit from some exercise. Exercise tones muscles, lowers stress, and improves health. Exercise programs differ between people based on their needs. Talk with your treatment team about which exercises would be best for you.

Being hooked on nicotine is one of the hardest addictions to stop. The stress of lung cancer may make it harder or easier to quit. Quitting is important since smoking can limit how well cancer treatment works. Talk with your treatment team about ways to quit.
Review

- Multiple primary tumors that have spread to N2 or N3 nodes or spread outside the chest area are treated the same as metastatic disease. Multiple primary tumors with N0 or N1 disease are treated based on traits of the cancer.

- If it is unlikely that cancer symptoms will appear, multiple primary tumors that appear at the same time don’t need treatment now.

- Signs that treatment is needed include current or soon-to-start symptoms and primary tumors that appear one after the other. In these cases, local treatments are an option if the cancer may be cured. Otherwise, chemotherapy with or without local treatments may be received.
Making treatment decisions
Having cancer is very stressful. While absorbing the fact that you have cancer, you have to learn about tests and treatments. In addition, the time you have to accept a treatment plan feels short. Parts 1 through 7 described the cancer and the test and treatment options recommended by NCCN experts. These options are based on science and agreement among NCCN experts. Part 8 aims to help you make decisions that are in line with your beliefs, wishes, and values.
It’s your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don’t know much about cancer. You’ve never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn’t any better than your doctors’.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You’ll likely get the treatment you want, at the place you want, and by the doctors you want.
Questions to ask your doctors

You may meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, or a friend with you at these visits. A patient advocate or navigator might also be able to come. They can help to ask questions and remember what was said. Suggested questions to ask include:

What’s my diagnosis and prognosis?

It’s important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1. Where did the cancer start? In what type of cell?
2. Is this cancer common?
3. What is the cancer stage? Does this stage mean the cancer has spread far?
4. Is this a fast- or slow-growing lung cancer?
5. What other tests results are important to know?
6. How often are these tests wrong?
7. Would you give me a copy of the pathology report and other test results?
8. How likely is it that I’ll be cancer-free after treatment?
What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Are you suggesting options other than what NCCN recommends? If yes, why?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options?
7. What if I am pregnant?
8. Which option is proven to work best?
9. Which options lack scientific proof?
10. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Less time-consuming? Less expensive?
11. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
12. What can be done to prevent or relieve the side effects of treatment?
13. What are my chances that the cancer will return?
What does each option require of me?

Many patients consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you:

1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
3. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
4. Should I bring someone with me when I get treated?
5. Will the treatment hurt?
6. How much will the treatment cost me? What does my insurance cover?
7. Will I miss work or school? Will I be able to drive?
8. Is home care after treatment needed? If yes, what type?
9. How soon will I be able to manage my own health?
10. When will I be able to return to my normal activities?
What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

1. Are you board certified? If yes, in what area?
2. How many patients like me have you treated?
3. How many procedures like the one you’re suggesting have you done?
4. Is this treatment a major part of your practice?
5. How many of your patients have had complications?
Weighing your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn’t been shown to work better than another, so science isn’t helpful. Some ways to decide on treatment are discussed next.

2nd opinion
The time around a cancer diagnosis is very stressful. People with cancer often want to get treated as soon as possible. They want to make their cancer go away before it spreads farther. While cancer can’t be ignored, there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion on which option is best can help.

Copies of the pathology report, a DVD of the imaging tests, and other test results need to be sent to the doctor giving the 2nd opinion. You may completely trust your doctor, but a 2nd opinion on which option is best can help.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What’s more, some health plans require a 2nd opinion. If your health plan doesn’t cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about the treatment you accept to have. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between your options. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Support groups
Besides talking to health experts, it may help to talk to patients who have walked in your shoes. Support groups often consist of people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with lung cancer.

Compare benefits and downsides
Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven’t thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.
My notes
## Websites

- **American Cancer Society**  
  cancer.gov/types/lung  

- **Lung Cancer Alliance**  
  lungcanceralliance.org  

- **Lung Cancer Research Council**  
  lungcancerresearchcouncil.org  

- **National Coalition for Cancer Survivorship**  
  www.canceradvocacy.org/toolbox  

- **National Cancer Institute**  
  www.cancer.gov/types/lung  

- **NCCN**  
  www.nccn.org/patients  

## Review

- Shared decision-making is a process in which you and your doctors plan treatment together.

- Asking your doctors questions is vital to getting the information you need to make informed decisions.

- Getting a 2nd opinion, attending support groups, and comparing benefits and downsides may help you decide which treatment is best for you.
Glossary

Dictionary

Acronyms
Dictionary

ablation
Treatment that destroys very small tumors with heat or cold.

adenocarcinoma
Cancer of cells that make fluids or hormones.

adjuvant treatment
Treatment that is given to lower the chances of the cancer returning.

adrenal gland
A small organ on top of each kidney that makes hormones.

alveoli
The tiny sacs in the lungs where gases are transferred in and out of the blood.

anaplastic lymphoma kinase (ALK)
Proteins on the edge of a cell that send signals for the cell to grow.

atelectasis
Collapse of a lung.

biomarker
Any molecule in your body that can be measured to assess your health.

biomarker testing
Tests of any molecule in your body that can be measured to assess your health. Also called molecular testing.

biopsy
Removal of small amounts of tissue or fluid to be tested for disease.

board certified
A status to identify doctors who finished training in a specialized field of medicine.

body plethysmograph
A test done in a small room with a small tube to measure how much air is in your lungs after inhaling or exhaling.

brachytherapy
Radiation received from a radioactive object placed near or in the tumor.

bronchi
The two airways extending from the windpipe into the lungs.

bronchioli
Branches of small airways within the lungs.

bronchoscope
A thin, long tube fitted with tools that is guided down the mouth.

bronchoscopy
Use of a thin tool guided down the mouth into the lungs.

bronchus
One of the two main airways that extends into the lungs.

cancer screening
The use of tests to find cancer before signs of cancer appear.

cancer stage
Rating of the growth and spread of tumors.

carcinoma
Cancer of cells that form the lining of structures or form glands.

carina
Firm, flexible, supportive tissue at the base of the windpipe.

chemoradiation
Treatment that combines chemotherapy with radiation therapy.

chemistry profile
Measurement of the amount of chemicals in the blood.

chemotherapy
Drugs that stop the life cycle of cells so they don't increase in number.

chest wall
The layer of muscles and bones under the skin that covers the chest area.

chronic obstructive pulmonary disease (COPD)
Trouble with breathing due to lung damage or too much mucus.

clinical stage
Rating the extent of a tumor based on tests before treatment.
clinical trial
Research on a test or treatment to assess its safety or how well it works.

complete blood count (CBC)
A test of the number of blood cells.

computed tomography (CT)
A test that uses x-rays to view body parts.

continuation maintenance
One or more first-line drugs is continued.

contrast
A dye put into your body to make clearer pictures during imaging tests.

conventional radiation therapy
Radiation that is given in small doses for weeks and targets both the tumor and some normal tissue.

core needle biopsy
Removal of a sample of solid tissue with a needle.

diagnosis
To identify a disease.

diaphragm
A sheet of muscles below the ribs that helps a person to breathe.

doublet chemotherapy
Treatment with two chemotherapy drugs.

Eastern Cooperative Oncology Group (ECOG) performance scale
A rating scale of one’s ability to do daily activities.

endobronchial ultrasound–guided transbronchial needle aspiration (EBUS-TBNA)
Removal of fluid with a needle guided with imaging into the main airway into the lung.

endoscopic ultrasound–guided fine needle aspiration (EUS-FNA)
Removal of fluid with a needle guided with imaging into the long organ between the mouth and stomach.

epidermal growth factor receptor (EGFR)
Proteins on the edge of a cell that send signals for the cell to grow.

esophagus
The tube-shaped organ between the mouth and stomach.

excision
Removal of a tumor but not too much healthy tissue.

external beam radiation therapy (EBRT)
Radiation therapy received from a machine outside the body.

fine-needle aspiration (FNA)
Use of a thin needle to remove fluid or tissue from the body to test for disease.

four-dimensional computed tomography (4D-CT)
An imaging test that can show movement of organs.

gas diffusion
A test that uses harmless gas to measure how much you breathe out.

gene
Instructions in cells for making and controlling cells.

gene rearrangement
The fusion of one gene with another gene to create a new gene.

general anesthesia
A controlled loss of wakefulness from drugs.

hilar lymph nodes
Groups of disease-fighting cells where the main airways enter the lungs.

human epidermal growth factor receptor 2 (HER2)
Proteins on the edge of a cell that send signals for the cell to grow.

image-guided radiation therapy (IGRT)
Radiation therapy that uses imaging tests during treatment to better target the tumor.

immunotherapy
Treatment that uses the body’s natural defense against disease.

intensity-modulated radiation therapy (IMRT)
Radiation therapy that uses small beams of different strengths based on the thickness of the tissue.

intrapulmonary lymph nodes
Groups of disease-fighting cells in the lungs around the small airways.

invasion
A mass of cancer cells that has grown from one structure into another.
large-cell lung carcinoma
A lack of features to classify the cancer as any other carcinoma.

lobe
A clearly seen division in the lungs.

lobectomy
Surgical removal of an entire lobe.

local anesthesia
A loss of feeling in a small area of the body caused by drugs.

low-dose computed tomography (LDCT)
A test that uses little amounts of radiation to make pictures of inside the body.

lymph
A clear fluid containing white blood cells.

lymph node
Small groups of special disease-fighting cells located throughout the body.

lymph node dissection
All groups of disease-fighting cells are removed from a cluster.

lymph node sampling
One group of disease-fighting cells is removed from a cluster.

magnetic resonance imaging (MRI)
A test that uses radio waves and powerful magnets to see the shape and function of body parts.

maintenance treatment
Treatment given to continue good treatment results.

mediastinal lymph nodes
Groups of disease-fighting cells in the middle of the chest.

mediastinal pleura
The lining of the lung at the center of the chest.

mediastinoscope
A thin, long tube fitted with tools to work inside the chest.

mediastinoscopy
Use of a thin tool inserted above the breastbone to do work in the middle of the chest.

mediastinum
The area of the chest between the lungs.

medical history
All health events and medications taken to date.

metastasis
The spread of cancer cells from the first tumor to another body part.

molecular testing
Tests of any molecule in your body that can be measured to assess your health. Also called biomarker testing.

multiple primary tumor
One or more unrelated masses of cancer cells.

mutation
Abnormal changes in the instructions within cells for making and controlling cells (genes).

navigational bronchoscopy
Use of a thin tool guided down the mouth into the smallest airways of the lung.

nodule
A small mass of tissue.

non-small cell lung cancer
A cancer that starts in lung cells that are not small.

non-solid nodule
A small mass of tissue of low density.

observation
A period of testing for cancer growth.

parietal pleura
The outer layer of the lining around the lungs.

part-solid nodule
A small mass of tissue with areas of low and high density.

pathologic stage
Rating the extent of a tumor based on tests after treatment.

pathologist
A doctor who’s an expert in testing cells to find disease.

percutaneous needle biopsy
Insertion of a needle through the skin into a mass to remove tissue for testing.

performance status
A rating of one’s ability to do daily activities.

peribronchial lymph nodes
Groups of disease-fighting cells in the lung around the main airway.
pericardial effusion
Excess fluid between the two tissue layers of the heart’s lining.

pericardiocentesis
Use of a needle inserted between the ribs to remove fluid around the heart.

pericardium
The tissue lining around the heart.

phrenic nerve
A bundle of fibers that sends signals between the spine and muscles used to breathe.

physical exam
A review of the body by a health expert for signs of disease.

platinum-doublet chemotherapy
Treatment with two chemotherapy drugs, one of which is platinum-based.

pleura
The tissue lining around the lungs.

pleural cavity
The space between the two layers of the lung’s lining.

pleural effusion
Excess fluid between the two tissue layers of the lung’s lining.

pleural fluid
The liquid in the space between the two layers of the lung’s lining.

pneumonectomy
Surgical removal of the entire lung.

pneumonitis
Swelling of the air sacs in a lung.

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

positron emission tomography/computed tomography (PET/CT)
A test that uses radioactive material and x-rays to view the shape and function of organs and tissues.

primary tumor
The first mass of cancer cells of their kind.

prognosis
The expected pattern and outcome of a disease based on tests.

proteomic testing
Tests that assess for patterns of proteins related to cancer.

proton therapy
Radiation therapy that uses protons to treat a disease. Also called hadron therapy.

pulmonary fibrosis
Major scarring of lung tissue.

pulmonary function tests
A set of breathing tests to test the strength of the lungs.

pulmonologist
A doctor who’s an expert in lung diseases.

radial endobronchial ultrasound (EBUS) bronchoscopy
Use of a thin tool that is guided down the mouth and into the lungs and is fitted with an imaging device to see through the walls of the lungs.

radiation oncologist
A doctor who’s an expert in treating cancer with radiation.

radiation therapy
The use of radiation to treat cancer.

recurrent laryngeal nerve
A bundle of fibers that sends signals between the spine and voice box.

respiratory system
The group of organs that transfers gases in and out of the body.

risk factor
Something that increases the chance of getting a disease.

ROS1
Proteins on the edge of a cell that send signals for the cell to grow.

scalene lymph nodes
Groups of disease-fighting cells in the neck.

secondary tumor
A mass of cancer cells that formed from the first mass of cancer cells.
sedative
A drug that helps a person to relax or go to sleep.

segmentectomy
Surgical removal of a large part of a lobe.

gine side effect
An unplanned physical or emotional response to treatment.

simulation
The steps needed to prepare for radiation therapy.

sleeve lobectomy
Surgical removal of an entire lobe and part of the bronchus.

small cell lung cancer
Lung cancer of small, round cells.

solid nodule
A small mass of tissue of high density.

spirometry
A test that uses a tube to measure how fast you breathe.

squamous cell carcinoma
A cancer of thin, flat cells that line many surfaces of the body.

stereotactic ablative radiotherapy (SABR)
Radiation therapy that uses precise, high-dose beams.

stereotactic radiosurgery (SRS)
Precise, high-dose photon beams used for brain tumors.

subcarinal lymph nodes
Groups of disease-fighting cells below the windpipe.

superior sulcus tumor
A mass of cancer cells at the top of the lung that has grown into the chest wall.

supportive care
Treatment for symptoms of a disease.

supraclavicular lymph nodes
Groups of disease-fighting cells above the collarbone.

surgical margin
The normal tissue around the tumor removed during surgery.

surgery
An operation to remove or repair a part of the body.

switch maintenance
All first-line drugs are stopped and a new drug is started.

targeted therapy
Drugs that stop the growth process of cancer cells.

thoracentesis
Use of a needle inserted between the ribs to remove fluid around the lungs.

thoracic radiologist
A doctor who’s an expert in reading imaging tests of the chest.

thoracic surgeon
A doctor who’s an expert in surgery within the chest.

thoracotomy
Surgery done through a large cut to remove all or part of the lungs.

three-dimensional conformal radiation therapy (3D-CRT)
Radiation therapy that uses beams that match the shape of the tumor.

trachea
The airway between the throat and bronchi; also called the windpipe.

transthoracic needle aspiration (TTNA)
Use of a needle inserted through the chest to remove fluid or tissue from the body to test for disease.

ultrasound
A test that uses sound waves to take pictures of the inside of the body.

vascular endothelial growth factor (VEGF)
A molecule that triggers the growth of blood vessels.

video-assisted thoracic surgery (VATS)
Use of thin tools inserted between the ribs to do work in the chest.

visceral pleura
The inner layer of the lining around the lungs.

wedge resection
Surgical removal of a small part of a lobe.

whole brain radiation therapy (WBRT)
Small amounts of radiation given to treat the entire brain for cancer.
## Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>3D-CRT</td>
<td>three-dimensional conformal radiation therapy</td>
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<tr>
<td>4D-CT</td>
<td>four-dimensional computed tomography</td>
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<tr>
<td>AJCC</td>
<td>American Joint Committee on Cancer</td>
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<tr>
<td>ALK</td>
<td>anaplastic lymphoma kinase</td>
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<tr>
<td>CAM</td>
<td>complementary and alternative medicine</td>
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<tr>
<td>CBC</td>
<td>complete blood count</td>
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<td>cm</td>
<td>centimeter</td>
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<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribonucleic acid</td>
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<td>ECOG</td>
<td>Eastern Cooperative Oncology Group</td>
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<tr>
<td>EGFR</td>
<td>epidermal growth factor receptor</td>
</tr>
<tr>
<td>EUS</td>
<td>endoscopic ultrasound</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>endoscopic ultrasound-guided fine-needle aspiration</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FNA</td>
<td>fine-needle aspiration</td>
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<tr>
<td>HER2</td>
<td>human epidermal growth factor receptor 2</td>
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<tr>
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<td>whole brain radiation therapy</td>
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## NCCN Abbreviations and Acronyms

- **NCCN**: National Comprehensive Cancer Network®
- **NCCN Patient Guidelines**: NCCN Guidelines for Patients®
- **NCCN Guidelines®**: NCCN Clinical Practice Guidelines in Oncology®
<table>
<thead>
<tr>
<th>Cancer Type</th>
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<tr>
<td>Acute Lymphoblastic Leukemia</td>
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<tr>
<td>Adolescents and Young Adults (AYAs) with Cancer</td>
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<td>Breast Cancer</td>
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<tr>
<td>Carcinoma in Situ (Stage 0)</td>
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<tr>
<td>Early-Stage (Stages I and II)</td>
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<tr>
<td>Stage III Breast Cancer</td>
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<tr>
<td>Stage IV Breast Cancer</td>
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<tr>
<td>Chronic Lymphocytic Leukemia</td>
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<tr>
<td>Chronic Myelogenous Leukemia</td>
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<td>Colon Cancer</td>
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<tr>
<td>Esophageal Cancer</td>
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<tr>
<td>Hodgkin Lymphoma</td>
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<tr>
<td>Kidney Cancer</td>
</tr>
<tr>
<td>Lung Cancer Screening</td>
</tr>
<tr>
<td>Malignant Pleural Mesothelioma</td>
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<tr>
<td>Melanoma</td>
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<tr>
<td>Multiple Myeloma</td>
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<td>Myelodysplastic Syndromes</td>
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<td>Non-Hodgkin’s Lymphomas</td>
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<td>Diffuse Large B-cell Lymphoma</td>
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<td>Follicular Lymphoma</td>
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<td>Mantle Cell Lymphoma</td>
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<td>Mycosis Fungoides</td>
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<td>Peripheral T-cell Lymphoma</td>
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<td>Non-Small Cell Lung Cancer</td>
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<td>Ovarian Cancer</td>
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<td>Pancreatic Cancer</td>
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<tr>
<td>Prostate Cancer</td>
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<tr>
<td>Soft Tissue Sarcoma</td>
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<td>Stomach Cancer</td>
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As of September 12, 2016
State Fundraising Notices

**FLORIDA:** A COPY OF THE OFFICIAL REGISTRATION AND FINANCIAL INFORMATION OF NCCN FOUNDATION MAY BE OBTAINED FROM THE DIVISION OF CONSUMER SERVICES BY CALLING TOLL-FREE WITHIN THE STATE 1-800-HELP-FLA. REGISTRATION DOES NOT IMPLY ENDORSEMENT, APPROVAL, OR RECOMMENDATION BY THE STATE. FLORIDA REGISTRATION #CH33263. **GEORGIA:** The following information will be sent upon request: (A) A full and fair description of the programs and activities of NCCN Foundation; and (B) A financial statement or summary which shall be consistent with the financial statement required to be filed with the Secretary of State pursuant to Code Section 43-17-5. **KANSAS:** The annual financial report for NCCN Foundation, 275 Commerce Drive, Suite 300, Fort Washington, PA 19034, 215-690-0300, State Registration # 445-497-1, is filed with the Secretary of State. **MARYLAND:** A copy of the NCCN Foundation financial report is available by calling NCCN Foundation at 215-690-0300 or writing to 275 Commerce Drive, Suite 300, Fort Washington, PA 19034. For the cost of copying and postage, documents and information filed under the Maryland charitable organizations law can be obtained from the Secretary of State, Charitable Division, State House, Annapolis, MD 21401, 1-410-974-5534. **MICHIGAN:** Registration Number MICS 45298. **MISSISSIPPI:** The official registration and financial information of NCCN Foundation may be obtained from the Mississippi Secretary of State’s office by calling 888-236-6167. Registration by the Secretary of State does not imply endorsement by the Secretary of State. **NEW JERSEY:** INFORMATION FILED WITH THE ATTORNEY GENERAL CONCERNING THIS CHARITABLE SOLICITATION AND THE PERCENTAGE OF CONTRIBUTIONS RECEIVED BY THE CHARITY DURING THE LAST REPORTING PERIOD THAT WERE DEDICATED TO THE CHARITABLE PURPOSE MAY BE OBTAINED FROM THE ATTORNEY GENERAL OF THE STATE OF NEW JERSEY BY CALLING (973) 504-6215 AND IS AVAILABLE ON THE INTERNET AT www.njconsumeraffairs.gov/ocp.htm#charity. REGISTRATION WITH THE ATTORNEY GENERAL DOES NOT IMPLY ENDORSEMENT. **NEW YORK:** A copy of the latest annual report may be obtained from NCCN Foundation, 275 Commerce Drive, Suite 300, Fort Washington, PA 19034, or the Charities Bureau, Department of Law, 120 Broadway, New York, NY 10271. **NORTH CAROLINA:** FINANCIAL INFORMATION ABOUT THIS ORGANIZATION AND A COPY OF ITS LICENSE ARE AVAILABLE FROM THE STATE SOLICITATION LICENSING BRANCH AT 888-830-4989 (within North Carolina) or (919) 807-2214 (outside of North Carolina). THE LICENSE IS NOT AN ENDORSEMENT BY THE STATE. **PENNSYLVANIA:** The official registration and financial information of NCCN Foundation may be obtained from the Pennsylvania Department of State by calling toll-free within Pennsylvania, 800-732-0999. Registration does not imply endorsement. **VIRGINIA:** A financial statement for the most recent fiscal year is available upon request from the State Division of Consumer Affairs, P.O. Box 1163, Richmond, VA 23218; 1-804-786-1343. **WASHINGTON:** Our charity is registered with the Secretary of State and information relating to our financial affairs is available from the Secretary of State, toll free for Washington residents 800-332-4483. **WEST VIRGINIA:** West Virginia residents may obtain a summary of the registration and financial documents from the Secretary of State, State Capitol, Charleston, WV 25305. Registration does not imply endorsement.

Consult with the IRS or your tax professional regarding tax deductibility. REGISTRATION OR LICENSING WITH A STATE AGENCY DOES NOT CONSTITUTE OR IMPLY ENDORSEMENT, APPROVAL, OR RECOMMENDATION BY THAT STATE. We care about your privacy and how we communicate with you, and how we use and share your information. For a copy of NCCN Foundation’s Privacy Policy, please call 215.690.0300 or visit our website at www.nccn.org.
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For disclosures, visit www.nccn.org/about/disclosure.aspx.
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