Lung Cancer

Treatment Guidelines for Patients

Version IV/February 2008





Current Cancer Treatment Guidelines for Patients

Advanced Cancer and Palliative Care Treatment Guidelines for Patients (English and Spanish)

Bladder Cancer Treatment Guidelines for Patients (English and Spanish)

Breast Cancer Treatment Guidelines for Patients (English and Spanish)

Cancer Pain Treatment Guidelines for Patients (English and Spanish)

Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients (English and Spanish)

Colon and Rectal Cancer Treatment Guidelines for Patients (English and Spanish)

Distress Treatment Guidelines for Patients (English and Spanish)

Fever and Neutropenia Treatment Guidelines for Patients with Cancer (English and Spanish)

Lung Cancer Treatment Guidelines for Patients (English and Spanish)

Melanoma Cancer Treatment Guidelines for Patients (English and Spanish)

Nausea and Vomiting Treatment Guidelines for Patients with Cancer (English and Spanish)

Non-Hodgkin's Lymphoma Treatment Guidelines for Patients (English and Spanish)

Ovarian Cancer Treatment Guidelines for Patients (English and Spanish)

Prostate Cancer Treatment Guidelines for Patients (English and Spanish)

Lung Cancer

Treatment Guidelines for Patients

Version IV/February 2008

The mutual goal of the National Comprehensive Cancer Network® (NCCN®) and the American Cancer Society (ACS) partnership is to provide patients and the general public with state-of-the-art cancer treatment information in an easy-to-understand language. This information, based on the NCCN's Clinical Practice Guidelines, is meant to help you when you talk with your doctor about treatment options that are best for you. These guidelines do not replace the expertise and clinical judgment of your doctor.

NCCN Clinical Practice Guidelines were developed by a diverse panel of experts. The guidelines are a statement of consensus of its authors regarding the scientific evidence and their views of currently accepted approaches to treatment. The NCCN guidelines are updated as new information becomes available. The Patient Information version is updated accordingly and is available on-line through the American Cancer Society and NCCN Web sites. To be sure you have the most upto-date version of the guidelines, check the Web sites of the ACS (www.cancer.org) or NCCN (www.nccn.org). You may also call the NCCN at 1-888-909-NCCN or the ACS at 1-800-ACS-2345 for the most recent information.

©2008 by the American Cancer Society (ACS) and the National Comprehensive Cancer Network (NCCN). All rights reserved. The information herein may not be reprinted in any form for commercial purposes without the expressed written permission of the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

Contents

Introduction	
Making decisions about lung cancer treatment	5
About the lungs	6
Types of lung cancer	
Tests and exams for the diagnosis of lung cancer	
Lung cancer staging	
Types of treatment for lung cancer	14
Complementary and alternative medicines	19
About clinical trials	19
Other things to consider during and after treatment	20
Work-up (evaluation) and treatment guidelines	23
Decision trees for non-small cell lung cancer:	
Initial work-up and staging	24
Evaluation of stages I and II	26
Treatment of stages I, II, and IIIA	28
Evaluation of stages IIB and IIIA	32
Treatment of stages IIB and IIIA	34
Evaluation of stages IIIA and IIIB	38
Treatment of stage IIIA	
Treatment of stage IIIB	
Evaluation and treatment of stage IIIB	
Treatment of stage IIIB	
Treatment of stage IV	
Follow-up and treatment of stage IV and recurrent cancer	
Treatment of stage IV and recurrent cancer	56
Treatment of stage IV with disease progression	58
Treatment of second primary	60
Decision trees for small cell lung cancer:	
Initial work-up and staging	64
Limited stage work-up	66
Treatment for limited stage	
Work-up and treatment for extensive stage	
Adjuvant treatment	
Treatment of recurrent disease	



Member Institutions

City of Hope

Dana-Farber/Brigham and Women's Cancer Center Massachusetts General Hospital Cancer Center

Duke Comprehensive Cancer Center

Fox Chase Cancer Center

Huntsman Cancer Institute at the University of Utah

Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance

Arthur G. James Cancer Hospital and Richard J. Solove Research Institute at The Ohio State University

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Memorial Sloan-Kettering Cancer Center

H. Lee Moffitt Cancer Center & Research Institute

Roswell Park Cancer Institute

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

St. Jude Children's Research Hospital/ University of Tennessee Cancer Institute

Stanford Comprehensive Cancer Center

University of Alabama at Birmingham Comprehensive Cancer Center

UCSF Helen Diller Family Comprehensive Cancer Center

University of Michigan Comprehensive Cancer Center

UNMC/Eppley Cancer Center at The Nebraska Medical Center

The University of Texas M.D. Anderson Cancer Center

Vanderbilt-Ingram Cancer Center

Introduction

With this booklet, patients have access to information on the way lung cancer is treated at the nation's leading cancer centers. Originally developed for cancer specialists by the National Comprehensive Cancer Network (NCCN), these treatment guidelines have now been translated for the lay public by the American Cancer Society (ACS).

Since 1995, doctors have looked to the NCCN for guidance on the highest quality, most effective advice on treating cancer. For more than 90 years, the public has relied on the American Cancer Society for information about cancer. The Society's books and brochures provide comprehensive, current, and understandable information to hundreds of thousands of patients, their families, and friends. This collaboration between the NCCN and ACS provides an authoritative and understandable source of cancer treatment information for the public.

These patient guidelines will help you better understand your cancer treatment options. We urge you to discuss them with your doctor. Here are some questions you might want to ask:

- What type of lung cancer do I have?
- · Has my cancer spread?
- What is the stage of my cancer and what does that mean?
- What are my treatment choices?
- What treatment do you suggest and why?
- What should I do to get ready for treatment, minimize side effects of treatment, and hasten my recovery?

- What is the goal of this treatment?
- What risks or side effects are there to the treatment you suggest?
- When will I be able to return to my normal activities?
- What are the chances of my cancer recurring (coming back) with the treatment options we have discussed?
- What rehabilitation and support services are available to me and my family?
- Is this the right time to discuss my living will or advance directives?

In addition to these questions, be sure to write down some of your own. For instance, you might want more information so that you can plan your work schedule. Or, you may want to ask if you qualify for any clinical trials.

Making decisions about lung cancer treatment

Although lung cancer is a very serious disease, it can be treated by a team of health care professionals. This team may include a surgeon, radiation oncologist, medical oncologist, lung specialist, oncology nurse, and social worker.

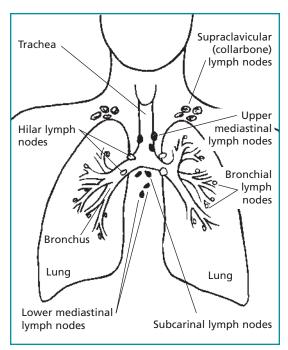
But not all people with lung cancer should have the same treatment. Doctors must consider each patient's specific medical situation. These guidelines are intended to help you understand the treatment options available to people with lung cancer so that you and your doctors can work together to identify which treatment best meets your medical and personal needs.

On the following pages, you will find flow charts that doctors call Decision Trees. They show how you and your doctor can use information about the type, location, and extent of the lung cancer to arrive at the choices you need to make about your treatment. Here you will also find background information on lung cancer with explanations of cancer stage, work-up, and treatment – all terms used in the flow charts.

About the lungs

Most cancers are named after the part of the body where the cancer first starts. Lung cancer begins in the lungs. Other cancers can spread (metastasize) to the lungs, but these cancers are named according to where they first developed. For example, breast cancer can spread to the lungs, but it is called metastatic breast cancer, not lung cancer. These guidelines only address cancers that start in the lungs.

The lungs are 2 sponge-like organs in the chest. They bring air into (inhale) the body and push it out (exhale), taking in oxygen and getting rid of carbon dioxide gas, a waste product. The right lung has 3 sections, called lobes. The left lung has 2 lobes. It is smaller because the heart takes up more room on that side of the body. The lining around the lungs, called the pleura, helps protect the lungs and allows them to move when you breathe. The trachea (windpipe) brings air down into the lungs. It divides into tubes called bronchi, which divide into smaller branches called bronchioles. At the end of



The lungs and nearby lymph nodes

these small branches are tiny air sacs known as alveoli. Most lung cancers start in the lining of the bronchi, but they can also begin in other areas such as the trachea, bronchioles, or alveoli.

Lymphatic vessels are like veins but carry lymph instead of blood. Lymph is a clear fluid that contains tissue waste products and immune system cells. Lymphatic vessels of the lungs lead to nearby lymph nodes inside the chest. These nodes are located around the bronchi and in the mediastinum (the area between the 2 lungs). Cancer cells may enter lymph vessels and spread out to reach lymph nodes. Lymph nodes are small, bean-shaped collections of immune system cells that are important in fighting infections. When lung cancer cells reach the lymph nodes, they can

continue to grow. If cancer cells have multiplied in the lymph nodes, they are more likely to have spread to other organs of the body too. One of the most important decisions about lung cancer treatment is based on whether the cancer has spread to the nearby lymph nodes in the mediastinum. The names, location, and importance of lymph nodes near the lungs are explained in the section on staging of lung cancer (see Lung Cancer Staging on page 11) and are shown in the diagram on the previous page.

Types of lung cancer

The lungs are made up of many kinds of cells that have different functions. The type of lung cancer depends on which cell type is affected. There are 2 major types of lung cancer. The first type is non-small cell lung cancer, or NSCLC. This term refers to a group of cancers that are categorized based on their similar treatment and outcomes. The other type is small cell lung cancer, or SCLC, which has a different prognosis and is treated very differently from NSCLC. Very rarely, lung cancers have features of both types—they are called mixed small cell/large cell cancer or combined small cell and non-small cell lung cancer.

Non-small cell lung cancer

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for 85% to 90% of lung cancers. There are 3 subtypes within this group which differ in size, shape, and chemical make-up when looked at under a microscope:

- squamous cell carcinoma (carcinoma is another word for cancer)
- adenocarcinoma (including bronchioloalveolar carcinoma)
- · large cell undifferentiated carcinoma.

The subtypes of NSCLC, however, have the same treatment options.

Small cell lung cancer

Small cell lung cancer (SCLC) accounts for 10% to 15% of all lung cancers. Other names for small cell lung cancer are oat cell carcinoma, small cell undifferentiated carcinoma, and poorly differentiated neuroendocrine carcinoma.

Other types of lung cancer

There are other rare types of lung cancer that are not covered in this booklet. For example, malignant mesothelioma, a type of cancer that develops from cells of the pleura, is treated differently from SCLC and NSCLC. Also, cancer that spreads to the lungs (metastatic cancer) but started in other organs (such as the breast, pancreas, kidney, or skin) is not covered. Treatment for metastatic cancer to the lungs depends on where it started. For information on these cancers, refer to other NCCN and/or ACS booklets.

Tests and exams for the diagnosis of lung cancer

If there is a reason to suspect you may have lung cancer, your doctor will use one or more methods to find out if the disease is really present. If these tests find lung cancer, more tests will be done to find out how far the cancer has spread.

Medical history and physical exam

Your doctor will ask you a series of questions about your health in general, any other conditions or disease you might have and about your symptoms and risk factors. This is called "taking your medical history." Although most lung cancers do not cause symptoms until they have spread, some of the most frequent symptoms are caused by the cancer growing in the lungs and its spread to nearby tissues. You should tell your doctor about any of these symptoms right away:

- · A cough that does not go away
- Chest pain, often made worse by deep breathing
- Shoulder pain with numbness in some fingers; with (or without) a droopy eyelid
- Hoarseness
- · Weight loss and loss of appetite
- Bloody or rust-colored sputum (spit or phlegm)
- · Shortness of breath
- · Fever without a known reason
- Infections that keep coming back, such as bronchitis and pneumonia
- New wheezing
- Headaches, dizziness; change in vision or speech
- Seizures

These problems are often caused by some other condition, but if lung cancer is found, prompt treatment could help you live longer and relieve symptoms. In many cases, lung cancer may have spread to distant organs before it causes any symptoms. Symptoms caused by cancer that has spread to other organs include:

- Bone pain
- Weakness or numbness of the arms or legs
- Dizziness
- Yellow coloring of the skin and eyes (jaundice)
- Lumps near the surface of the body, caused by cancer spreading to the skin or to lymph nodes (often in the neck or above the collarbone)
- Clusters of symptoms (called paraneoplastic syndromes) caused by the cancer that can point to a possible lung cancer

The medical history and physical exam are the first steps towards finding out whether a lung cancer is present and finding out how far it may have spread. Information about problems other than lung cancer such as bronchitis, emphysema, or heart disease will help doctors decide what treatment options are best for you.

Performance status

Because the side effects of chemotherapy can be severe, recommendations for chemotherapy are often based on a patient's overall general health. This is called a patient's performance status. NCCN doctors use precise definitions of "good health" or "poor health," based on the Eastern Cooperative Oncology Group (ECOG) Performance Scale. The ECOG Performance Scale ranks the health of people with cancer on a scale of 0 to 4. A rank of 0 means that the patient has no symptoms and is able to do

the same things he or she could do before being diagnosed with cancer. At the other end of the scale, a rank of 4 means that the patient cannot take care of his or her daily self-care activities (such as feeding, bathing, dressing, or going to the bathroom) and cannot get out of bed. A rank of 3 means that the patient can do some self-care activities, but spends more than half of his or her waking hours in bed because of feeling too sick or weak. In the Decision Trees presented here, an EGOG performance scale ranking of 0-2 is good health, while a ranking of 3 or 4 is poor health.

Imaging tests

These tests use x-rays, magnetic fields, or radioactive substances to create pictures of the inside of the body to look at the extent or spread of the cancer.

Computed tomography

Computed tomography, or a CT scan, is an x-ray test that produces detailed cross-sectional pictures of your body. Instead of taking one picture, as does a usual chest x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied.

Often after the first set of pictures is taken, you will get an intravenous (IV) injection of a radio-contrast agent or dye, which helps to better outline structures in your body. A second set of pictures is then taken. Some people get hives or, rarely, a few people can have more serious allergic reactions like

trouble breathing and low blood pressure. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for a test.

The CT scan can give precise information about the size, shape, and position of a tumor and can help find enlarged lymph nodes that might contain cancer. CT scans are more sensitive than a routine chest x-ray in finding early lung cancers.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) scans use radio waves and strong magnets instead of x-rays to take pictures. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into very detailed cross-sectional images of parts of the body. A contrast material might be injected just as with CT scans. These images are useful in finding lung cancer that has spread to the brain or spinal cord.

Radionuclide bone scan

This procedure helps show if a cancer has spread to bones. You will get an injection of radioactive material (usually technetium diphosphonate). The amount of radioactivity used is very low and causes no long-term effects. The radioactive substance is attracted to diseased bone cells throughout the entire skeleton. Areas of diseased bone will be seen on the bone scan image as dense, gray to black areas, called "hot spots." These areas may suggest the presence of metastatic cancer, but arthritis, infection, or other bone diseases can also cause a similar pattern.

Positron emission tomography

Positron emission tomography (PET) scans use a form of sugar (glucose) that contains a radioactive atom. A small amount of the radioactive material is injected into your arm. Because of the high amount of energy that lung cancer cells use, areas of cancer in the body absorb large amounts of the radioactive sugar. Then you are put into the PET machine where a special camera can detect the radioactivity. Newer devices combine PET scans and CT scans.

Procedures used to diagnose and check for spread of lung cancer

Depending on the results of the imaging tests, one or more of the following procedures may be used to collect samples and check them for cancer cells. A pathologist, a doctor who specializes in laboratory tests to diagnose diseases such as cancer, will examine the cells using a microscope. If you have any questions about your pathology results or any diagnostic tests, do not hesitate to ask your doctor. You can get a second opinion of your pathology report, called a pathology review, by having your tissue specimen sent to a consulting pathologist at an NCCN center or other laboratory recommended by your doctor.

Sputum cytology

A sample of phlegm (mucus you cough up from the lungs) is checked to see if cancer cells are present.

Fine needle biopsy

A thin needle can be guided between the ribs into the area of concern while the lungs are

being viewed with fluoroscopy (fluoroscopy is like an x-ray, but the image is looked at on a screen rather than on film). CT scans can also be used to direct needle placement. Once doctors are certain the needle tip is within the target area, a biopsy (sample) is removed and sent to the laboratory. A thin needle can also be inserted through the wall of the trachea using a bronchoscope in order to sample nearby lymph nodes. This procedure, called transtracheal fine needle aspiration, is often used to take samples of subcarinal lymph nodes (around the point where the windpipe branches into the left and right bronchi) and mediastinal lymph nodes (along the windpipe and the major bronchial tube areas).

Bone marrow biopsy

A bone marrow biopsy is done to look for lung cancer cells that may have spread to bone marrow. A needle is used to remove a small piece of bone and a sample of bone marrow, usually from the back of the hip bone. A bone marrow biopsy is only done for some patients with small cell lung cancer (SCLC).

Bronchoscopy

Bronchoscopy can help find tumors and take samples of tissue or fluids to see if cancer cells are present. A lighted, flexible tube called a bronchoscope is passed through the mouth into the bronchi. After a lung cancer has been diagnosed, bronchoscopy is used to thoroughly check the lining of other airways in the lungs. If another cancer is found that is not close to the first one, surgery may not be able to remove all of the cancerous tissue.

Mediastinoscopy

For a mediastinoscopy a hollow, lighted tube is inserted under the breastbone (sternum), through a small cut in the base of the neck. Special instruments operated through this tube can be used to take a tissue sample from the mediastinal lymph nodes (along the windpipe and the major bronchial tube areas).

Thoracentesis

Thoracentesis is done to check whether fluid around the lungs is caused by cancer that has spread to the pleural membranes (the delicate membranes that cover the lungs) or caused by a non-cancerous condition, such as heart failure or an infection. A needle is placed between the ribs to drain the fluid, which is checked under a microscope to look for cancer cells. If fluid collects around the lungs, it can keep the lungs from filling with air, so thoracentesis can help improve the patient's breathing.

Thoracoscopy

A thoracoscopy procedure uses a thin, lighted tube connected to a video camera and monitor to look at the space between the lungs and the chest wall. This allows the doctor to see tumors on the surface of the lungs. The doctor can also take a biopsy of any areas that look suspicious.

Blood tests

When cancer spreads to the liver and bones, it may cause certain chemical abnormalities in the blood. Certain blood tests are often done to see if the lung cancer has spread to

these areas. These tests include a complete blood count (CBC) and blood chemistry. A CBC determines whether the patient's blood has the correct number of various cell types. Doctors repeat this test regularly in patients treated with chemotherapy, because these drugs temporarily affect blood-forming cells of the bone marrow. To find these changes, doctors perform blood chemistry tests.

Lung cancer staging

Staging is the process of finding out how far the cancer has spread. This is very important, because your treatment and the outlook for your recovery and chances of cure depend on the stage of your cancer. For example, some stages of lung cancer may be best treated with surgery, while others are best treated with combinations of chemotherapy and radiation therapy. There are different staging systems for small cell and non-small cell lung cancer.

Your treatment and prognosis (the outlook for chances of survival) depend, to a large extent, on your cancer's stage and cell type. Tests such as MRI, CT scans, bone marrow biopsy, mediastinoscopy, and blood tests are used to stage the cancer.

Be sure to ask your doctor to explain your stage in a way you understand. Once you know your stage, you will know which Decision Trees in this booklet apply to you. Reviewing these Decision Trees can help you and your doctor decide which treatments are best suited for you.

Staging of non-small cell lung cancer

The system most often used to describe the growth and spread of non-small cell lung cancer (NSCLC) is the **TNM** staging system, also known as the American Joint Committee on Cancer (AJCC) system. In TNM staging, information about the tumor, nearby lymph nodes, and distant organ metastases is combined and a stage is assigned to that specific grouping. The grouped stages are described using Roman numerals from I to IV.

In TNM staging **T** stands for tumor (its size and how far it has spread within the lung and to nearby organs), **N** stands for spread to lymph nodes, and **M** is for metastasis (spread to distant organs).

T categories for non-small cell lung cancer

T categories are based on the lung cancer's size, its spread and location within the lungs, and its spread to nearby tissues.

Tis: Cancer is found only in the layer of cells lining the air passages. It has not spread into other lung tissues. This stage is also known as carcinoma in situ.

T1: The cancer is no larger than 3 centimeters (slightly less than 1½ inches), has not spread to the visceral pleura (membranes that surround the lungs), and does not affect the main branches of the bronchi.

T2: The cancer has one or more of the following features:

- It is larger than 3 cm across.
- It has grown into a main bronchus but is not closer than 2 cm (about ¾ inch) from the point where the trachea (windpipe) branches into the left and right main bronchi.

- It has spread to the membranes that surround the lungs.
- The cancer may partially block the airways, but this has not caused the entire lung to collapse or develop pneumonia.

T3: The tumor is any size and has one or more of the following features:

- It has spread to the chest wall, the diaphragm (breathing muscle that separates the chest from the abdomen), the mediastinal pleura (membranes surrounding the space between the 2 lungs), or parietal pericardium (membranes of the sac surrounding the heart).
- It has grown into a main bronchus, and it is closer than 2 cm (about ¾ inch) from the point where the trachea (windpipe) branches into the left and right main bronchi, but has not grown into this area.
- It has grown into the airways enough to cause one lung to entirely collapse or to cause pneumonia of the entire lung.

T4: The cancer has one or more of the following features:

- It has spread to any of the following: the mediastinum (space behind the chest bone and in front of the heart), the heart, the trachea (windpipe), the esophagus (tube connecting the throat to the stomach), the backbone, or the point where the windpipe branches into the left and right main bronchi.
- Two or more separate tumors are present in the same lobe of a lung.

T category	N category	M category
Tis (In situ)	N0	MO
T1	NO	MO
T2	NO	MO
T1	N1	MO
T2	N1	M0
T3	N0	M0
T1	N2	MO
T2	N2	MO
T3	N1	MO
T3	N2	M0
Any T	N3	M0
T4	Any N	M0
Any T	Any N	M1
	Tis (In situ) T1 T2 T1 T2 T3 T1 T2 T3 T1 T2 T3 T1 T4	Tis (In situ) N0 T1 N0 T2 N0 T1 N1 T2 N1 T3 N0 T1 N2 T2 N2 T3 N1 T3 N1 T3 N1 T3 N2 Any T T4 Any N

 There is a malignant pleural effusion (fluid containing cancer cells in the space surrounding the lung).

N categories for non-small cell lung cancer

The N category depends on which, if any, of the lymph nodes near the lungs are affected by the cancer.

N0: The cancer has not spread to lymph nodes.

N1: The cancer has spread to lymph nodes within the lung, or the hilar lymph nodes (located around the area where the bronchus enters the lung). Metastases affect lymph nodes only on the same side as the cancerous lung.

N2: The cancer has spread to subcarinal lymph nodes (around the point where the windpipe branches into the left and right

bronchi) or to lymph nodes in the mediastinum (space behind the chest bone and in front of the heart). Affected lymph nodes are on the same side of the lung with the tumor.

N3: The cancer has spread to lymph nodes near the collarbone on either side, and/or to hilar or mediastinal lymph nodes on the side opposite the lung with the tumor.

M categories for non-small cell lung cancer

The M category describes whether the cancer has spread to any distant tissues and organs.

M0: No distant cancer spread.

M1: Cancer has spread to one or more distant sites. Sites considered distant include other lobes of the lungs, lymph nodes further than those mentioned in N stages, and other organs or tissues such as the liver, bones, or brain.

Stage grouping for non-small cell lung cancer

Once the T, N, and M categories have been assigned, this information is combined (stage grouping) to assign an overall stage of 0, I, II, III, or IV (see Table 1). Various T and N categories are combined into stages. The stages identify tumor types that have a similar prognosis and are treated in a similar way. As noted in the table, a tumor that has metastasized to distant areas (M1) is considered Stage IV, regardless of the tumor's size or if the lymph nodes are involved. Patients with lower stage cancers have a more favorable outlook for survival (that is, patients with Stage I disease tend to live longer than those with Stage IV disease).

Staging of small cell lung cancer

Although small cell lung cancer can be staged like NSCLC, most doctors have found that a much simpler 2-stage system works better choosing treatment. This system divides SCLC into "limited stage" and "extensive stage."

- Limited stage means that the cancer is only in one lung and in lymph nodes on the same side of the chest.
- Extensive stage means that the cancer
 has spread outside the other lung and
 to other parts of the body such as the
 lymph nodes on the other side of the
 chest, or to distant organs; or there is
 malignant fluid surrounding the lung.

Types of treatment for lung cancer

There is a lot for you to think about when choosing the best way to treat or manage your cancer. There may be more than one treatment to choose from. Planning lung cancer treatment is very complex. A team of cancer care professionals should be available to discuss all of the options. Combinations of chemotherapy, radiation therapy, targeted therapy, or surgery may be of greater value than any single treatment alone. You may feel that you need to decide on a treatment quickly. But give yourself time to understand your options. Talk with your doctor. Look at the list of questions on page 5 to get some ideas. Then add your own.

You may want to get a second opinion. Your doctor should not mind if you want to do this. In fact, some insurance companies require a second opinion. If your first doctor has done tests, the results can be sent to the second doctor so that you will not have to have them done again. Before making any plans check your health insurance company's policy about second opinions.

The treatment options for lung cancer are surgery, radiation therapy, chemotherapy, and targeted therapy either alone or in combination, depending on the stage of the tumor.

Surgery

Depending on the type and stage of the cancer, surgery may be used to remove the tumor and some of the lung tissue around it. If a lobe (section) of the lung is removed, the surgery is called a lobectomy. If the entire lung is removed,

the surgery is called a pneumonectomy. These operations are done with the patient asleep under general anesthesia. A hospital stay of about 1 week is usually needed. Because the surgeon has to cut or spread the ribs to get to the lungs, the patient will have some pain after the surgery. There are many ways to control pain. (See the ACS/NCCN *Cancer Pain Treatment Guidelines for Patients* for more information on pain management.)

People who do not have any other lung problems (other than the cancer) can often return to their normal activities after a lobe or even an entire lung is removed. However, if they also have diseases such as emphysema or chronic bronchitis (common among heavy smokers), they may find that their shortness of breath gets worse. For people who can't have surgery because they are in poor general health, have other medical problems, or because the cancer is widespread, other types of therapy (for example, radiation therapy, chemotherapy, and supportive care) can be given to relieve symptoms.

Surgery may be the first step in treating your lung cancer. Or, surgery may be considered after chemotherapy and radiation therapy. In either case, your initial work-up before beginning any treatment should include evaluation by a surgeon.

Chemotherapy

Chemotherapy refers to the use of drugs to kill cancer cells. Usually the drugs are given into a vein or by mouth. Once the drugs enter the bloodstream, they reach all parts of the body. Often several drugs are given at the same time. Depending on the type and stage of lung cancer, chemotherapy may be given as the

main treatment or in addition to surgery and/ or radiation therapy. When it is used with surgery, chemotherapy is called adjuvant therapy. It is added to surgery to reduce the risk that the cancer will recur (come back) or spread outside the lung.

Doctors who prescribe these drugs (called medical oncologists) most often use a combination of medicines that have proven to be more effective than a single drug. Doctors give chemotherapy in cycles, with each cycle of treatment followed by a recovery period. Chemotherapy cycles generally last about 21 to 28 days, and initial treatment typically involves 4 to 6 cycles. Chemotherapy is not recommended for patients in poor health (performance status 3–4). Advanced age is not a barrier, as long as the patient is not in poor health.

All chemotherapy agents have side effects. Temporary side effects might include loss of appetite, nausea and vomiting, mouth sores, and hair loss. Chemotherapy can damage the cells of the bone marrow that make blood, causing a decrease in white blood cells that can increase a patient's risk of infection; a shortage of blood platelets that can cause bleeding or bruising after minor cuts or injuries; and a decrease in red blood cells (low blood hemoglobin levels) that can lead to fatigue. (For more information see the ACS/NCCN Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients).

Things can be done to prevent or lessen these side effects. For example, there are several drugs that can prevent or reduce nausea and vomiting (see the ACS/NCCN Nausea and Vomiting Treatment Guidelines for Patients with Cancer). A group of drugs called growth

factors can help bone marrow recover after chemotherapy and shorten the period of time that a person's blood counts are low.

Patients can also have long-term effects from cancer drugs such as premature menopause, infertility, or heart or lung damage.

Your doctor or nurse will discuss possible side effects and what can be done to reduce them, with you and your family before you start treatment. Once treatment is started, your doctor and nurse will expect you to tell them about any side effects that you have.

Non-small cell lung cancer

The drug combinations most frequently used for initial chemotherapy (also called first-line therapy) for NSCLC are cisplatin combined with one of the following:

- Docetaxel
- Etoposide
- Gemcitabine
- Vinblastine
- Vinorelbine

Some patients cannot tolerate cisplatin therapy. If this is the case, the patient may be given other drugs, including carboplatin combined with either gemcitabine, paclitaxel, or docetaxel. Docetaxel can also be combined with gemcitabine.

For some patients, bevacizumab, a drug that blocks the growth of blood vessels that feed the cancer, can be combined with chemotherapy drugs. After chemotherapy, bevacizumab may be continued until the cancer progresses.

First-line chemotherapy for advanced or metastatic NSCLC includes cisplatin or carboplatin combined with any of the following drugs:

- Docetaxel
- Etoposide
- Gemcitabine
- Irinotecan
- Paclitaxel
- Vinblastine
- Vinorelbine

Patients who cannot tolerate combination chemotherapy, can have single-agent chemotherapy (that is, using just one drug). However, chemotherapy is not recommended for patients in poor general health (performance status 3–4).

Chemotherapy or targeted therapy used for second-line therapy (medicines used if the cancer continues to grow during or after initial chemotherapy) for NSCLC includes all the drugs listed before, and also:

- Docetaxel alone
- Erlotinib alone
- Pemetrexed alone

Small cell lung cancer

The drug combinations most frequently used for initial chemotherapy for limited stage small cell lung cancer are:

- Cisplatin and etoposide
- Carboplatin and etoposide

The drug combinations most frequently used for initial chemotherapy for extensive stage small cell lung cancer are:

- · Cisplatin and etoposide
- · Carboplatin and etoposide
- Cisplatin and irinotecan

Chemotherapy drugs used if the small cell lung cancer comes back within 6 months of initial treatment include:

- Topotecan
- Irinotecan
- Paclitaxel
- Docetaxel
- Gemcitabine
- · Oral etoposide
- Cyclophosphamide, doxorubicin, and vincristine (CAV)
- Vinorelbine
- Ifosfamide

For relapses more than 6 months after the initial treatment, the original chemotherapy can be repeated.

Targeted therapy

In the past few years, lung cancer research has focused on drugs that are specifically targeted at cancer cells and interfere with their ability to grow. For example, erlotinib (Tarceva*) has been recently approved by the Food and Drug Administration (FDA) to be used in NSCLC patients who are no longer responding to chemotherapy (this is usually determined after 1 or 2 different chemotherapy combinations have been tried). Tarceva is taken by mouth. Common side effects this drug include skin rash and diarrhea.

Bevacizumab (Avastin*) is another targeted therapy that has been most commonly used to treat colon cancer but has also been recently approved by the Food and Drug Administration (FDA) as a treatment for NSCLC. Bevacizumab can cause bleeding, which means it cannot be used in patients who are coughing up blood, whose cancer has spread to the brain, or who are on blood thinners (anticoagulation therapy). Patients

with squamous cell cancer also cannot use it because it leads to bleeding from this type of lung cancer. Other rare but serious side effects include blood clots and high blood pressure. Bevacizumab is given intravenously (IV) every 3 weeks with chemotherapy.

Radiation therapy

Radiation therapy uses high-energy rays (such as x-rays) to kill or shrink cancer cells. The radiation may be given from outside the body (external radiation) or from radioactive materials placed directly in the tumor (internal or implant radiation, also called brachytherapy). External radiation is the type most often used to treat lung cancer.

Combination therapy

Lung cancer is often initially treated with a combination of different therapies; that is, the combination of surgery with chemotherapy, or radiation therapy, or both, given either before or after the surgery. Chemotherapy and radiation therapy can be combined in several different ways. This is called chemoradiation. For example, the chemotherapy can be given at the same time as the radiation therapy. And sometimes more chemotherapy will be given after the combined therapy. In other situations, the chemotherapy and radiation therapy are given in sequence. Typically chemotherapy is given before radiation therapy, but sometimes the radiation therapy may come first. The T and N status of the tumor (see the staging section on page 11) are used to determine whether chemoradiation therapy is needed.

Palliative and supportive care

Most of these guidelines identify ways to cure some people with lung cancer or to help others live longer by removing or destroying lung cancer cells. But it is also important to realize that controlling symptoms and helping you continue to do the things you want and need to do is another key goal. Don't hesitate to discuss your symptoms or how you are feeling with your cancer care team. There are effective and safe ways to treat pain, most other symptoms of lung cancer, and most of the side effects caused by lung cancer treatments. Treatment to help relieve symptoms is sometimes called palliative care, or supportive care.

Pain is a significant concern for patients with lung cancer. If the cancer grows around certain nerves it may cause severe pain. It is important that patients tell their doctors right away if they have pain. For most patients, treatment with morphine or other opioids will reduce the pain considerably. Opioids are prescription medicines and the strongest pain relievers available. For more information on managing cancer pain, look at the ACS Web site, www.cancer.org, or call 1-800-ACS-2345 and request a copy of the *NCCN Cancer Pain Treatment Guidelines for Patients*.

In addition to the general supportive care measures for any type of advanced cancer, you may also benefit from specific ways to relieve some symptoms of lung cancer that are relatively rare with other cancers. For example, some small cell lung cancers may secrete a hormone (called antidiuretic hormone). The pituitary gland normally makes small amounts of this hormone, but large amounts produced by a cancer may cause fluid to collect in the body. Limiting how

much fluid you take in may help. Drug therapy with demeclocycline also helps. Other hormone-like substances produced by lung cancer cells can cause high levels of the hormones produced by the adrenal glands. These hormones cause a condition known as Cushing's syndrome. Patients with this problem may notice weight gain (especially around the chest and abdomen), fat deposits behind the neck and shoulders, fatigue, easy bruising, depression and/or moodiness, and weakened bones. This condition may be treated with a drug called ketoconazole. Other hormone-like substances that may be produced by NSCLC can affect blood calcium levels, leading to muscle weakness and other nervous system problems. Intravenous fluids and medicines can help relieve some of these symptoms.

Sometimes patients may be given cancer treatment that is intended to reduce or prevent symptoms but is not expected to cure the cancer. This palliative care may include radiation or chemotherapy treatments that relieve symptoms by shrinking the tumor. Some other palliative treatments for lung cancer include laser surgery and photodynamic therapy.

Laser surgery can vaporize the part of a tumor that is blocking an airway and interfering with breathing. But it does not destroy all of the cancer.

Photodynamic therapy uses a drug which is only attracted to cancer cells. The drug is injected into a vein in an inactive form. It is then activated by shining a certain color light on it. Beams of laser light can be aimed through a bronchoscope and activate the drug there to help destroy the part of a tumor that is blocking an air passage. Patients must

avoid sunlight for a time to avoid side effects to the skin.

Complementary and alternative medicines

Complementary and alternative medicines are different kinds of health care practices and products that are not part of your usual medical treatment. They may include herbs, special supplements, acupuncture, massage, and a host of other types of treatment. You may hear about different treatments from your family and friends. People may offer all sorts of suggestions, such as vitamins, herbs, stress reduction, and more, as a treatment for your cancer or to help you feel better.

The American Cancer Society defines complementary medicine or methods as those that are used along with your regular medical care. If these treatments are carefully managed, they may add to your comfort and well-being. Some of these methods have been tested, while others have not. Some have shown possible benefit, while others have not proven helpful. Some of these treatments have harmful effects too.

Alternative medicines are defined as those that are used instead of regular medical care. Some of them have been proven harmful, but are still promoted as "cures." If you choose these alternatives, it is important to know that even the methods that do not cause harm may reduce your chance of fighting your cancer by delaying or replacing regular cancer treatment.

There is a great deal of interest today in complementary and alternative treatments

for cancer. Many are being studied to find out if they are helpful to people with cancer.

Before changing your treatment or adding any of these methods, it is best to discuss this openly with your doctor or nurse. Some methods can be safely used along with standard medical treatment. Others, however, can interfere with standard treatment or cause serious side effects. That is why it's important to talk with your doctor. More information about complementary and alternative methods of cancer treatment is available through the American Cancer Society's toll-free number at 1-800-ACS-2345 or on our Web site at www.cancer.org.

About clinical trials

All drugs used to treat cancer or other diseases must undergo clinical trials in order to determine their safety and effectiveness before the Food and Drug Administration (FDA) can approve them for use. Treatments used in clinical trials are often found to have real benefits. Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment helpful?
- How does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Do the benefits outweigh the risks, including side effects?
- Which patients will the treatment most likely help?

During cancer treatment, the doctor may suggest taking part in a clinical trial. Scientists conduct clinical trials only when they believe that the treatment being studied may be better than other treatments.

All patients in a clinical trial are closely watched by a team of experts to monitor their progress very carefully. The study is done to find out if the new treatment will work better than the standard treatment and if the side effects are worse or less. The new treatment may have some side effects, which the doctor will discuss with you before the clinical trial is started.

Deciding to enter a clinical trial

Taking part in any clinical trial is completely voluntary. Doctors and nurses explain the study in detail and provide a consent form to read and sign. This form states that the patient understands the risks and wants to participate. Even after signing the form and the trial begins, the patient may leave the study at any time, for any reason.

Taking part in the study will not keep anyone from getting other medical care they may need. You should always check with your health insurance company to find out whether it will cover the costs of taking part in a clinical trial.

Participating in a clinical trial evaluating new, improved methods for treating cancer may help the patient directly, and it may help other people with cancer in the future. For these reasons, members of the National Comprehensive Cancer Network and the American Cancer Society encourage participation in clinical trials.

How can I find out more about clinical trials that might be right for me?

The American Cancer Society offers a clinical trials matching service that will help you find a clinical trials that is right for you. You can reach this service at 1-800-303-5691 or through the Web site http://clinicaltrials.cancer.org. Based on the information you give about your cancer type, stage, and previous treatments, this service compiles a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinical_trials/.

More information about clinical trials is available through the American Cancer Society's toll-free number at 1-800-ACS-2345 or on our Web site at www.cancer.org.

Other things to consider during and after treatment

During and after treatment for your lung cancer, you may be able to speed up your recovery and improve your quality of life by taking an active role. Learn about the benefits and disadvantages of each of your treatment options and ask questions if there is anything you do not understand. Learn about and look out for side effects of treatment and report

these promptly to your cancer care team so that they can take steps to reduce them.

Remember that your body is as unique as your personality and your fingerprints. Although understanding your cancer's stage and learning about your treatment options can help predict the health problems you may face, no one can say precisely how you will respond to cancer or its treatment.

You may have special strengths such as a history of excellent nutrition and physical activity, a strong family support system, or a deep faith, and these strengths may make a difference in how you respond to cancer treatment. There are also experienced professionals in mental health services, social work services, and pastoral services who may assist you and your family in coping with your illness.

You can also help in your own recovery from cancer by making healthy lifestyle choices. If you use tobacco, stop now. Quitting will improve your overall health, and the full return of your sense of smell may help you enjoy a healthy diet during recovery. If you use alcohol, limit how much you drink. Have no more than 1 or 2 drinks per day.

Good nutrition can help you get better after treatment. Eat a nutritious and balanced diet, with plenty of fruits, vegetables, and whole grain foods. If you are having nutrition problems, ask your cancer care team if you may benefit from talking with a dietician.

If you are being treated for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy add to the fatigue caused by the disease itself. To help you with the fatigue, plan your daily activities around when you feel your best. Get plenty of sleep at night. Don't be afraid to ask others for help. And ask your cancer care team about a daily exercise program to help you feel better.

A cancer diagnosis and its treatment is a major life challenge that has an impact on you and everyone who cares for you. Before you get to the point where you feel overwhelmed, consider attending a meeting of a local support group. If you need assistance in other ways, contact your hospital's social service department or the American Cancer Society.

NOTES

Work-up (evaluation) and treatment guidelines

Decision trees

The Decision Trees (or flow charts) on the following pages represent different stages of lung cancer. Each one shows you step-by-step how you and your doctor can arrive at the choices you need to make about your treatment.

Keep in mind, this information is not meant to be used without the expertise of your own doctor who is familiar with your situation, medical history, and personal preferences. You may want to review this booklet together with your doctor, who can show you which of the Decision Trees apply to you. We've left some blank spaces in the Decision Tree section for you or your doctor to add notes about the treatments. You might also use this space to write down some questions to ask your doctors about the treatments.

Participating in a clinical trial is an option for patients at any stage of lung cancer. Taking part in a study does not prevent you from getting other medical care you may need.

The NCCN guidelines are updated as new significant data become available. To ensure you have the most recent version, consult the Web sites of the ACS (www.cancer.org) or NCCN (www.nccn.org). You may also call the NCCN at 1-888-909-NCCN or the ACS at 1-800-ACS-2345 for the most recent information on these guidelines. If you have questions about your cancer or cancer treatment, please call the ACS any day at any time at 1-800-ACS-2345.

Treatment Guidelines for Patients

Diagnosis

Initial work-up (evaluation)

Patient has non-small cell lung cancer based on test results (biopsy or cytology of main lung tumor or of a metastatic site)

- Medical history and physical exam to assess general health and cancer symptoms
- Pathology review
- CT scan of chest, upper abdomen, and adrenal glands
- Blood cell counts
- Blood chemistry tests
- Counseling on smoking cessation

Non-small cell lung cancer: Initial work-up and staging

This Decision Tree begins when you have just been diagnosed with non-small cell lung cancer. This diagnosis is based on the results of a biopsy (a small piece of tissue that has been removed from the tumor) or cytology (examination of cell samples, such as cells in sputum, cells in the fluid that has collected around the lungs, or cells that have been scraped from the lining of the airways).

The next step after diagnosis is a series of examinations and tests that doctors call the initial work-up. The medical history and physical exam focus on symptoms that may suggest spread outside the lung. Your doctor also reviews your overall health and discusses

the results of your biopsy. Your biopsy tissue may also be sent for another pathologist to review so that you can be sure of the diagnosis. You then have a group of tests that are used to find the extent of the cancer. For example, a chest CT scan can show the tumor's size and location and also allows the doctor to look at the lymph nodes in the chest. If these lymph nodes are enlarged, they may contain cancer cells that have spread from the lung tumor. The CT scan also includes views of your liver and adrenal glands, because lung cancers may spread to these areas. A variety of blood tests are done to see how well your liver and kidneys are working and to make sure your blood cell counts are not too low. Low blood cell counts or problems with internal

Non-small cell lung cancer: Initial work-up and staging

Clinical stage Additional work-up and treatment Determine clinical stage Depends on clinical stage

©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

organs could mean that you are especially at risk for problems and side effects of certain lung cancer treatments, so these tests must be done before your treatment begins. Other blood test results can suggest a cancer has spread outside the lung. Depending on your medical history, symptoms, and physical exam results, extra testing of your heart, lungs, kidneys, or other organs may be needed to see if you are likely to have serious problems from certain lung cancer treatments. If you smoke tobacco, your doctor will ask that you quit and will talk with you about ways to do this.

based on initial work-up

The results of your initial evaluation are used to determine the clinical stage (T, N, and

M status) of your cancer. These results determine which of the Decision Trees are most relevant to your treatment. If you have any questions about your clinical stage after checking the information on pages 11–14 ask your doctor.

Based on your clinical stage, the guidelines recommend that you have other tests to learn more about whether your cancer has spread. These tests may include other imaging studies (MRI scans, bone scans) or procedures to get tissue samples from your lungs, lymph nodes, or other organs. Your stage may change after biopsies and surgery.



Treatment Guidelines for Patients

Clinical stage and tumor location

Work-up and results

Stage I (T1–T2, N0) Located in the outer part of the lungs OR

Located in the center of the lungs near large airways

OR

Stage II (T1–T2, N1)

- Pulmonary function tests if not previously done
- Bronchoscopy to look for additional tumors
- Mediastinoscopy to look for spread of cancer to lymph nodes in the chest
- PFT scan
- Brain MRI (only if stage II nonsquamous cell cancer)

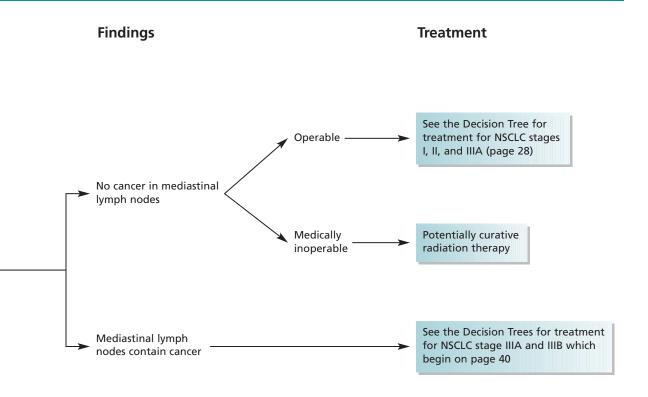
Non-small cell lung cancer: Evaluation of stages I and II

Stage I and some stage II cancers are generally small tumors and may have spread to lymph nodes within the lung. For more detailed information on staging, see pages 11–14.

If your initial clinical stage is T1 or T2, and N0 or N1, the guidelines recommend some tests and scans to see if surgery is a good treatment option. Pulmonary function tests

measure how well the lungs take in and exhale air and how efficiently they transfer oxygen into the blood. Bronchoscopy looks for cancer in other parts of the lungs or to get tissue for biopsy and diagnosis. Mediastinoscopy checks whether cancer has spread to mediastinal lymph nodes. The PET scan also shows spread to mediastinal lymph nodes, as well as spread anywhere else in the body. MRI of the brain is needed if stage II nonsquamous cell cancer is present because

Non-small cell lung cancer: Evaluation of stages I and II



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

this type of cancer more frequently spreads to the brain.

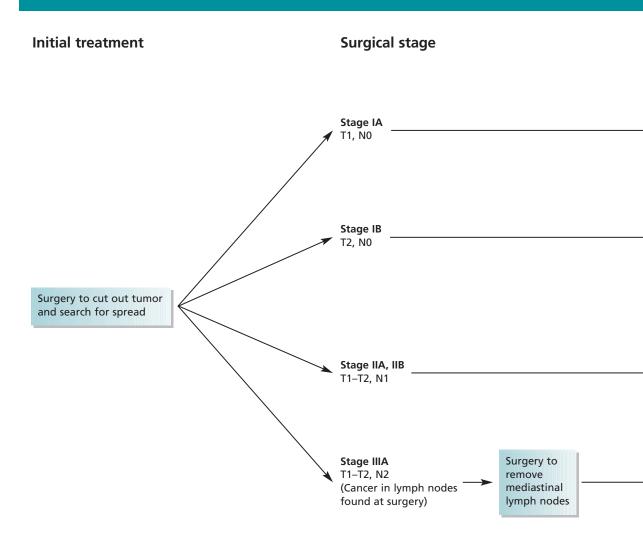
If there is no cancer in the mediastinal nodes and the cancer can be removed with surgery, treatment is discussed on the Decision Tree on page 28.

If there is no cancer in the mediastinal nodes or no distant spread but surgery can't be done because of other medical conditions, radiation therapy is an option that may cure the cancer.

If cancer is found in the mediastinal nodes, the cancer is stage III, and surgery may or may not be a good option. See the Decision Trees beginning on page 40 that fit your T and N categories.



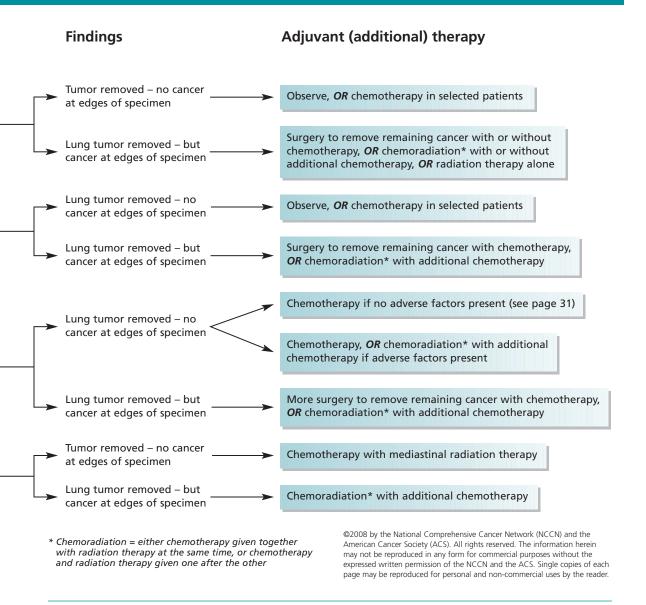
Treatment Guidelines for Patients



Non-small cell lung cancer: Treatment of stages I, II, and IIIA

If the initial test results show the cancer has not spread, exploratory surgery is recommended to remove the cancer and look at the area around the tumor. The surgeon tries to completely remove the cancer whenever possible, since this offers the best chance for a cure. The surgical margin (the edge of the tissue removed by the surgeon) is checked under the microscope for cancer cells. If cancer cells are present at the edge (positive surgical margin), it is likely that some cancer cells may have been left behind. This can happen even when

Non-small cell lung cancer: Treatment of stages I, II, and IIIA



the surgeon removes all cancer that was visible during surgery. In this case, your doctor will recommend more treatment. A negative surgical margin is usually a sign that no cancer was left behind in the area the tumor was removed from. A negative surgical margin does not mean a cure is a sure thing, because cancer cells may have spread to other areas of the body before surgery.

Treatment Guidelines for Patients

After surgery has completely removed the tumors, if no cancer was found at the edges of the specimens, patients with T1, N0 and many patients with T2, N0 tumors will be watched carefully.

Patients with tumor cells that look very different from normal cells, or patients with tumors that have grown into nearby blood vessels, or have very narrow surgical margins are considered to be high risk and should consider chemotherapy.

Chemotherapy is a systemic therapy that can kill cancer cells that have spread beyond the lung. Chemotherapy is strongly recommended for larger tumors. This is because larger tumor size is associated with a greater risk of spread beyond the lung. For example, there is disagreement about the use of chemotherapy for T2, N0 tumors, but it is recommended for T1/T2, N1/N2 tumors.

Radiation therapy and surgery are known as "local" therapies, because they do not attempt to treat cancer that has spread outside the lung. Additional local therapy is needed following surgery whenever the margins or edges of the removed tissue are found to contain cancer.

The radiation may also be combined with chemotherapy in different ways. This is called chemoradiation. For example, chemotherapy can be given at the same time as the radiation therapy, or chemotherapy and radiation therapy can be given one after the other. Sometimes additional chemotherapy

NOTES

Non-small cell lung cancer: Treatment of stages I, II, and IIIA (continued)

is added after the chemoradiation therapy, and this is referred to as chemoradiation with additional chemotherapy,

In one instance, radiation therapy is an option even when the tumor margins are negative. If the tumor has spread to lymph nodes near the lung, the treatment depends on whether certain adverse factors are present or not. Adverse factors are:

- the lymph nodes in the mediastinum cannot be evaluated as needed
- the cancer has grown outside the lymph nodes
- there are many lymph nodes involved with cancer
- the margins may be very close to the edge of the cancer

If no adverse factors are present and the surgical margins are not involved with cancer, then only chemotherapy is recommended. If there are adverse factors, there is a higher risk that the surgery did not remove all of the tumor. In this case chemotherapy alone, or chemoradiation followed by additional chemotherapy may be advised.

If cancer is found in the lymph nodes during surgery (T1,T2, N2) the cancerous nodes should be removed along with the tumor. If there is no cancer at the edge of the tumor specimen, chemotherapy with radiation to the mediastinum is recommended. If cancer is found at the specimen edge, chemoradiation followed by additional chemotherapy may be suggested.

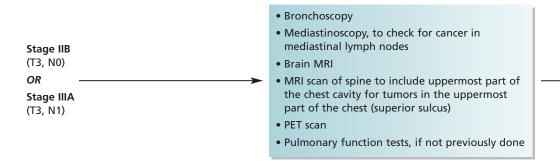
NOTES



Treatment Guidelines for Patients

Clinical stage

Additional work-up (evaluation)



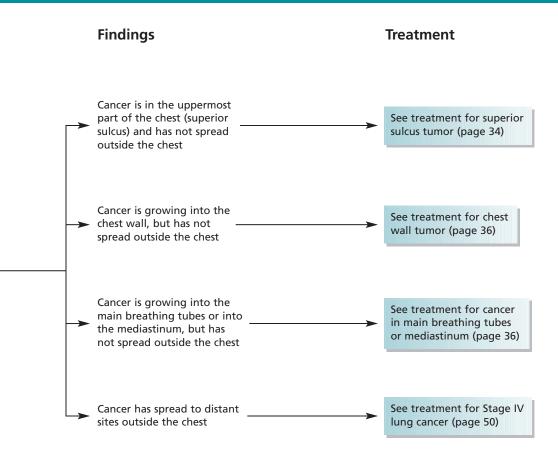
Non-small cell lung cancer: Evaluation of stages IIB and IIIA

This Decision Tree is for patients with tumors that invade the chest wall, either in the superior sulcus (upper part of the lung) or elsewhere; or tumors invading the main bronchus near the trachea. Lymph nodes near the tumor may or may not have cancer cells (N0 or N1). These cancers are larger than those in the previous Decision Tree. This means your doctor will

need to make an extensive evaluation before treatment can be started to make sure the cancer hasn't spread to mediastinal lymph nodes or distant sites in the body.

Bronchoscopy is done to check for more tumors in other areas of the lungs. Mediastinoscopy is recommended to find out if cancer has spread to the mediastinal lymph nodes. MRI of the brain and, for superior sulcus tumors, the spine, is done to look for

Non-small cell lung cancer: Evaluation of stages IIB and IIIA



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

spread to these tissues. A PET scan is also done to look for spread. Finally, if not already done, pulmonary function tests are recommended to measure how well the lungs take in and exhale air and how efficiently they transfer oxygen into the blood.

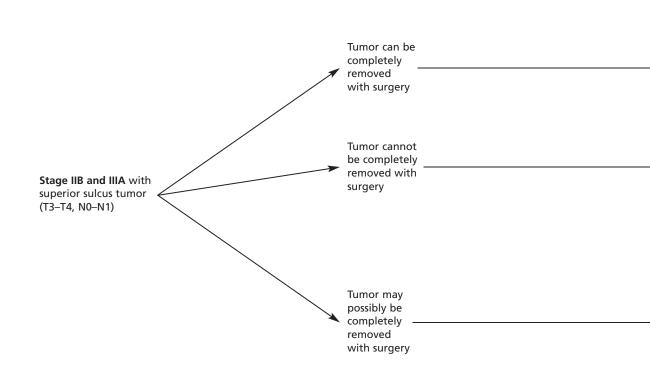
This Decision Tree refers you to others with more specific details depending on the findings the additional tests. If it is found that the cancer has spread to distant areas, the cancer is reclassified as M1, and you should see the Decision Tree on page 50.



Treatment Guidelines for Patients



Clinical assessment

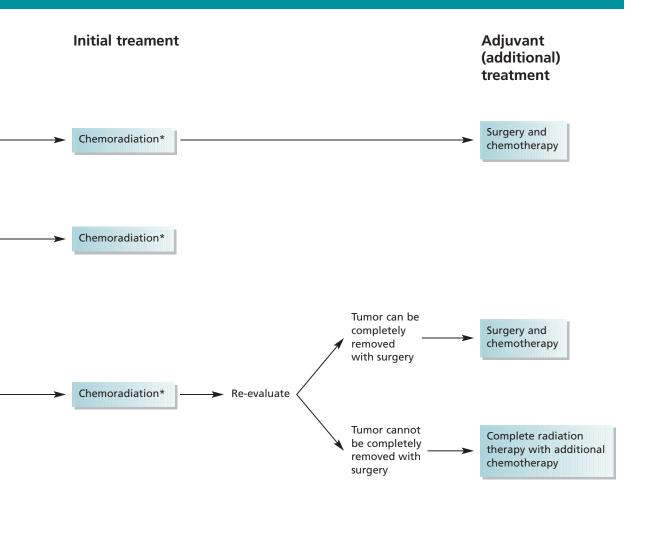


Non-small cell lung cancer: Treatment of stages IIB and IIIA

Tumors in the very top part of the lung, called superior sulcus tumors, often grow into nerves and other tissues in that area. This makes it difficult to remove them completely with surgery. If the surgeon thinks the tumor can be completely removed (it is resectable), the recommendation is first to give chemotherapy with radiation to shrink the tumor, followed by surgery and more chemotherapy.

If the tumor cannot be removed with surgery (it is unresectable), then chemotherapy with a full dose of radiation therapy is recommended.

Non-small cell lung cancer: Treatment of stages IIB and IIIA



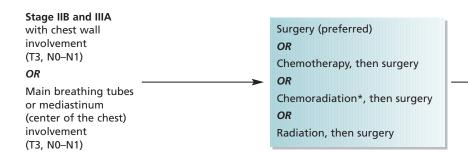
* Chemoradiation = either chemotherapy given together with radiation therapy at the same time, or chemotherapy and radiation therapy given one after the other ©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

Sometimes in cases where the chance of removal is uncertain, chemotherapy is given with radiation therapy, followed by surgery and then more chemotherapy if the tumor becomes resectable. If the tumor still cannot be removed, then radiation therapy is recommended as the primary therapy followed by chemotherapy.



Stage and site of tumor

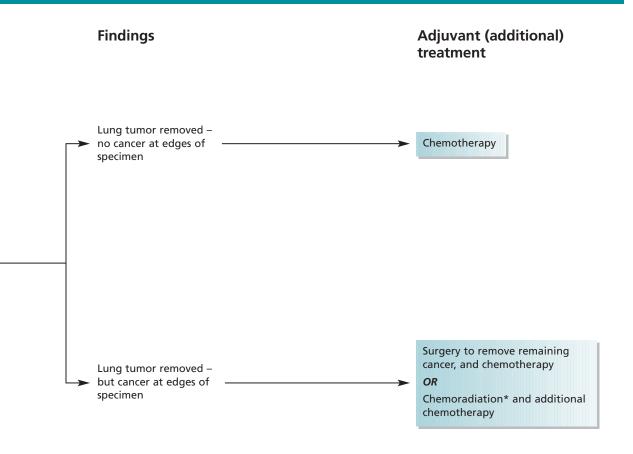
Initial treament



Non-small cell lung cancer: Treatment of stages IIB and IIIA (continued)

Tumors growing into the chest wall, into main breathing tubes near the trachea, or into the mediastinum may be treated with surgery first (which is preferred). Other options include chemotherapy alone, chemotherapy together with radiation therapy, or radiation therapy alone; all of these options are followed by surgery.

Non-small cell lung cancer: Treatment of stages IIB and IIIA (continued)

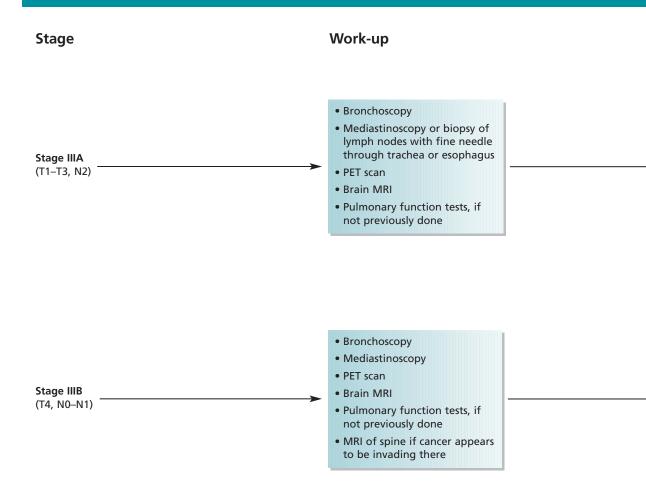


©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

If, after surgery, the specimen margins (edges) are free of cancer, more chemotherapy is recommended. If the edges of the specimen contain cancer, then either further surgery and chemotherapy or chemoradiation followed

by more chemotherapy is recommended. If a large amount of tumor remains after surgery, the radiation therapy is typically given before the chemotherapy.

^{*} Chemoradiation = either chemotherapy given together with radiation therapy at the same time, or chemotherapy and radiation therapy given one after the other



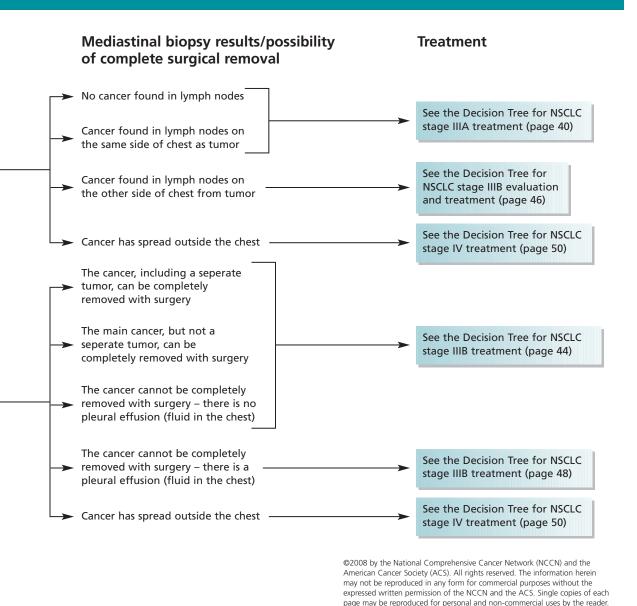
Non-small cell lung cancer: Evaluation of stages IIIA and IIIB

This Decision Tree is for evaluating patients with stage IIIA cancers that appear to have spread to mediastinal lymph nodes (N2), as well as those with stage IIIB cancers with a large tumor (T4), but minimal lymph node spread (N0–N1). The stage IIIA patients should have bronchoscopy and biopsy of mediastinal

lymph nodes, either by mediastinoscopy or fine needle aspiration. PET scan and MRI of the brain are done to look for spread to distant areas. If not previously done, pulmonary function tests are recommended to measure how well the lungs take in and exhale air and how efficiently they transfer oxygen into the blood.

The patient with a stage IIIB tumor should also have bronchoscopy, mediastinoscopy,

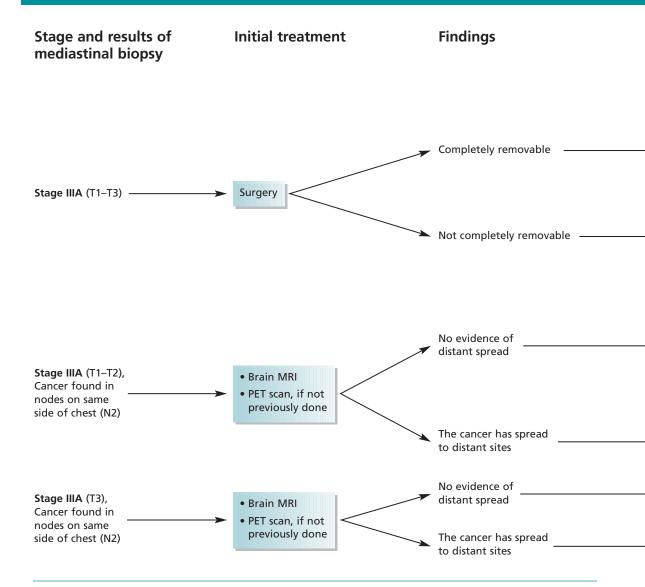
Non-small cell lung cancer: Evaluation of stages IIIA and IIIB



PET scan, MRI of the brain, and pulmonary function tests, if not already done. Because a large T4 tumor can invade the spine, an MRI of the spine may be recommended.

Further treatment, as outlined on the Decision Tree, depends on the findings of these tests.





Non-small cell lung cancer: Treatment of stage IIIA

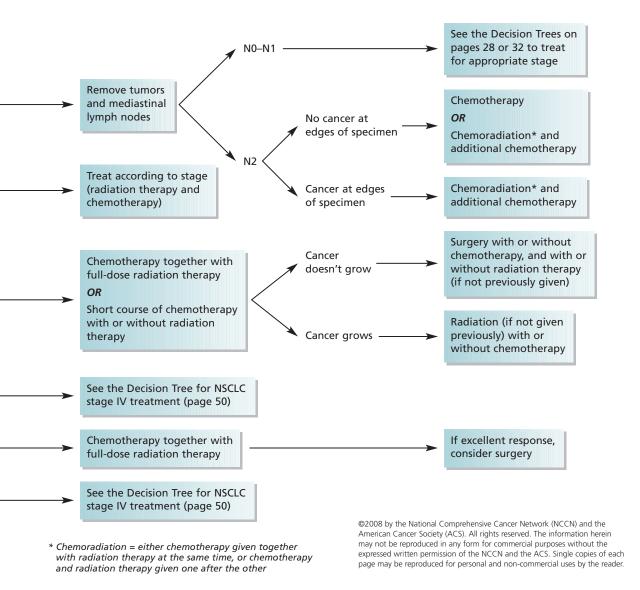
Three different stages are described here. The first one is T1–T3 with no cancer cells found in the biopsy of the mediastinal lymph nodes

(N0). Surgery with removal of the mediastinal nodes is recommended.

• If the tumor is completely removable and the mediastinal lymph nodes do not contain cancer, then further treatment is as described on page 28.

Non-small cell lung cancer: Treatment of stage IIIA

Adjuvant (additional) treatment



 If cancer is found in mediastinal lymph nodes (N2) and the surgical margins do not contain cancer, chemotherapy alone or chemoradiation with additional chemotherapy can be given.



- If the margins do contain cancer cells chemoradiation with additional chemotherapy is recommended.
- If the original tumor couldn't be removed, the tumor should be treated according to the stage as described in earlier Decision Trees.

The next group is those patients with T1 and T2 tumors with cancer found in the mediastinal lymph nodes on the same side as the tumor (N2). If the brain MRI and PET scan show that the cancer has not spread, there are 2 options: chemotherapy with a full dose of radiation therapy, or a short course of chemotherapy with (or without) radiation

NOTES

Non-small cell lung cancer: Treatment of stage IIIA (continued)

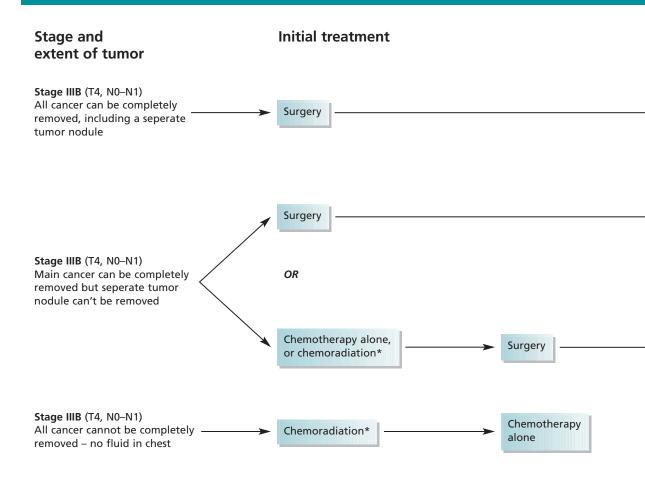
can be given to determine if surgery is possible. If the disease has not progressed during this treatment, surgery with or without chemotherapy and with or without radiation (if not given before) is an option

The final patient group is those with T3 tumors with cancer cells found in the medi-

astinal lymph nodes on the same side as the tumor (N2). If the scans show no evidence of spread to distant areas or organs, patients can be initially treated with chemotherapy with a full course of radiation therapy. If there is an excellent response, surgery can be considered in rare cases.

NOTES





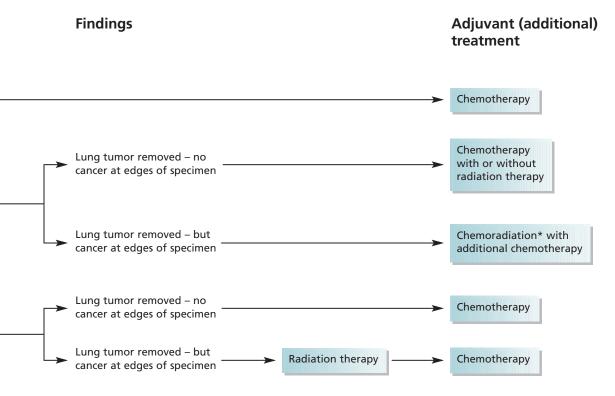
Non-small cell lung cancer: Treatment of stage IIIB

This Decision Tree describes the treatment for patients with separate tumor nodules or very large tumors (T4) that have spread into structures within the chest, but have little spread to lymph nodes (N0, N1). While not having the cancer spread to mediastinal lymph nodes is good news, the extent of tumor growth may still make it difficult or impossible for a surgeon to completely remove the tumor.

Whenever possible, the surgeon tries to remove the tumor and any satellite tumors (separate tumors spread within the same lobe of the lung). If this is successful, then chemotherapy is recommended after the surgery.

If the main tumor can be removed but the other tumor (or tumors) cannot be, options include initial surgery, or initial chemotherapy or chemoradiation and then surgery. If initial surgery is selected, further treatment depends on the status of the tumor margins. If the

Non-small cell lung cancer: Treatment of stage IIIB



* Chemoradiation = either chemotherapy given together with radiation therapy at the same time, or chemotherapy and radiation therapy given one after the other

©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

margins do not contain cancer cells, chemotherapy with optional radiation therapy is recommended. If the edges of the specimen do show cancer cells, then chemoradiation with additional chemotherapy is recommended.

For those not choosing to have surgery first, options include either initial chemotherapy or chemoradiation. Both of these options are then followed by surgery with additional treatment depending on whether the tumor margins are positive or negative. If there are

no cancer cells at the edge of the specimen, only chemotherapy is recommended. If there are cancer cells at the edges of the specimen, radiation therapy followed by chemotherapy is recommended.

If the surgeon concludes that it is not possible to completely remove the tumor and there is no fluid in the patient's chest, chemoradiation followed by chemotherapy is recommended.

Stage and extent of tumor

Additional tests and results



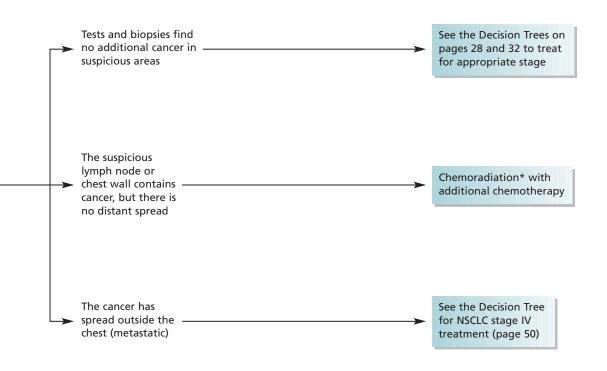
- Biopsy of any suspicious lymph node to check for cancer in mediastinum (mediastinoscopy), or other side of chest, or supraclavicular (above the collarbone), or in the neck, or elsewhere
- Thoracoscopy, if suspected spread of cancer in the lining of the chest cavity
- PET scan
- Brain MRI
- Pulmonary function tests (if not previously done)

Non-small cell lung cancer: Evaluation and treatment of stage IIIB

This Decision Tree describes work-up and treatment for patients who appear to have cancer that has spread to lymph nodes on the opposite side of the mediastinum or above the collar bone (N3). N3 disease must be confirmed through biopsy of any suspicious lymph nodes. A thoracoscopy is done to look for cancer cells in the space between the lungs and the chest wall. A PET scan, brain MRI, and pulmonary function tests may also be done. If all these test results are normal,

Non-small cell lung cancer: Evaluation and treatment of stage IIIB

Initial treatment



* Chemoradiation = either chemotherapy given together with radiation therapy at the same time, or chemotherapy and radiation therapy given one after the other

©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

meaning the enlarged lymph nodes did not contain cancer and the cancer has not spread to distant areas or organs, then the cancer is treatable with surgery. Refer to the decision trees on pages 28 and 32. If the biopsies do show cancer cells but there is no distant

metastasis, then chemoradiation followed by more chemotherapy, is recommended. If the tests show the cancer has spread to distant areas, then treatment for widespread disease should be considered, as outlined on page 50.

Stage and extent of tumor

Additional tests and results



- Biopsy of any suspicious lymph node to check for cancer in mediastinum (mediastinoscopy), or other side of chest, or supraclavicular (above the collarbone), or in the neck, or elsewhere
- Thoracoscopy, if suspected spread of cancer in the lining of the chest cavity
- Brain MRI
- PET scan

Remove chest fluid and possibly remove fluid around heart

Thoracoscopy may be needed to check for spread of cancer in the lining of the chest cavity

Non-small cell lung cancer: Treatment of stage IIIB

Two different types of T4 tumors are discussed here. T4 means the tumor has spread to other structures in the chest or it is producing fluid that surrounds the lung (pleural effusion) or heart (pericardial effusion), and surgery is generally not an option.

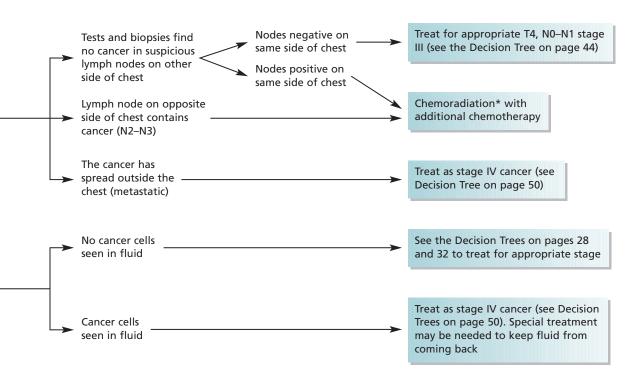
If your doctor suspects you have a T4 tumor that has spread widely to lymph nodes (N2 or N3), then these nodes should be biopsied by mediastinoscopy, or with needle aspiration, or biopsy guided by ultrasound, or perhaps by removing a node above the collarbone. Looking in the chest cavity with a lighted tube,

called thoracoscopy, tells how far the cancer has grown. Tests should also be done to look for spread outside the chest (brain MRI and PET scan).

If the lymph nodes do not contain cancer cells, the cancer is classified as T4, N0, N1 and may be treated with surgery or as recommended on page 44. If the lymph nodes on the same or opposite side of the chest do contain cancer (N2 or N3), then treatment with chemoradiation, followed by additional chemotherapy is recommended. Finally, if the tests show the cancer has spread outside the chest to distant sites, then treatment should be as discussed for stage IV on page 50.

Non-small cell lung cancer: Treatment of stage IIIB

Initial treatment



^{*} Chemoradiation = either chemotherapy given together with radiation therapy at the same time, or chemotherapy and radiation therapy given one after the other

©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

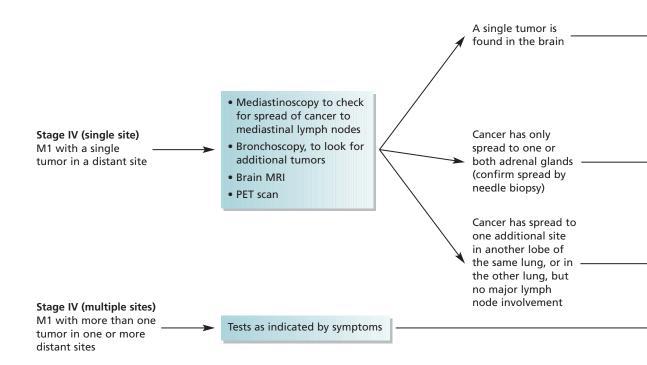
If there is fluid around the lungs or the heart, a sample of the fluid can be removed and examined for cancer cells. If cancer can't be diagnosed from cells in the fluid, it may be necessary to perform a thoracoscopy to make sure that the fluid is not related to cancer that has spread to the lining of the chest. If there are no cancer cells in the fluid, then the cancer should be treated according to its T

and N stage as discussed on pages 28 and 32. If there are cancer cells in the fluid, surgery is not a treatment option. The fluid should be drained with a catheter (a tube used to withdraw fluids). Sometimes a small piece of the sac around the heart needs to be removed so that the fluid pressure doesn't build up. Then treatment should be given as for stage IV disease (page 50).



Stage and extent of tumor

Additional tests and results

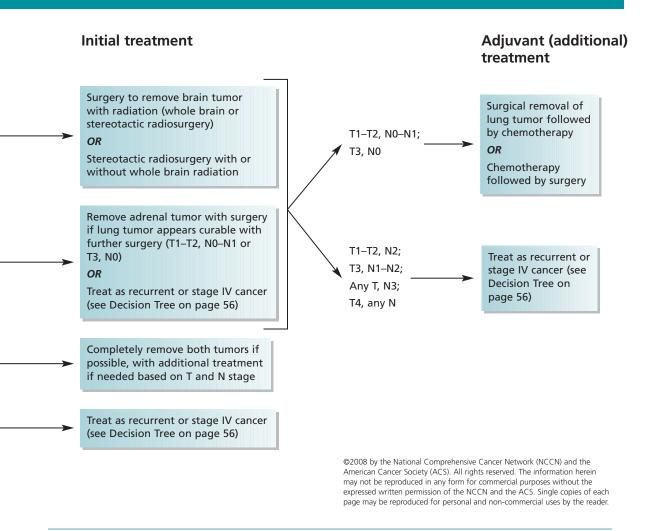


Non-small cell lung cancer: Treatment of stage IV

Sometimes there is only 1 tumor nodule in one site of distant spread. This can only be determined after a complete evaluation with mediastinoscopy, bronchoscopy, brain MRI, and PET scan. Treatment options depend on where the cancer has spread.

If the cancer has spread only to the brain and there is only 1 tumor, one option is surgery followed by radiation therapy. Two different types of radiation therapy may be recommended, either radiation therapy to the entire brain, or radiation therapy focused specifically at the site where the metastasis was removed. This second type of radiation therapy is called stereotactic radiosurgery. As another option, stereotactic radiosurgery can be the first treatment, followed by radiation to the entire brain. After treatment of the brain metastases, surgical removal of the lung tumor depends on its stage, as noted in the Decision Tree.

Non-small cell lung cancer: Treatment of stage IV



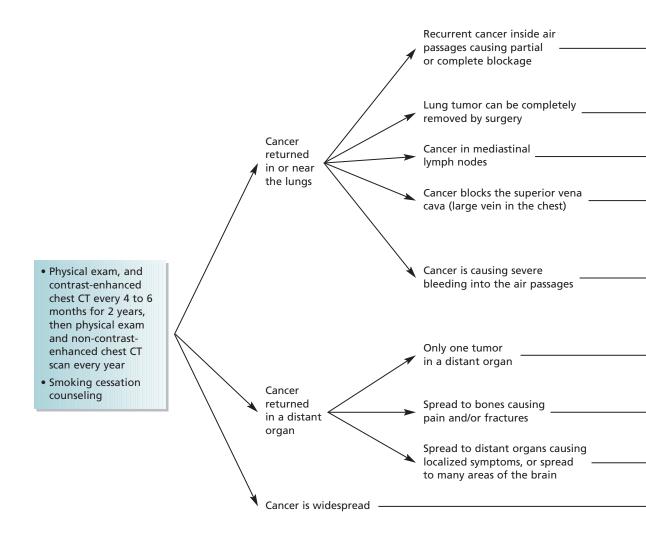
If the cancer has only spread to the adrenal glands, which is confirmed by a biopsy, and the cancer in the lung is T1, T2; N0, N1; or T3, N0 (which means it can be completely removed by surgery), then both the adrenal gland tumors and the lung cancer can be removed or treatment for stage IV cancer (see page 56) can be given. Additional treatment then depends on the stage of the disease.

Sometimes there is a separate cancer in another lobe of the lung or in the other lung. Both tumors should be removed if the cancer has not spread to the lymph nodes or to distant sites and then further treated according to their T and N stage.

If there are multiple sites of spread, then surgery is not recommended. For further treatment recommendations, see page 56.



Follow-up and findings after initial treatment



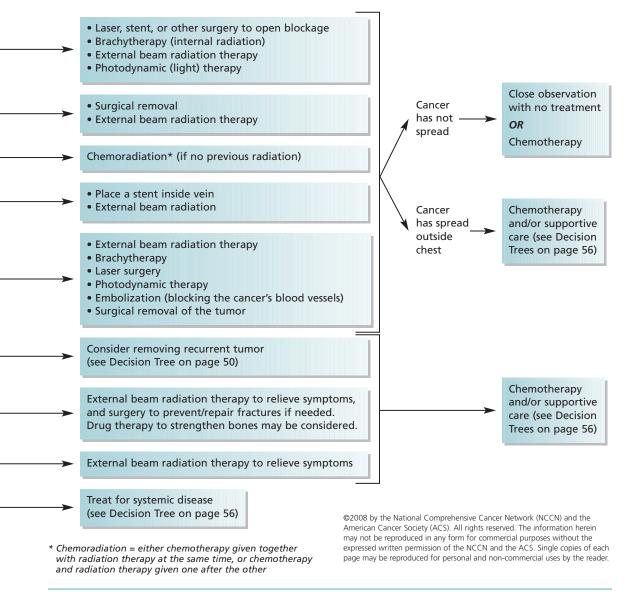
Non-small cell lung cancer: Followup and treatment of stage IV and recurrent cancer

After your initial treatment with surgery, chemotherapy, and/or radiation therapy, the

guidelines recommend that you have regular follow-up tests and exams (physical exam and chest CT scan) to check for recurrence (cancer coming back). Tumors may recur locally (in the lung), regionally (near the lungs), or distantly

Non-small cell lung cancer: Follow-up and treatment of stage IV and recurrent cancer

Treatment for recurrent cancer and metastasis



(in distant organs). It is very important that you to stop smoking and your doctor should talk to you about ways to do this.

If the tumor recurs in or near the lung, treatment depends on exactly where it is located and what symptoms it may be causing.

The tumor may recur in the airways and block breathing passages. Treatment options include vaporizing the tumor with a laser; having a stent (hollow tube) placed inside the airway to keep it open; radiation therapy, with either brachytherapy (placing a small radioactive pellet inside the airway) or external beam radiation; and photodynamic therapy (see description on page 18).

It may be possible to have surgery to remove the recurrence in some cases. Radiation therapy is another option. If the tumor is located in the mediastinum, chemotherapy together with radiation is recommended, but only if the patient has not had radiation therapy in the past.

If the cancer is pressing on the large vein leading to the heart (the superior vena cava), a stent (hollow tube) can be placed inside the vein to keep it from collapsing. Radiation therapy is another option for shrinking tumors pressing on this vein. When cancer presses on and collapses this vein, blood flow from the head and arms is reduced, and there may be severe swelling in both the face and arms, which is uncomfortable.

If the tumor is causing bleeding into the airways, treatment options are similar to when

NOTES

Non-small cell lung cancer: Follow-up and treatment of stage IV and recurrent cancer (continued)

the airway is blocked, but bleeding can also be controlled by blocking off the blood supply to the tumor (called tumor embolization).

If the lung cancer comes back at only 1 distant site, the treatment options depend on the number and location of the recurrent tumors. If only 1 tumor is found, surgery to remove it may be an option (see pages 50).

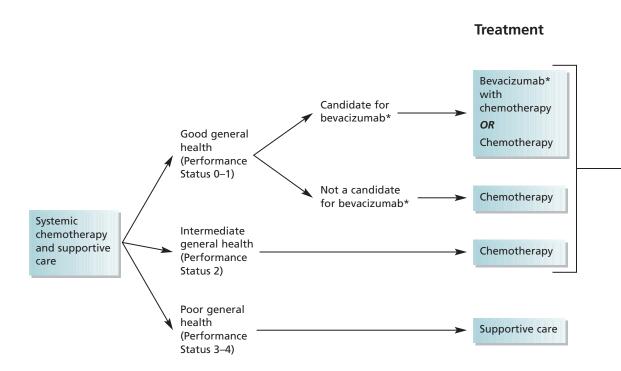
If cancer that has spread to the bones is causing pain, external beam radiation can help relieve the pain. If the cancer has weakened the bone enough that a fracture (broken bone) might occur, doctors may also recommend surgery to strengthen it. This can help relieve

pain and help the patient resume usual activities. Drug therapy may also be used to strengthen bones weakened by tumor. If the cancer has spread to distant organs or more than 1 brain metastasis, external beam radiation therapy is used to relieve symptoms.

Although these treatments are described in the section on follow-up and recurrence, they also apply to patients who have distant metastases when their lung cancer is first diagnosed. Doctors may also recommend systemic therapy – treatment, usually chemotherapy, that goes throughout the body to attack the cancer (see page 56).

NOTES





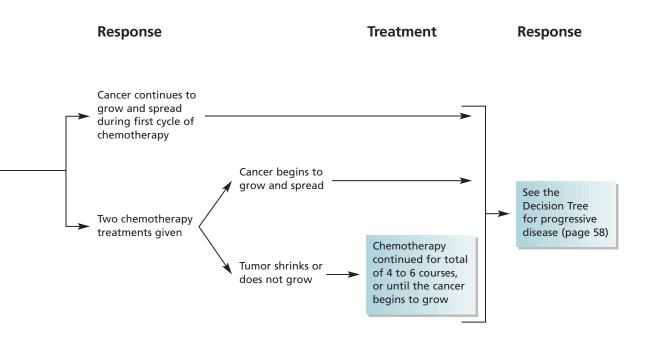
Non-small cell lung cancer: Treatment of stage IV and recurrent cancer

This Decision Tree focuses on the role of chemotherapy and how long the treatments should continue. Because chemotherapy can cause severe side effects, it is recommended only for people in relatively good health. Patients in very poor health may have serious, life-threatening complications of chemotherapy.

In deciding which patients should receive chemotherapy, NCCN doctors use precise definitions of good health or poor health based on the Eastern Cooperative Oncology Group (ECOG) Performance Scale. See page 8 for more information about the ECOG Performance Scale.

The NCCN recommends chemotherapy for patients with widespread disease who are in good health. The targeted therapy bevacizumab in addition to chemotherapy is an option for patients who are in good health and who have nonsquamous NSCLC (and do not have any history of coughing up blood or brain metastasis, and are not using any blood thinning drugs). Chemotherapy alone is given for patients with a good or intermediate performance status. Patients are then evaluated after completing the first round of chemotherapy. If the cancer grows after the first

Non-small cell lung cancer: Treatment of stage IV and recurrent cancer



^{*} Bevacizumab is used only for patients with nonsquamous NSCLC and no history of bleeding problems or brain metastasis and not on anticoagulation therapy (see page 17 of text)

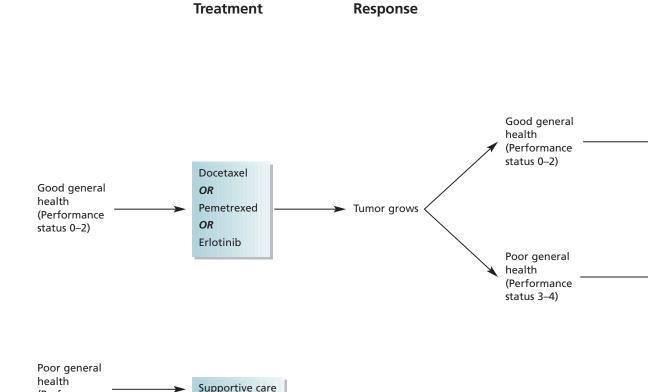
©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (AcS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

cycle, the patient should be treated according to the guidelines for progressive disease (see page 58). If the cancer shrinks or at least doesn't grow, another cycle of therapy is given. If there is no tumor growth after 2 treatments, chemotherapy should be continued for 4 to 6 total cycles or until the tumor begins to grow again. Further treatment after the cancer begins to grow is outlined on page 58.

For patients in poor health, the guidelines recommend supportive care. Supportive care is intended to relieve symptoms and to help keep patients as comfortable as possible, but it is not intended to directly attack the cancer.

Although participation in clinical trials is a good option for any patient with lung cancer, a study of a very new treatment in early stages of testing (called a phase I or phase II clinical trial) may be a good option for patients who get sicker while on chemotherapy. Deciding on the right time to discontinue chemotherapy and focus on supportive care is never easy. Good communication with doctors, nurses, family, and clergy, as well as discussions with hospice staff can help people facing this situation.





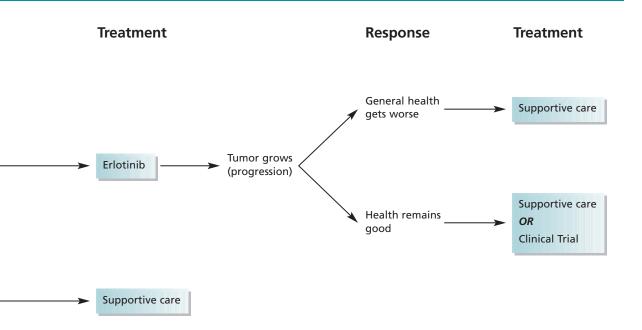
Non-small cell lung cancer: Treatment of stage IV with disease progression

(Performance status 3–4)

This Decision Tree describes treatment after the cancer has begun to grow again. A different type of chemotherapy may be given for those in good health. Docetaxol, pemetrexed, or the targeted therapy, erlotinib are treatment options at this point. If the tumor grows while on this therapy, erlotinib is an option for those who remain in good health (performance status 0 to 2), if the patient has not already received this drug. If the patient taking erlotinib has further tumor growth, supportive care is an option. If the patient remains in good health, then participation in a clinical trial is another option.

Supportive care is recommended for patients in poor health (performance status 3 to 4).

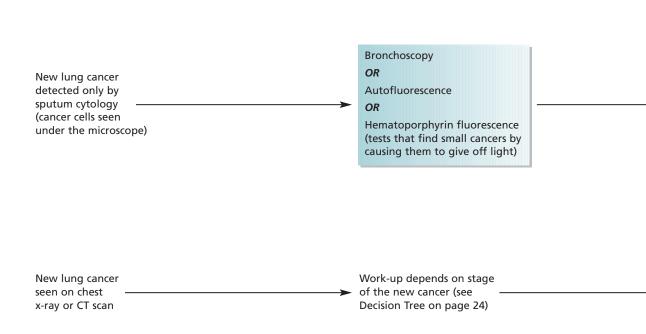
Non-small cell lung cancer: Treatment of stage IV with disease progression



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

NOTES	

Results of follow-up



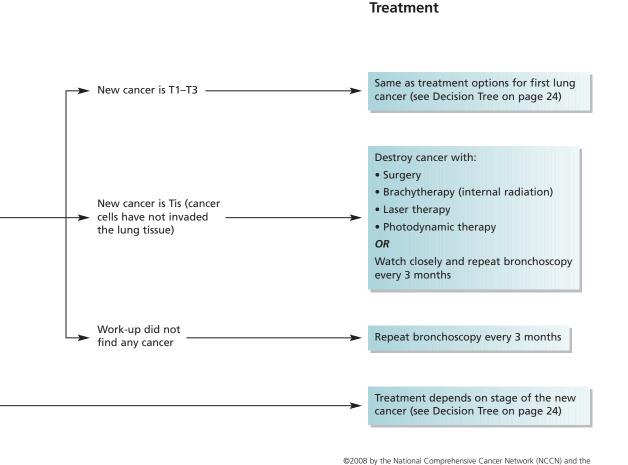
Non-small cell lung cancer: Treatment of second primary

Concern about the cancer coming back (this is called recurrence) is an important issue for people with lung cancer and their doctors. But, there is another follow-up issue that many patients don't think about: the risk of developing a second lung cancer. The risk factors that contributed to your lung cancer (such as smoking, in most cases) have already

changed many cells throughout your lungs. It is possible for people with 1 lung cancer to develop a second cancer. This is a possibility that your doctors are watching out for, so if a second cancer does develop they can find it at the earliest possible stage and start treatment when a cure is still possible.

Sputum cytology (using a microscope to look for cancer cells in the mucus you cough up) is one way of finding a second lung cancer.

Non-small cell lung cancer: Treatment of second primary



Sometimes sputum cytology finds new lung cancers so small that they can't be seen on a chest x-ray or a CT scan. In that case, bronchoscopy is used to thoroughly check the lining of your airways. Shining a special light through the bronchoscope may cause cancers to glow, so they can be more easily recognized.

This test is called an autofluorescence test. A similar test called hematoporphyrin fluorescence also uses a chemical that makes small cancers more likely to glow under a special light. This test is very similar to photodynamic therapy, which is mentioned as a treatment option (see page 18). Tissue samples (biopsies)

American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

are taken from any abnormal areas found by these tests.

If cancer cells are found and a tumor can also be seen (T1-T3), your work-up (starting on page 24) is the same as when your first cancer was diagnosed. Once the stage is determined, treatment is similar, but not identical. Because the treatments of your first lung cancer affected the health and amount of your remaining lung tissue, your options for treatment of a second cancer may be limited.

If these areas turn out to be small cancers that have not spread (Tis), doctors try to remove

NOTES

Non-small cell lung cancer: Treatment of second primary (continued)

or destroy them by local surgery, brachytherapy (placing small radioactive pellets inside the airway next to the cancer), laser surgery, or photodynamic therapy. As another option the areas with cancer can be closely watched by doing a bronchoscopy every 3 months.

If results of sputum cytology tests are positive, but no tumors are found, doctors will

be concerned that a cancer is present but is still too small to detect. They will repeat bronchoscopy every 3 months so that they can find the source of the cancer cells and destroy the tumor as soon as possible.

If a new cancer is seen on chest x-ray or CT scan, work-up and treatment depends on the stage of the new cancer.

NOTES

Diagnosis

Initial work-up (evaluation)

Patient has small cell lung cancer based on biopsy or cytology test results of main lung tumor or of a metastatic site

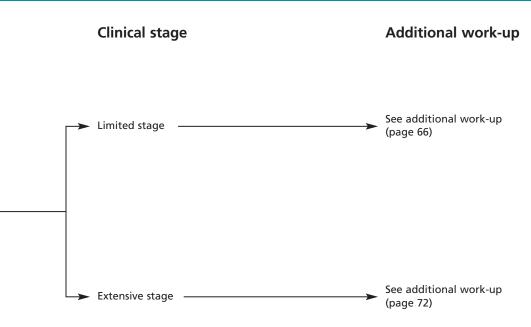
- Medical history and physical exam
- Pathology review
- CT scan of chest, liver, and adrenal glands
- MRI or CT scan of head (MRI is preferred)
- Bone scan (optional if PET scan done)
- PET scan is optional
- Chest x-ray (optional)
- Blood cell counts
- Blood chemistry tests including LDH
- Smoking cessation counseling and intervention

Small cell lung cancer: Initial workup and staging

This Decision Tree begins when small cell lung cancer (SCLC) has been diagnosed, based on the results of a biopsy (a small piece of tissue that has been removed from the tumor) or cytology (examination of cell samples, such as cells in sputum, cells in the fluid that has collected around the lungs, or cells that have been scraped from the lining of the airways).

The next step after diagnosis is a series of examinations and tests that doctors call the initial work-up. The medical history and physical exam focus on symptoms that may suggest spread beyond your lungs and also consider your overall health. Several tests are done to determine the clinical stage of the cancer. For example, a chest CT scan helps determine your tumor size and location, and also evaluates the size of lymph nodes within the chest. If these lymph nodes are enlarged, they may contain cancer cells that have spread from the lung tumor. SCLC frequently spreads to the liver, adrenal glands, brain, and bone. Various tests are done to look at these areas; such as a CT scan of your liver and adrenal glands, a brain MRI or CT scan, and a bone scan. Another test that is sometimes done is

Small cell lung cancer: Initial work-up and staging



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

a PET scan, which may be combined with a CT scan. If a PET scan is done, the bone scan is optional.

A variety of blood tests are done to check how well your liver and kidneys are working and to make sure your blood cell counts are not too low. Low blood cell counts or problems with internal organs could mean that there is a higher risk of complications and side effects of certain lung cancer treatments, so these tests must be done before your treatment begins. Other blood test results can suggest a cancer has spread outside the lung. For example, such spread is more likely when blood levels of an enzyme called LDH (lactate dehydrogenase) are too high.

The results of your initial work-up are used to determine the clinical stage of your cancer. The clinical stage tells you which of the Decision Trees are most relevant to your treatment. If you have any questions about your clinical stage, check the information on page 14, and talk to your doctor.

Clinical stage

Additional work-up



- Pulmonary function tests, if indicated
- X-rays or MRI of bone if the bone scan shows possible cancer spread
- Bone marrow biopsy and aspiration may be recommended in some cases
- If fluid around the lung is found, the fluid should be checked for cancer cells. If cancer not found in fluid, thoracoscopy may be done

Small cell lung cancer: Limited stage work-up

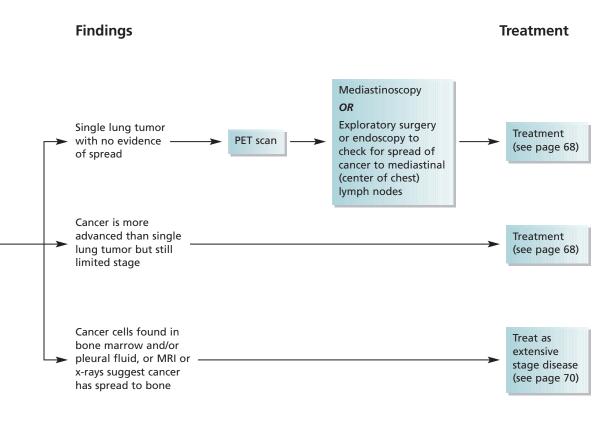
If your clinical stage appears limited after initial tests, the guidelines recommend more tests to make sure that your cancer is not more advanced.

Pulmonary function tests may be necessary to measure how well the lungs take in and exhale air and how efficiently they transfer oxygen into the blood. If the bone or PET scan showed any areas that may be cancer, additional x-rays are done to further evaluate the abnormal areas. An MRI may be done if the x-rays still cannot determine whether

there has been tumor spread. A sample of your bone marrow may be checked under the microscope to look for lung cancer cells.

If your chest x-ray shows fluid around your lungs (pleural effusion), some of the fluid is removed through a needle inserted through the ribs into the space next to the lungs. A sample of the fluid is looked at under the microscope to see if cancer cells are present. If no cancer cells are found, a surgeon may also look into the chest cavity with a small telescope-like tube called a thoracoscope to further look for cancer there. If any of these tests find lung cancer cells, then your cancer

Small cell lung cancer: Limited stage work-up



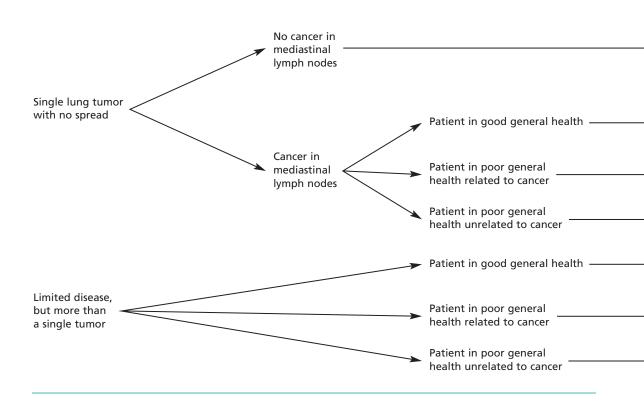
©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

is reclassified as extensive stage rather than limited stage. See page 70 for a discussion of your treatment options.

If no evidence of cancer spread is found and there appears to be only 1 tumor nodule, then a PET scan will be done to see if the cancer has spread to the mediastinal lymph nodes or anywhere else. If needed, the PET scan can also be used to guide a biopsy procedure. For example, a procedure known as mediastinoscopy (see page 11) may be done. This procedure removes some lymph nodes inside the chest. These lymph nodes can also be removed during exploratory surgery. The lymph nodes can then be examined to see if they contain any cancer cells.

Sometimes there is more than 1 lung tumor, but no lymph node spread. These cases are still treated as limited stage SCLC.

Test results



Small cell lung cancer: Treatment for limited stage

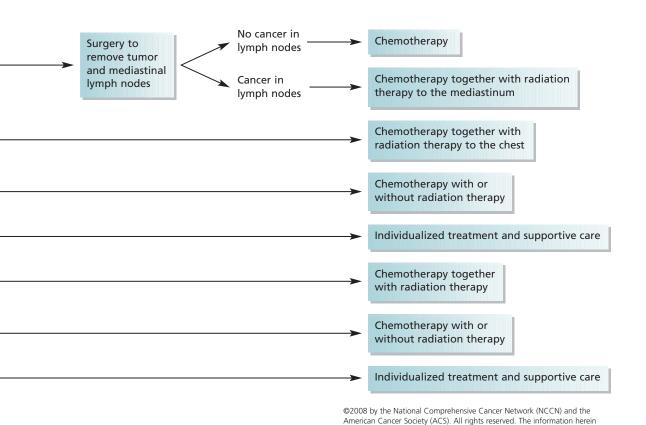
People with small cell lung cancer (SCLC) are not commonly treated with surgery because their cancer usually has spread at the time of diagnosis. However, if the imaging tests show only 1 lung tumor and there is no evidence of spread elsewhere in the body (based on imaging tests, bone marrow biopsy, thoracoscopy, etc.), you might benefit from surgery. If no spread to mediastinal lymph nodes is found by mediastinoscopy, the guidelines

recommend that you have an operation to remove your lung tumor and the mediastinal nodes. Chemotherapy is then given after the operation. Radiation is added to the chemotherapy if the lymph nodes removed at surgery contain cancer cells.

If the mediastinoscopy shows that lung cancer cells have spread to your mediastinal lymph nodes or there is more than 1 tumor, your cancer has spread too far to be removed by surgery and your treatment will be determined by your health status. NCCN doctors

Small cell lung cancer: Treatment for limited stage

Treatment

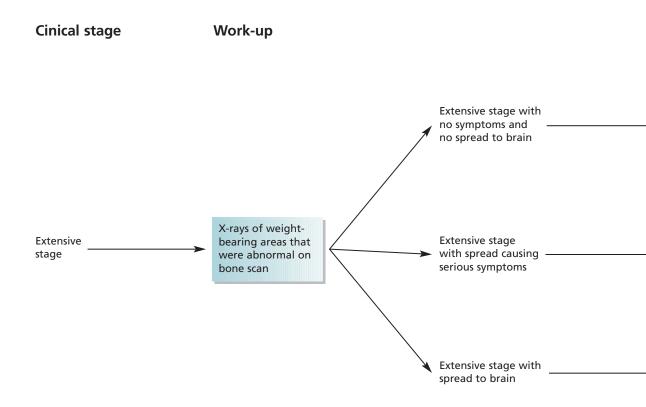


use precise definitions of good health or poor health based on the Eastern Cooperative Oncology Group (ECOG) Performance Scale. (Refer to page 8 for more information about the ECOG Performance Scale.) For example, if your performance status is good, chemotherapy with radiation therapy is recommended because this combination is more effective in helping patients live longer and in preventing

or treating symptoms of SCLC. Poor performance status may be related either to the tumor or to other health problems. Chemotherapy with (or without) radiation therapy is recommended if your poor performance status is related to the tumor. If you have significant other medical problems, then individualized treatment and supportive care is recommended.

may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.





Small cell lung cancer: Work-up and treatment for extensive stage

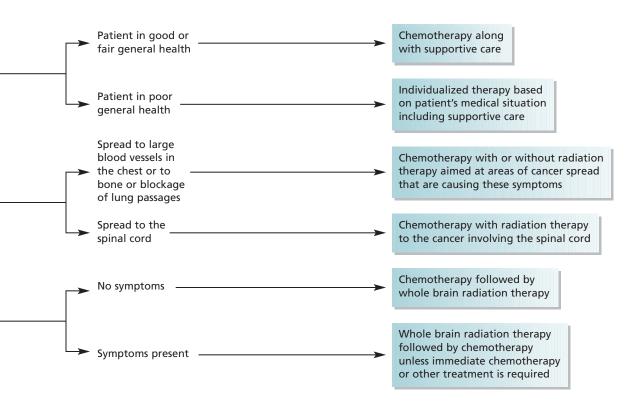
If you have extensive stage small cell lung cancer (SCLC), your treatment depends on exactly where your cancer has spread and your general state of health. In deciding which patients should receive chemotherapy, NCCN doctors use precise definitions of good health or poor health (that is, your performance status), as described on page 8. Chemotherapy has been shown to help patients with extensive

stage SCLC who are in good or fair general health to live longer. It can also relieve some symptoms and delay the onset of others. However, if your general health is very poor, you may not be able to withstand the side effects of chemotherapy or benefit from it. In this case, your doctor may select a treatment plan based on your individual medical situation.

In addition to having chemotherapy, the guidelines recommend radiation therapy aimed at any areas causing symptoms. Such

Small cell lung cancer: Work-up and treatment for extensive stage

Initial treatment



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

areas would include blood vessels or airways that are blocked by tumor, metastases in leg or hip bones, or metastases pressing on the spinal cord or spinal nerves causing paralysis or pain.

If the cancer has spread to the brain, whole brain radiation therapy and chemotherapy are recommended, but the order of the treatment depends on whether symptoms are present. If there are no symptoms, chemotherapy is given first, followed by whole brain radiation therapy. If the brain metastases are symptomatic, whole brain radiation therapy is given first, followed by the chemotherapy, unless the tumor outside the brain needs immediate treatment.



Treatment Guidelines for Patients

Additional work-up **Findings** Limited stage Complete response (main lung tumor no longer visible) or has • Chest x-ray (optional) shrunk to 10% or less • CT scans of chest, liver, Extensive and adrenal glands stage MRI scan (preferred) or CT scan of head for patients who will receive brain radiation to prevent brain Partial response (tumors metastases shrank by 50% but did Other imaging tests to not completely disappear) check status of known cancer spread CBC and blood chemistry tests Progressive disease (cancer continued to grow or spread)

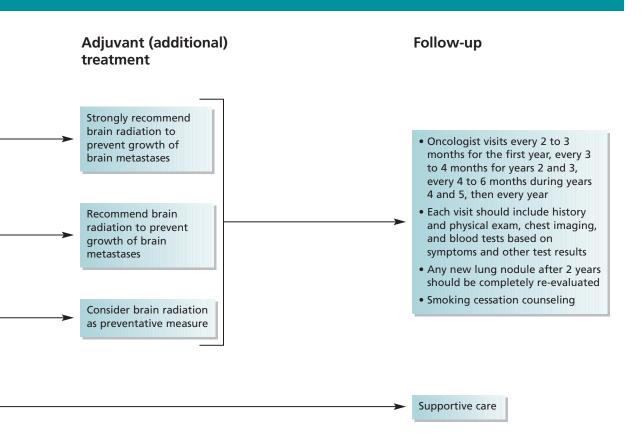
Small cell lung cancer: Adjuvant treatment

After your initial treatment has been completed, the guidelines recommend that you have follow-up tests and exams that include an optional chest x-ray; CT scan of the chest, liver, and adrenal glands; brain CT or MRI (MRI is preferred); imaging tests of known areas of disease; and blood tests to check for recurrence (cancer coming back). Based on

results of the imaging tests, the cancer's response to treatment is classified as complete response, partial response, or progressive disease.

A complete response means that all tumors in your body seem to have completely disappeared or are less than 10% of the size they were on the original imaging tests, such as CT scans. This response does not guarantee that all of your cancer cells have been

Small cell lung cancer: Adjuvant treatment



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

destroyed. In fact, most patients with a complete response still have some cancer cells scattered throughout their body. Doctors worry about a recurrence in the brain, because chemotherapy doesn't easily cross from the bloodstream into the brain. For this reason, brain radiation is recommended, even if CT

or MRI scans of the brain do not detect any tumors. This form of radiation is known as prophylactic (preventive) cranial irradiation (PCI). In patients with a complete response who initially had limited stage disease, PCI is strongly recommended. The guidelines also recommend PCI for patients with a complete

Treatment Guidelines for Patients

response who originally had extensive disease. It can be considered for patients with a partial response, but the benefits of this approach are not as clear for these patients.

If you have either a complete or partial response to initial therapy, you should have

frequent check-ups (that is, follow-up with an oncologist) according to the schedule in this Decision Tree. Every visit should include a medical history, physical exam, chest imaging, and blood tests. If you have any new symptoms or if your chest imaging results or

NOTES

Small cell lung cancer: Adjuvant treatment (continued)

physical exam is abnormal, additional tests are done to check whether the cancer has come back. If a cancer is found after 2 years, it will be assumed to be a new second cancer and should be treated as such with a biopsy and re-evaluation as described on page 64. It is

also very important to stop smoking. Your doctor can give you information to help you with this.

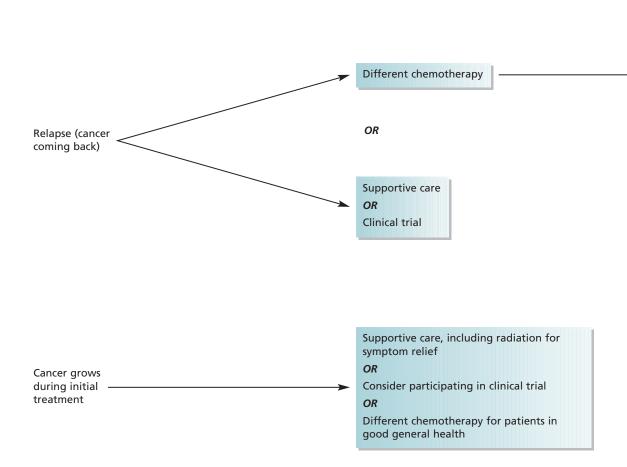
If the cancer continues to grow with treatment, supportive care is recommended.

NOTES		



Treatment Guidelines for Patients





Small cell lung cancer: Treatment of recurrent disease

This Decision Tree discusses what to do if the cancer comes back after it has shrunk or disappeared, or if it continues to grow during chemotherapy. If the cancer shrank or disappeared with chemotherapy and comes back,

new (and different) chemotherapy can be given. This different therapy is continued until the cancer begins to grow, at which time the choices are either a clinical trial of new treatments or supportive care to relieve any symptoms and keep the patient comfortable. If the cancer comes back and chemotherapy

Small cell lung cancer: Treatment of recurrent disease



©2008 by the National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS). All rights reserved. The information herein may not be reproduced in any form for commercial purposes without the expressed written permission of the NCCN and the ACS. Single copies of each page may be reproduced for personal and non-commercial uses by the reader.

is not a good option then a clinical trial or supportive care is the recommended treatment. If the cancer did not respond to the initial chemotherapy (that is, did not shrink or increased in size), then the guidelines recommend supportive care (including radiation therapy for symptom relief), or a clinical trial, or a different chemotherapy regimen if you are in good health.

NOTES

NOTES

The Lung Cancer Treatment Guidelines for Patients were developed by a diverse group of experts and were based on the NCCN clinical practice guidelines. These patient guidelines were translated, reviewed, and published with help from the following individuals:

Terri Ades, MS, APRN-BC, AOCN

American Cancer Society

Kimberly A. Stump-Sutliff,

MSN, AOCNS

American Cancer Society

Miranda Hughes, PhD

National Comprehensive

Cancer Network

Joan McClure, MS

National Comprehensive Cancer Network

Mary Dwyer Rosario, MS

National Comprehensive

Cancer Network

Dottie Shead, MS

National Comprehensive

Cancer Network

David S. Ettinger, MD

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Gregory P. Kalemkerian, MD

University of Michigan

Comprehensive Cancer Center

The original NCCN Lung Cancer Clinical Practice Guidelines were developed by the following **NCCN Panel Members:**

Non-Small Cell Lung **Cancer Panel**

Wallace Akerley, MD

Huntsman Cancer Institute at the University of Utah

Gerold Bepler, MD, PhD

H. Lee Moffitt Cancer Center &

Research Institute

Andrew Chang, MD

University of Michigan Comprehensive Cancer Center

Richard T. Cheney, MD

Roswell Park Cancer Institute

Lucian R. Chirieac, MD

Dana-Farber/Brigham and Women's Cancer Center | Massachusetts

General Hospital Cancer Center

Thomas A. D'Amico, MD

Duke Comprehensive Cancer Center

Todd L. Demmy, MD

Roswell Park Cancer Institute

David S. Ettinger, MD / Chair

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Steven J. Feigenberg, MD, FACS

Fox Chase Cancer Center

Robert A. Figlin, MD

City of Hope

Ramaswamy Govindan, MD

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Frederic W. Grannis, Jr., MD

City of Hope

Thierry Jahan, MD

UCSF Comprehensive Cancer Center

Mohammad Jahanzeb, MD

St. Jude Children's Research Hospital/University of Tennessee

Cancer Institute

Anne Kessinger, MD

UNMC Eppley Cancer Center at The Nebraska Medical Center

Ritsuko Komaki, MD, FACR

University of Texas M. D. Anderson

Cancer Center

Mark G. Kris, MD

Memorial Sloan-Kettering

Cancer Center

Corey J. Langer, MD Fox Chase Cancer Center

Ouvnh-Thu Le, MD Stanford Comprehensive

Cancer Center

Renato Martins, MD

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Gregory A. Otterson, MD

Arthur G. James Cancer Hospital & Richard J. Solove Research Institute at The Ohio State University

Jyoti D. Patel, MD

Robert H. Lurie Comprehensive Cancer Center of Northwestern

University

Francisco Robert, MD

University of Alabama at Birmingham Comprehensive Cancer Center

David J. Sugarbaker, MD

Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center

Douglas E. Wood, MD

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance

Small Cell Lung Cancer Panel

Wallace Akerley, MD Huntsman Cancer Institute at the University of Utah

Robert J. Downey, MD Memorial Sloan-Kettering Cancer Center

David S. Ettinger, MD
The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins

Frank Fossella, MD University of Texas M. D. Anderson Cancer Center

John C. Grecula, MD Arthur G. James Cancer Hospital & Richard J. Solove Research Institute at The Ohio State University Thierry Jahan, MD UCSF Helen Diller Family Comprehensive Cancer Center

Bruce E. Johnson, MD Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center

Gregory P. Kalemkerian, MD / Chair University of Michigan Comprehensive Cancer Center

Anne Kessinger, MD UNMC Eppley Cancer Center at The Nebraska Medical Center

Marianna Koczywas, MD City of Hope

Corey J. Langer, MD Fox Chase Cancer Center

Renato Martins, MD Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance Harvey B. Niell, MD St. Jude Children's Research Hospital/ University of Tennessee Cancer Institute

Charles C. Pan, MD University of Michigan Comprehensive Cancer Center

Nithya Ramnath, MD Roswell Park Cancer Institute

Neal Ready, MDiv, PhD Duke Comprehensive Cancer Center

Francisco Robert, MD University of Alabama at Birmingham Comprehensive Cancer Center

Charles C. Williams, Jr., MD H. Lee Moffitt Cancer Center & Research Institute



1.800.ACS.2345 www.cancer.org



1.888.909.NCCN www.nccn.org