Patient information: Non-small cell lung cancer treatment; stage I to III cancer (Beyond the Basics)

Author
Howard J West, MD

Section Editor
James R Jett, MD

Deputy Editor
Michael E Ross, MD

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NON-SMALL CELL LUNG CANCER OVERVIEW — Non-small cell lung cancer (NSCLC) accounts for between 85 and 90 percent of all lung cancers; the remaining 10 to 15 percent are small cell lung cancers. This distinction is important when considering treatment.

This article will discuss the treatment of non-small cell lung cancer confined to the chest (stage I, stage II, and stage III disease). The treatment of non-small cell lung cancer that has spread more widely (stage IV) is discussed separately, as are the risks, symptoms, and diagnosis of non-small cell lung cancer are also discussed separately. (See "Patient information: Non-small cell lung cancer treatment; stage IV cancer (Beyond the Basics)" and "Patient information: Lung cancer risks, symptoms, and diagnosis (Beyond the Basics)".)

STAGING NON-SMALL CELL LUNG CANCER — Once lung cancer is diagnosed, the next step is to review its size, to determine its exact location and to find out if it has spread. This process is called staging. Determining the stage of a lung cancer can be complicated because many features of the tumor are used at the same time. The stage of non-small cell cancer is based on:

- The size and location of the tumor
- Whether the tumor has invaded lymph nodes and tissues inside the chest
- Whether the tumor has spread to places outside the chest (for example lung cancer can spread (metastasize) to places like the lymph nodes or adrenal glands or elsewhere)

Non-small cell lung cancer stages range from I to IV. In general, the lower number (stages I and II) suggest that the tumor is smaller and has not spread far. In comparison, the higher numbers (stage III and IV) suggest that the tumor is larger or has metastasized.

- Stage I – The tumor is smaller than or equal to 5 cm (about 2 inches) in maximum diameter and has not spread to any other tissues or lymph nodes (figure 1).
- Stage II – Stage II means that the tumor is either between 3 and 7 cm (between about 1.2 to 3 inches) in size, or it has spread to the lymph nodes, or it has invaded the tissues surrounding the lung, or it has started to invade the large bronchial tubes (figure 2).

- Stage IIIA – Stage IIIA disease means that the tumor can be bigger than 7 cm (about 3 inches), or has spread to the lymph nodes in the center of the chest (called the mediastinum) or has spread to the rib cage, heart, swallowing tube (called the esophagus) or to the trachea (figure 3).

- Stage IIIB – Stage IIIB disease means that the tumor has spread to lymph nodes on the other side of the mediastinum or to the lymph nodes above or behind the clavicle (collar bone). Stage IIIB also includes large tumors that have spread to the rib cage, heart, swallowing tube (called the esophagus) or to the trachea when there is involvement of the mediastinal lymph nodes (figure 4).

- Stage IV – Stage IV means that the cancer has spread outside of the chest or has spread to a critical location or has caused some complication. Possible complications are that the cancer has caused fluid to collect around the lung or heart (called a malignant effusion), or it has spread to the opposite side of the chest, has spread to outside the chest (figure 5). (See "Patient information: Non-small cell lung cancer treatment; stage IV cancer (Beyond the Basics)".)

In general, lower-stage cancers require less treatment than higher-stage cancers. Stage I to III non-small cell lung cancers are referred to as localized cancers, while stage IV is called advanced cancer.

STAGE I AND II TREATMENT — Whenever possible, surgery is recommended as the first treatment in people with stage I or II non-small cell lung cancer (NSCLC). Radiation therapy may be recommended for people who are not good candidates for surgery due to severe lung disease or other underlying medical problems. In some cases, the initial surgery or radiation therapy may be followed by adjuvant (postoperative) chemotherapy.

Surgery — Surgery to remove the cancer is the preferred treatment for stage I and stage II NSCLC. Options for surgery include the following, depending upon the size and position of the tumor in the chest:

- Lobectomy, which involves removal of one lobe of the lung.

- Segmentectomy (the removal of an anatomical division of one lobe) or wedge resection (the removal of a non-anatomically defined area of lung around the tumor) may be considered in some patients with a small tumor of 2 cm or smaller. This form of surgery may also be favored for some people who could not tolerate conventional lobectomy. This might happen in a person whose lungs do not work well.

- In some people, it is necessary to remove the entire affected lung (called pneumonectomy) because lobectomy cannot completely remove the tumor. Pneumonectomy requires that the remaining lung be relatively healthy.

Radiation therapy — Radiation therapy involves the use of X-rays to destroy cancer cells. Radiation therapy may be recommended for people with stage I or II NSCLC in the following situations:

- After surgery, radiation therapy may be recommended for patients with tumor left behind at the margins of the surgical resection or for patients felt to have a high risk for locoregional (nearby) recurrence. It is not a clear standard therapy, and it is relatively contraindicated in patients with lung cancer and no lymph node involvement, with some evidence suggesting that it can have a net harmful effect in such patients.

- Radiation therapy may be used alone or with chemotherapy, without surgery, in people who are unable to tolerate or who do not want surgery.

Radiation treatments are brief and not painful, similar to having an X-ray. Treatments are usually done five days per week for several weeks.

A different technique to give radiation, called stereotactic body radiation therapy (SBRT), involves giving more

radiation to a small area over a few daily treatments (five or fewer). Studies of SBRT demonstrate very promising outcomes in patients with node-negative tumors, particularly those that are relatively small (<3-4 cm). Long-term efficacy and side effects for this relatively new approach compared with conventional surgery remains unclear.

Radiation side effects — Radiation therapy can cause side effects during treatment. Side effects usually resolve after treatment ends. The most common side effects of radiation therapy for lung cancer are:

- Difficulty swallowing due to swelling and irritation of the esophagus (the tube between the mouth and stomach); this is called esophagitis.
- Swelling and irritation of the normal lung surrounding the tumor (called pneumonitis).
- Fatigue.
- Skin irritation in the area being treated; this can look like a sunburn on the chest.
- Hair loss just in the area being treated.

Adjuvant chemotherapy — Postoperative chemotherapy is a treatment given to slow or stop the growth of cancer cells. Even after a cancer has been removed with surgery, cancer cells can remain in the body, increasing the risk of a relapse.

Chemotherapy can get rid of these cancer cells and increase the chance of cure, but it is indicated only in patients with a high enough risk of recurrence to justify the side effects of chemotherapy. Chemotherapy in the postoperative setting is called adjuvant therapy, meaning “helper”.

Chemotherapy is not given every day but instead is given in cycles. A cycle of chemotherapy, which is typically 21 or 28 days, refers to the time it takes to give the treatment and then allow the body to recover from the side effects of the medicines. Most treatments involve a combination of two chemotherapy drugs (called a doublet chemotherapy regimen). The best studied options include the agent cisplatin, though the potential for challenging side effects may make it a less ideal choice than the related drug carboplatin for some patients. Most of the drugs are given into a vein (intravenous, IV). Typically, adjuvant treatment regimens for non-small cell lung cancer last about three months. (See "Patient information: Non-small cell lung cancer treatment; stage IV cancer (Beyond the Basics)", section on 'Chemotherapy'.)

Your healthcare provider can describe which specific chemotherapy drugs will be recommended.

Side effects — The most common side effects of chemotherapy used for NSCLC include:

- A lowered white blood cell count (which can increase the risk of infection). Chemotherapy is associated with a 1 to 2 percent risk of fatal infections.
- Fever related to a low white blood cell count
- Nausea and vomiting
- Bowel changes, which may include constipation or diarrhea

Other side effects may occur, and these vary with the exact regimen of therapy being administered. Fortunately, the common side effects of chemotherapy are, with rare exception, only temporary.

STAGE III TREATMENT — There is no one "best" treatment for people with stage III non-small cell lung cancer (NSCLC). Treatment depends upon the size and location of your tumor, lymph node involvement, and whether surgery has been done. The options generally include:

- Radiation therapy (see 'Radiation therapy' above)
- Chemotherapy (see 'Adjuvant chemotherapy' above)
- Surgery (see 'Surgery' above)

In many people with stage III NSCLC, a combination of chemotherapy and radiation therapy are recommended as the cornerstone of treatment, and in some cases, surgery may be pursued after initial chemotherapy or chemotherapy with radiation (this is called chemoradiotherapy). Chemotherapy and radiation therapy may be given together (called concurrent chemoradiotherapy) or one treatment after the other (called sequential chemoradiotherapy). It is appropriate for recommendations for stage III disease to be individualized by a multi-speciality team to a particular patient's needs, based on the extent of the tumor, the pattern of spread, and the patient's underlying health.

PANCOAST TUMORS — The term Pancoast tumor (also called superior sulcus tumor) refers to a non-small cell lung cancer that is located in the top part of one of the lungs, in a region called the superior sulcus (figure 6). Pancoast tumors can involve nerves, causing a unique set of symptoms referred to as Pancoast syndrome.

Initially, symptoms may include shoulder or arm pain, weakness of the muscles of the hand, and flushing or excessive sweating on one side of the face. As the tumor progresses, the flushing can disappear, the eyelid may droop, and the involved side may not sweat.

As long as there is no evidence of distant spread, treatment of Pancoast tumors usually consists of a combination of chemotherapy and radiation, followed by surgery, as long as there is no evidence of distant spread.

CLINICAL TRIALS — Progress in treating lung cancer requires that better treatments be identified through clinical trials, which are conducted all over the world. A clinical trial is a carefully controlled way to study the effectiveness of new treatments or new combinations of known therapies. Whenever possible, patients with lung cancer are encouraged to enroll in a clinical trial. Ask for more information about clinical trials, or read about clinical trials at:

- http://clinicaltrials.gov/

WHERE TO GET MORE INFORMATION — Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (www.uptodate.com/patients). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient information: Non-small cell lung cancer (The Basics)
Patient information: Lung cancer (The Basics)
Patient information: Lung cancer screening (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient information: Non-small cell lung cancer treatment; stage IV cancer (Beyond the Basics)

Patient information: Lung cancer risks, symptoms, and diagnosis (Beyond the Basics)
Patient information: Small cell lung cancer treatment (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

Overview of the initial evaluation, treatment and prognosis of lung cancer
Diagnosis and staging of non-small cell lung cancer
Pathology of lung malignancies
Management of stage I and stage II non-small cell lung cancer
Management of stage III non-small cell lung cancer
Adjuvant systemic therapy in resectable non-small cell lung cancer
Superior pulmonary sulcus (Pancoast) tumors
Bronchioloalveolar carcinoma, including adenocarcinoma in situ

The following organizations also provide reliable health information.

- The National Library of Medicine

(www.nlm.nih.gov/medlineplus/lungcancer.html)

- National Cancer Institute

(www.cancernet.nci.nih.gov/)

- American Society of Clinical Oncology

(www.cancer.net/portal/site/patient)

- Global Resource for Advancing Cancer Education (GRACE)

(www.cancerGRACE.org/lung)

- Lung Cancer Alliance

(www.lungcanceralliance.org)

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