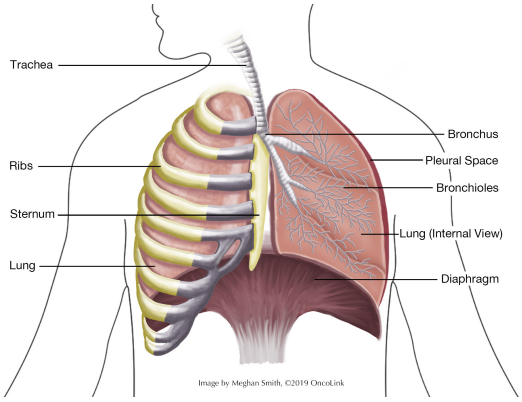
Non-Small Cell Lung Cancer: Staging and Treatment

What is staging for cancer?

Staging is the process of learning how much cancer is in your body and where it is. For non-small cell lung cancer (NSCLC), a bronchoscopy, biopsy, chest x-ray, CT scan, MRI of the brain, and/or PET scan may be used to stage your cancer. Staging helps your providers learn about your cancer and your health so they can plan the best treatment for you.



Anatomy of the chest.

Staging looks at the size of your tumor, where it is, and if it has spread to other organs.

The “TNM system” is used to stage NSCLC. It has three parts:

- **T**- Describes the size/location/extent of the "primary" tumor in the lung.
- **N**- Describes if the cancer has spread to the lymph nodes.
- **M**- Describes if the cancer has spread to other organs (metastases).

Your healthcare provider will use the results of the tests you had to figure out your TNM result and combine these to get a stage from 0 to IV (four).

How is non-small cell lung cancer staged?

Staging is important because it helps to guide your treatment options.

Staging for non-small cell lung cancer is based on:

- The size of your tumor and its location in the lung(s).
- If your lymph nodes have cancer cells in them.
- If the cancer has spread to other organs (metastasis).

The staging system is very complex. Below is a summary. Talk to your provider about the stage of your cancer.

- **Stage 0** (Tis, N0, M0): The cancer is only in the top layers of the airway and has not spread deeper into the lung (Tis). It has not spread to the lymph nodes (N0) or other parts of the body (M0).
- **Stage Ia1** (T1a/mi, N0, M0): The tumor is a minimally invasive adenocarcinoma. The tumor is not larger than 3 centimeters (cm) and the part that has invaded into deeper lung tissues is not larger than ½ cm (T1mi). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0); **OR** (T1a, N0, M0) The tumor is no bigger than 1 cm in size. It hasn’t spread to the area around the lungs (pleura) and it hasn’t grown into the main parts of the bronchi (T1a). It has not spread to the lymph nodes (N0) or other parts of the body (M0).

- **Stage IA2** (T1b, N0, M0): The tumor is between 1 and 2 cm in size. It hasn't spread to the area around the lungs (pleura) and it hasn't grown into the main parts of the bronchi (T1b). It has not spread to the lymph nodes (N0) or other areas of the body (M0).
- **Stage IA3** (T1c, N0, M0): The tumor is 2 to 3 cm in size. It hasn't spread to the area around the lungs (pleura) and it hasn't grown into the main parts of the bronchi (T1c). It has not spread to the lymph nodes (N0) or other areas of the body (M0).
- **Stage IB** (T2a, N0, M0): The tumor is 1 or more of the following (T2a): (1) The tumor is 3 to 4 cm in size, (2) it has grown into a main bronchus but not the carina (where the windpipe splits into the left and right bronchi) and is less that 4 cm in size, (3) it has grown into the area around the lungs (pleura) and is less than 4 cm in size, or (4) it is partly blocking the airways and is less than 4 cm in size.
  It has not spread to the lymph nodes (N0) or other areas of the body (M0).
- **Stage IIA** (T2b, N0, M0): The tumor is 1 or more of the following (T2b): (1) it is 4 to 5cm in size, (2) it has grown into the main bronchus but not the carina (where the windpipe splits into the left and right bronchi) and is 4 to 5 cm in size, (3) the tumor has grown into the area around the lungs (pleura) and is 4 to 5 cm in size, or (4) it is partly blocking the airways and is less than 5 cm in size.
  It has not spread to the lymph nodes (N0) or other areas of the body (M0).
- **Stage IIB**
  - (T1a/T1b/T1c, N1, M0): The tumor is 3 cm or less in size. It has not grown into the area around the lungs (pleura) and does not affect the main branches of the bronchi (T1). It has spread to lymph nodes within the lung or in the area where the bronchus enters the lung.
    These lymph nodes are on the same side as the tumor (N1). The cancer has not spread to other parts of the body (M0).
  - (T2a/T2b/ N1, M0): The tumor is 1 or more of the following: (1) It is 3 to 5 cm in size, (2) It has grown into a main bronchus but not the carina (where the windpipe splits into the left and right bronchi) and is less than 5 cm in size, (3) it has grown into the area around the lungs (pleura) and is less than 5 cm in size, or (4) it is partly blocking the airways and is less than 5 cm in size.
    It has spread to lymph nodes within the lung or in the area where the bronchus enters the lung.
    These lymph nodes are on the same side as the tumor (N1). The cancer has not spread to other parts of the body (M0).
  - (T3, N0, M0): The tumor is one or more of the following: (1) The tumor is 5 to 7 cm in size, (2) it has grown into the chest wall, the inner lining of the chest wall, the phrenic nerve, or the area around the heart (parietal pericardium), or (3) there are 2 or more separate tumor nodules in the same lobe of a lung. It has not spread to the lymph nodes (N0) or other areas of the body (M0).
- **Stage IIIA**
  - (T1a, T1b, T1c, N2, M0): The tumor is no bigger than 3 cm in size. It hasn't grown into the pleura and does affect the main parts of the bronchi (T1). The cancer has spread to the lymph nodes below the carina (where the windpipe splits into the left and right bronchi) or in the space between the lungs (the mediastinum). These lymph nodes are on the same side as the lung with the main tumor (N2). The cancer has not spread to other areas of the body (M0).
  - (T2a/T2b, N2, M0): The tumor is one of more of the following: (1) It is 3 to 5 cm in size, (2) it has grown into the main bronchus but not the carina (where the windpipe splits into the left/right bronchi) and is less than 5 cm in size, (3) it has grown into the pleura and is less than 5 cm in size, or 4) it is parly blocking the airways and is less than 5 cm in size.
    The cancer has spread to the lymph nodes below the carina and the mediastinum. These lymph nodes are on the same side as the lung with the main tumor (N2). The cancer has not spread to other parts of the body (M0).

- (T3, N1, M0): The tumor is one or more of the following: (1) it is 5 to 7 cm in size, (2) the tumor has grown into the chest wall, the inner lining of the chest wall (parietal pleura), the phrenic nerve, or the area around the heart (parietal pericardium), or (3) there are 2 or more separate tumors in the same part of the lung.
  The tumor has also spread to the lymph nodes in the lung and around the lung. These lymph nodes are on the same side as the lung with the tumor (N1). The cancer has not spread to other areas of the body (M0).
- (T4, N0 or N1, M0): The tumor is one or more of the following: (1) It is bigger than 7 cm in size, (2) the tumor has grown into the space between the lungs (the mediastinum), the heart, the blood vessels near the heart, the windpipe (trachea), the diaphragm, the esophagus, the spine, or the carina, or (3) there are 2 or more tumors in different lobes of the same lung.
  The cancer may have also spread to the lymph nodes in the lung or near the bronchus. These lymph nodes are on the same side of the body as the tumor (N0 or N1). The cancer has not spread to other parts of the body (M0).

- **Stage IIIB**
  - (T1a/T1b/T1c, N3, M0): The tumor is no bigger than 3 cm in size. It has not grown into the pleura or the bronchi's main branches (T1). The cancer has spread to lymph nodes above the collarbone on either side of the body or to the lymph nodes near the other lung from the main tumor site (N3). It has not spread to other parts of the body (M0).
  - (T2a/T2b, N3, M0): The tumor is one or more of the following (T2): The tumor is 3 to 5 cm in size, (2) it has spread into the main bronchus, but not the carina (where the windpipe splits into the left and right bronchi) and it is less than 5 cm in size, (3) it has grown into the pleura and is less than 5 cm in size, or (4) is partly blocking the airways and is less than 5 cm in size.
    The cancer has spread to lymph nodes above the collarbone on either side of the body, and/or to the lymph nodes near the other lung on the other side of the body from the main tumor site (N3). It has not spread to other parts of the body (M0).
  - (T3, N2, M0): The tumor is one or more of the following (T3): (1) it is 5 to 7 cm in size, (2) it has grown into the chest wall, the inner lining of the chest wall (parietal pleura), the phrenic nerve, or the area around the heart (parietal pericardium), or (3) there are 2 or more separate tumors in the same lobe of the lung.
    The cancer has also spread to the lymph nodes below the carina (where the windpipe splits into the left and right bronchi) or in the space between the lungs (the mediastinum). These lymph nodes are on the same side as the lung with the main tumor (N2). The cancer has not spread to other parts of the body (M0).
  - (T4, N2,M0): The tumor is one or more of the following (T4): (1) It is bigger than 7 cm in size, (2) it has grown into the mediastinum, the heart, the blood vessels near the heart, the windpipe (trachea), the diaphragm, the esophagus, the spine, or the carina (where the windpipe splits into the left and right bronchi), or (3) there are 2 or more tumors in different lobes of the same lung.
    The cancer has also spread to the lymph nodes below the carina and the mediastinum. These lymph nodes are on the same side as the lung with the main tumor (N2). The cancer has not spread to other areas of the body (M0).
- **Stage IIIC**
  - (T3, N3, M0): The tumor is one or more of the following (T3): (1) it is 5 to 7 cm in size, (2) it has grown into the chest wall, the inner lining of the chest wall (parietal pleura), the phrenic nerve, or the area around the heart (parietal pericardium), or (3) there are 2 or more separate tumors in the same lobe of the lung.
    The cancer has spread to lymph nodes above the collarbone on either side of the body and/or to

the lymph nodes near the other lung on the other side of the body from the main tumor site (N3). It has not spread to other parts of the body (M0).

- (T4, N3, M0): The tumor is one or more of the following (T4): (1) It is bigger than 7 cm in size, (2) the tumor has grown into the space between the lungs (the mediastinum), the heart, the blood vessels near the heart, the windpipe (trachea), the diaphragm, the esophagus, the spine, or the carina (where the windpipe splits into the left and right bronchi), or (3) there are 2 or more tumors in different lobes of the same lung.
  The cancer has spread to lymph nodes above the collarbone on either side of the body and/or to the lymph nodes near the other lung on the other side of the body from the main tumor site (N3). It has not spread to other parts of the body (M0).

- **Stage IVA**
  - (Any T, Any N, M1a): The tumor can be any size and may have grown into the pleura, bronchi, mediastinum, or other nearby parts of the body (Any T). It may have spread to nearby lymph nodes (Any N). It may also (M1a) (1) have spread to the other lung, (2) have spread to either the lining around the lungs (pleura) or the pericardium (lining around the heart), or (3) have caused cancer cells in the fluid around the lung (malignant pleural effusion), or (4) cancer cells in the fluid around the heart (malignant pericardial effusion).
  - (Any T, Any N, M1b): The tumor can be any size and may have grown into the pleura, bronchi, mediastinum, or other nearby parts of the body (Any T). It may have spread to nearby lymph nodes (Any N). The tumor has also spread as a single tumor outside of the chest. This could be a lymph node in another part of the body, or in an organ such as the brain, liver, or bone (M1b).
- **Stage IVB**
  - (Any T, Any M, M1c): The tumor can be any size and may have grown into the pleura, bronchi, mediastinum, or other nearby parts of the body (Any T). It may have spread to nearby lymph nodes (Any N). The tumor has also spread to more than 1 tumor outside of the chest. This could be a lymph node in another part of the body, and/or the brain, the liver, or the bone (M1c).

How is non-small-cell lung cancer treated?

Treatment for NSCLC depends on the stage of your cancer. If you smoke, quit as soon as possible. Smoking may lessen how well your cancer treatments work and can make the side effects of treatment worse.

Your treatment may include some or all of the following:

- Surgery.
- Chemotherapy.
- Targeted therapy.
- Immunotherapy.
- Radiation therapy.
- Ablative treatments.
- Palliative treatment.
- Clinical trials.

Surgery

Surgery can be used in the treatment of NSCLC. The goal of surgery is to remove as much of the cancer as possible. There are many different surgical procedures used in the treatment of NSCLC. These procedures include:

- Wedge resection: the surgeon will remove a small part of the lung affected by the cancer.
- Lobectomy: the surgeon will remove the lobe of the lung affected by the cancer.
- Pneumonectomy: the surgeon will remove the whole lung.

The type of surgery you may have depends on the location and size of your tumor and your overall health. You may also have pulmonary function tests (PFTs) before surgery to make sure you can tolerate the surgery.

Surgery may also be used if the cancer has spread (metastasis). This might include the removal of tumors that have spread to parts of the body like the brain, spine, or adrenal gland.

Chemotherapy

Chemotherapy is the use of anti-cancer medicines that go through your whole body. These medicines may be given through a vein (IV, intravenously) or by mouth. Chemotherapy for NSCLC may be used with immunotherapy and/or radiation therapy. What treatment you receive and how often you have treatment will depend on the stage of your cancer.

The medications used to treat NSCLC include: cisplatin, carboplatin, pemetrexed, paclitaxel, docetaxel, etoposide, gemcitabine, and vinorelbine. Your provider will work with you to find the best chemotherapy plan for your cancer and the potential side effects of your treatment.

Targeted Therapy

Some cancers have biomarkers that help providers to focus your treatment on certain genetic mutations or receptors in your tumor. These treatments are called targeted therapies. They target those genetic mutations. Your provider will test your tumor for these markers.

Targeted therapies used in the treatment of specific genetic mutations include:

- EGFR positive: Amivantamab, afatinib, dacomitinib, erlotinib, gefitinib, lazertinib, and osimertinib.
- ALK positive: Alectinib, brigatinib, ceritinib, crizotinib, ensartinib**,** and lorlatinib.
- KRAS G12C mutation: Sotorasib and adagrasib.
- ROS1 positive: Ceritinib, crizotinib, entrectinib,lorlatinib, and repotrectinib.
- BRAF V600E positive: Dabrafenib with trametinib, encorafenib with binimetinib, and vemurafenib.
- RET Rearrangement positive: Cabozantinib, pralsetinib, and selpercatinib.
- MET Exon 14 Skipping mutation: Capmatinib, Crizotinib, and tepotinib.
- ERBB (HER2) mutations: Ado-tratuzumab emtansine, fam-trantuzumab deructecan-nxki, and zenocutuzumab.
- NTRK Gene Fusion positive: Entrectinib, larotrectinib, and repotrectinib.
- Anti-angiogenesis agents/VEGF inhibitors: Bevacizumab and ramucirumab.

Your provider will talk to you about if targeted therapy can be used to treat your cancer and any side effects that you may have. Other targeted therapy medications are being studied in clinical trials.

Immunotherapy

Immunotherapy medications work with the immune system to kill cancer cells. Immunotherapy medications that may be used in the treatment of NSCLC are nivolumab, ipilimumab, cemiplimab**,**tremelimumab,pembrolizumab, atezolizumab, and durvalumab. Your provider will talk to you about if these medications will help treat your cancer and what side effects that you may have. Other immunotherapy medications are being studied in clinical trials.

Radiation Therapy

Radiation therapy is the use of high-energy X-rays to kill cancer cells. For NSCLC, radiation may be used before surgery to shrink the tumor to make it easier to remove. It may also be used with chemotherapy/targeted therapy/immunotherapy at the same time. Radiation to the chest may also be used to help prevent the cancer from coming back.

Sometimes, lung cancer spreads to other parts of the body (metastasis). Radiation may be used to treat the spread of lung cancer to these places as well as to help lessen the pain from the cancer spreading.

Ablative Treatment

- **Radiofrequency ablation (RFA)** is used to treat some types of tumors with a needle and heat. The heated needle kills cancer cells. You can have more than one tumor heated during the procedure.
- **Cryoablation** uses liquid nitrogen or argon gas to freeze and kill cancer cells.
- **Microwave ablation** uses microwaves that go into the tumor through a probe. The heat kills cancer cells.

Palliative Treatment

Palliative treatment is used to lessen symptoms that are caused by the cancer. It does not cure the cancer. There are many options for palliative treatments, such as chemotherapy, radiation, surgery, stent placement, laser therapies, and removal of extra fluid from around the heart or lungs. Talk to your provider about your options for helping your symptoms.

Clinical Trials

You may be offered a clinical trial as part of your treatment plan. To find out more about current clinical trials, visit the OncoLink Clinical Trials Matching Service.

Making Treatment Decisions

Your care team will make sure you are included in choosing your treatment plan. This can be overwhelming as you may be given a few options to choose from. Take the time to meet with different providers and think about your options and what is best for you. This is a personal decision. Friends and family can help you talk through the options and the pros and cons of each, but they cannot make the decision for you. You need to be comfortable with your decision – this will help you move on to the next steps. If you ever have any questions or concerns, be sure to call your team.