

Lung Cancer

What is lung cancer?

Lung cancer is a disease in which malignant (cancer) cells of the lung tissue grow in an uncontrolled way and form tumors. Lung cancer can arise in any part of the lung but in most cases, begins in the airways of the lung (the bronchi and bronchioles). There are two main types of lung cancer - small cell lung cancer (SCLC) and the more common non-small cell lung cancer (NSCLC). There are four subtypes of NSCLC: squamous cell carcinoma (SCC), large cell carcinoma (LCC), undifferentiated lung cancer and adenocarcinoma. Each type has different kinds of cancer cells, which grow and spread in different ways.

Useful statistics

- Worldwide, lung cancer is the most common cause of cancer-related deaths in men and the second most common in women (after breast cancer) (*Vir: 1*)
- Worldwide, it is estimated that approximately 975,000 men and 376,000 women die from the disease each year (*Vir: 2*)
- NSCLC accounts for approximately 80% of lung cancers (*Vir: 3*)
- Smoking is responsible for approximately 80% of lung cancer cases in men and 50% in women worldwide (*Vir: 4*)
- Overall five-year survival rate for lung cancer is about 16%, compared to 65% for colon cancer, 89% for breast cancer and 99% for prostate cancer (*Vir: 5*)
- Most patients with NSCLC present with advanced disease which is difficult to treat (*Vir: 6*)

Symptoms (*Vir: 7*)

Lung cancer may not exhibit any symptoms. Common symptoms can also be similar to those related to other conditions so may be ignored. Symptoms include:

- A persistent cough
- Shortness of breath
- Persistent chest pain
- Wheezing, hoarseness
- Coughing up blood
- Swelling of the face and neck
- Loss of appetite
- Unexplained weight loss, fever or tiredness

Risk factors (*Vir: 8*)

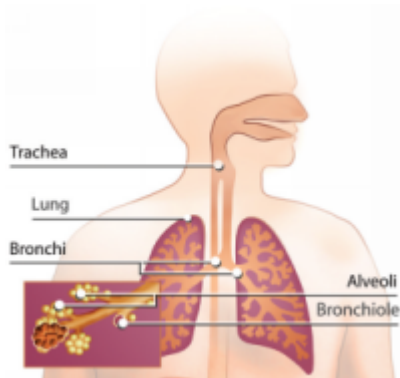
- **Smoking:** Smoking is by far the leading risk factor for lung cancer
- **Passive smoking:** Breathing in the smoke of others also puts people at increased risk of lung cancer
- **Family/medical history:** Family history and some genetic predispositions increase risk levels of lung cancer
- **Cancer-causing chemicals:** Carcinogens such as asbestos, radon, arsenic, polycyclic hydrocarbons, nickel and chromium can increase lung cancer risk
- **Air pollution:** Continued exposure to air pollution may also be a risk factor
- **Fibrosis/scars:** Fibrosis or scars after surgery or tuberculosis can increase lung cancer risk levels
- **Radiation:** People who have had radiation therapy to the chest for cancer (e.g. for Hodgkin's disease or breast cancer) are at higher risk of lung cancer, particularly if they smoke

Stages (*Vir: 7*)

Stages of NSCLC are graded according to the Tumor, Nodes and Metastases (TNM) staging system.

- **Stage I:** The lung cancer is confined to the lungs and surrounded by normal tissue, there is no cancer in any lymph nodes

- Stage II: The lung cancer has spread to regional lymph nodes
- Stage III: The lung cancer has spread to the chest wall, diaphragm or other nearby organs or blood vessels, and may have spread to lymph nodes in the mediastinum (central compartment of the chest containing the heart and the trachea) or the other side of the chest or neck
- Stage IV: The lung cancer has spread to more distant sites in the body



The respiratory system

Treatment options

Treatment for NSCLC is dependent on the size, location, type and stage of the disease, as well as the overall health and wellbeing of the patient.⁷

Treatment options include:

Surgery

Only early-stage (I and II) NSCLC tumors can be surgically removed. This option offers the best five-year survival rates. However, most patients who undergo surgery eventually relapse. Therefore, an adjuvant cisplatin-based chemotherapy is added. In more advanced stages (III) pre-operative treatment is often needed before the tumor can be removed surgically.

Radiotherapy

Radiotherapy may be used curatively, before surgery (neoadjuvant setting) to reduce the tumor size, after surgery to reduce relapse rate (adjuvant setting) or for advanced NSCLC cases (combined with surgery or chemotherapy).

Chemotherapy

Chemotherapy is mainly used in the treatment of metastatic NSCLC. It improves overall survival and contributes to symptom improvement. However, the optimal number of chemotherapy cycles that provide both survival and quality of life advantages is unclear. Chemotherapy may also be given before or after surgery, also in combination with radiation. The overall response rate to chemotherapy is just over 40% for patients with metastatic NSCLC. (Vir: 9) Current standard treatments in 1st-line NSCLC include a variety of platinum-based chemotherapy doublets which demonstrate comparable efficacy.

Targeted therapies

Targeted anti-cancer therapies, such as monoclonal antibodies or so-called small molecules, block the growth of cancer cells by interfering with specific molecules needed for tumor growth and division. They may be more effective and tolerable than current treatments as they specifically

attack cancer cells, leaving healthy cells unharmed. With these characteristics they raise the hope to overcome the efficacy plateau that has been reached by the currently used platinum-based doublets. Cetuximab is an IgG1 monoclonal antibody that specifically targets the epidermal growth factor receptor and tumor angiogenesis (blood vessel growth). In the treatment of 1st-line lung cancer Erbitux has been shown in Phase II and III trials to improve overall survival in combination with standard chemotherapy agents cisplatin and vinorelbine (*Vir*: 10,11,12) as well as gemcitabine plus cisplatin or carboplatin and to be well tolerated by the patients.

Cancer vaccine therapies

Merck KGaA is also investigating an innovative therapeutic cancer vaccine, (BLP25 liposome vaccine), which stimulates the body's immune system to identify and destroy MUC1-expressing tumor cells. Stimuvax is currently in Phase III development in the START (Stimulation Targeted Antigenic Responses To NSCLC) trial, assessing the efficacy and safety of Stimuvax. Over 30 countries will participate in the START trial most of which are now open for enrollment.

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**For more information on Erbitux in colorectal, head & neck and non-small cell lung cancer,
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