Background information

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Non-small cell lung cancer

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Lung cancer is the leading cause of cancer death globally; it kills more people than breast, colon, kidney, liver, melanoma and prostate cancers combined.[i] Each year 1.18 million people die as a result of the disease,[ii] equating to more than 3,000 deaths worldwide every day and approximately two deaths every minute.[iii] The majority of patients with lung cancer are diagnosed when the disease is at an advanced stage and has spread to other parts of the body (known as having 'metastasised').[iv]

What is non-small cell lung cancer (NSCLC)?

Lung cancer is caused by the uncontrolled growth (proliferation) of abnormal cells inside the lung. There are two main forms of the disease, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is the most common form of the disease, accounting for approximately 85% of all cases.[v]

Early-stage NSCLC does not always have obvious symptoms. Therefore, approximately two thirds of patients are not diagnosed until the disease is at an advanced stage,[vi] when the possibility of finding a cure is much smaller. NSCLC can be further divided into adenocarcinoma, squamous cell carcinoma and large cell carcinoma (Figure 1). Adenocarcinoma develops in the outer areas of the lungs and is the most common type of NSCLC.[vii]

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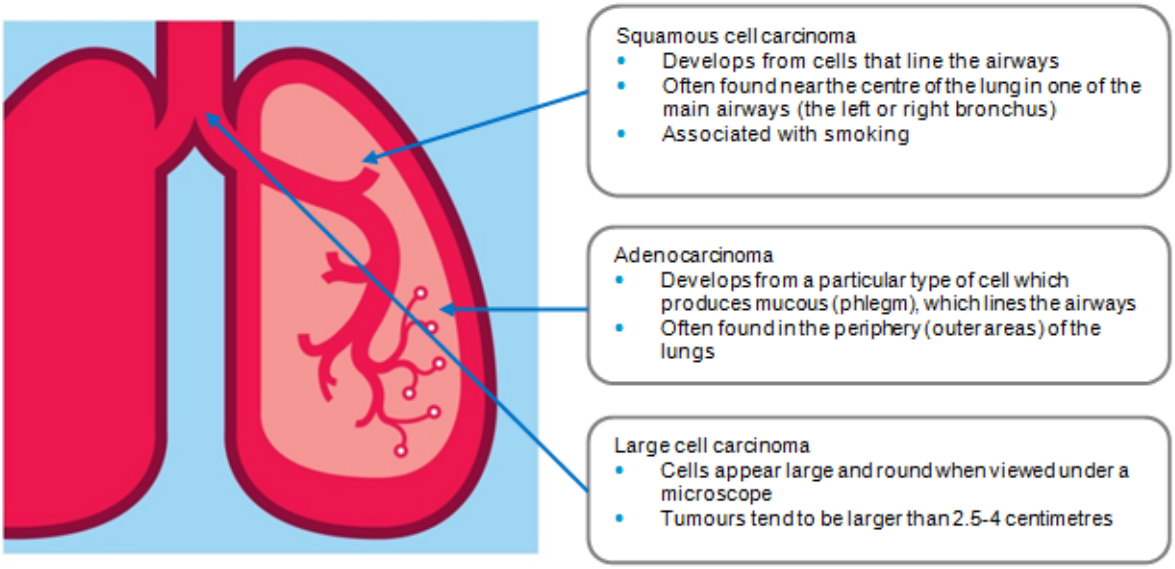

Figure 1: Diagram showing the location of different types of non-small cell lung cancer (NSCLC).

How common is NSCLC?

Lung cancer is one of the most common cancers worldwide, with 1.35 million new cases diagnosed every year.[viii] It is estimated that lung cancer accounts for an average of 20% of all cancer deaths.[ix] Almost half of the cases of lung cancer occur in developing countries, with men being affected more than women (globally, 36 per 100,000 men compared with12 per 100,000 women).[vi]

In Europe, lung cancer is also a leading cause of cancer-related death. In the year 2000, there were approximately 375,000 cases of lung cancer.[x] The average estimated age-standardised incidence per 100,000 populations is 72 for men and 22 for women, across the European Union (25-member states).[xi]

What causes NSCLC?

Lung cancer is caused by abnormal growth and replication of cells. Cell growth and replication is controlled by signalling pathways that relay information from the outside to the inside of cells via specialised antennae, known as 'receptors'.

A type of receptor that is important in NSCLC is called the 'MET' receptor. MET sits on the surface of epithelial and endothelial cells and is activated by a protein called hepatocyte growth factor (HGF). Inappropriate activation of MET receptors leads to over-stimulation of signalling pathways that drives cell growth and replication. This, in turn, can cause normal healthy cells to become cancerous.

Another type of receptor that is important in NSCLC is called the epidermal growth factor receptor (EGFR). EGFR is present on the surface of the cell and is activated when a protein called epidermal growth factor (EGF) binds to it. Binding of EGF to EGFR triggers a signalling pathway inside the cells that tells them to grow and replicate. Genetic defects (mutations) in the EGFR can lead to over-activation of the EGFR pathway and give rise to certain types of cancer. Over-activation of EGFR can also cause cancerous cells to spread from their original location to other parts of the body, and stimulate the formation of new blood vessels, in a process called angiogenesis.

Angiogenesis occurs naturally in the body and involves the growth of new blood vessels during, for example, development and wound healing. Growing lung cancer tumours can release chemicals to encourage this blood vessel growth so that the new blood supply brings them the oxygen and nutrients they need to grow. A protein called VEGF (vascular endothelial growth factor) is the key driver of tumour angiogenesis. Inhibiting the formation of these new blood vessels helps starve the tumour of the essential oxygen and nutrients it needs to grow and spread. By controlling angiogenesis, tumour growth is controlled.

What are the risk factors for developing NSCLC?

There are several factors associated with increased risk of developing NSCLC:

- Smoking is associated with 80% of cases in men and 50% of cases in women[x]
- Passive smoking: There is a 20% increase in the likelihood of developing lung cancer in spouses of smokers[xii]
- A family history of lung cancer[xiii]
- Exposure to asbestos and radon gas[ix]
- Urban and indoor air pollution, particularly in poorly ventilated homes where coal, wood or other solid fuels are regularly burnt[xiv]

What are the symptoms?

Common symptoms of lung cancer are mostly non-specific and can be similar to other illnesses or conditions. Because of this, symptoms are sometimes disregarded and patients do not go to their doctor until their disease has become advanced. Common symptoms of lung cancer include:

- Shortness of breath and/or wheezing
- Chronic cough and/or repeated bouts of bronchitis
- Hoarseness of voice, chest pain
- Loss of weight and appetite for no apparent reason

How is NSCLC treated?

Treatment options vary according to the type, stage, size and location of the cancer in the lung, whether it has spread to other parts of the body, and the physical condition of the patient. In general the treatment options for NSCLC are as follows:

Surgery

Patients with early stage, localised NSCLC may be successfully treated using surgery. Up to two thirds of patients with early stage, localised NSCLC survive for at least five years after diagnosis if treated at this stage, with a proportion of these patients being cured.[xv]

Chemotherapy

The majority of NSCLC cases are diagnosed at an advanced stage,[xvi] when the cancer has already spread to another part of the body. At this stage, the cancer can no longer be successfully removed by surgery alone and chemotherapy is required to treat patients. The most common chemotherapies for the treatment of NSCLC are those which contain platinum, often used in combination with another therapy. Combinations of chemotherapy tend to work better than single drugs. The drugs commonly used include ifosfamide, cisplatin, docetaxel and etoposide. Treatment can be given for four to six cycles. Side effects can accumulate with successive rounds of therapy and can outweigh the benefits achieved with continued treatment.

Biological therapy

Biological therapies (also called targeted therapies) are a relatively new approach to cancer treatment. Biological therapy can include monoclonal antibodies, vaccines and gene therapies. Some types of biological therapy help the body's own immune system to seek out and destroy cancerous cells. Others help stop the progression and spread of cancer directly by preventing the cancerous cells from growing, replicating and surviving.

Biological therapies target cancer-specific processes. These include bevacizumab, erlotinib and gefitinib among others. They have the potential to be more effective than conventional types of treatment (e.g., chemotherapy and radiotherapy) and cause fewer side effects because they are less toxic to healthy, non-cancerous cells.[xvii] Several types of biological therapy exist for the treatment of advanced NSCLC. These are either given as monotherapy or together with other therapies, depending on the various stages of advanced disease and according to their approved label.

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