

# LUNG CANCER

## B A C K G R O U N D E R

1. What is lung cancer?
2. How common is lung cancer?
3. What are the risk factors for lung cancer?
4. What are the signs and symptoms of lung cancer?
5. How is lung cancer diagnosed?
6. What are the available treatment options?

## 1. WHAT IS LUNG CANCER?

Lung cancer is the term used to describe the growth of abnormal cells lining the air passages inside the lung tissue. These cells divide and grow more rapidly than normal cells and combine to form a cluster or tumour.

Lung cancer is not just one disease. There are two main types of lung cancer:

### 1. Non-small cell lung cancer (NSCLC)

NSCLC is the most common form of lung cancer, comprising over 85% of lung cancer cases.<sup>1,2</sup> NSCLC can be further divided into several different subtypes which are determined by the types of cells and the location of the tumour. The different subtypes need to be treated differently. The most common subtypes are outlined below:

- **Adenocarcinoma** (40-50% of NSCLC)<sup>1,2</sup> – both the most common type of lung cancer and the most common form of NSCLC. It develops within the mucus-producing cells in the lining of the airways. Epidermal growth factor receptor (EGFR) mutations are present in approximately 40% of Asian adenocarcinoma NSCLC patients, and in 10-15% of Caucasian patients.<sup>3</sup> This sub-group of patients may benefit from targeted therapies, including EGFR inhibition by tyrosine kinase inhibitors (TKI) or ErbB Family blockers.
- **Squamous-cell carcinoma** (25-40% of NSCLC)<sup>1,2</sup> – develops in the squamous cells that line the airways and tends to spread locally. It is often caused by smoking, and has limited treatment options.
- **Large cell carcinoma** (3-5% of NSCLC)<sup>1,2</sup> – named after the large, rounded cells that are seen when examined microscopically. It is sometimes known as undifferentiated carcinoma and has a high tendency to spread to other parts of the body.
- **Not otherwise specified** (<5% of NSCLC).<sup>1,2</sup>

### 2. Small cell lung cancer (SCLC)

About 14% of all lung cancers are small cell lung cancer.<sup>2</sup> In this type, the cancerous cells are small cells in which the nucleus (the control centre of cells) dominates. SCLC is almost always caused by smoking and generally spreads quickly at an early stage. Due to its aggressive nature, there are only two stages of SCLC: limited disease and extensive disease, and prognosis is generally poor.

# LUNG CANCER

## BACKGROUND

### 2. HOW COMMON IS LUNG CANCER?

Lung cancer is the most common cancer in the world, accounting for 1.8 million new cancer cases each year.<sup>4</sup> It is also the biggest cancer killer in the world with incidence rates higher in men than women and with particularly high prevalence rates seen in Central Eastern and Southern Europe, Northern America and Eastern Asia.<sup>5</sup>

- 1.6 million deaths each year are attributable to lung cancer.<sup>6</sup>
- Overall lung cancer is the cause of 19% of all cancer deaths.<sup>6</sup>
- 13% of all new cases of cancer are lung cancers.<sup>7</sup>
- More than two-thirds of lung cancers are diagnosed at a late stage and only 7% of lung cancer patients survive for at least five years after diagnosis.<sup>8</sup>
- 8 in 10 lung cancer cases occur in people aged 60 and over.<sup>8</sup>
- Recent studies indicate that despite a higher incidence of the disease in men, women are more susceptible to developing lung cancer than men, and female smokers are twice as likely to develop lung cancer as male smokers. Even among non-smokers, women are at higher risk of developing lung cancer than men.<sup>9</sup>

### 3. WHAT ARE THE RISK FACTORS FOR LUNG CANCER?

Cigarette smoking is the primary cause of most lung cancers, contributing to nearly 85% of cases,<sup>10</sup> although many people diagnosed with NSCLC have never smoked.<sup>6</sup> Other causes include prolonged contact with asbestos, radon gas or certain other chemicals. Prior non-malignant (non-cancerous) lung diseases also increase the risk for lung cancer.<sup>11</sup>

### 4. WHAT ARE THE SIGNS AND SYMPTOMS OF LUNG CANCER?

The signs and symptoms of lung cancer may take many years to appear, and are often confused with symptoms of less serious conditions, such as flu or bronchitis. A chronic cough can be an early symptom of lung cancer. Other symptoms can include coughing up blood, shortness of breath, and pain or aching in the shoulder, back, chest or arm (lung cancers may press on nerves, resulting in pain even before they cause a cough or difficulty breathing).

Due to the unspecific nature and the late onset of symptoms, approximately two-thirds of lung cancer patients present in a late, advanced stage when there is a very poor rate of cure.<sup>12-14</sup>

### 5. HOW IS LUNG CANCER DIAGNOSED?

A wide range of diagnostic procedures are used to diagnose lung cancer. These include:

#### **Imaging studies**

X-rays, ultrasound, CAT (computerised axial tomography) scans, MRI (magnetic resonance imaging) scans, PET (positron emission tomography) scans and bone scans.

#### **Sputum tests**

Samples of mucus from the lower airways (sputum) are checked for cancer cells.

# LUNG CANCER

## BACKGROUND

### **Blood tests**

Baseline blood tests, which include renal and liver function tests, calcium and lactate dehydrogenase (LDH) levels, which can indicate the existence and severity of acute or chronic tissue damage.

### **Biopsies**

A biopsy (sample of tumour tissue) is taken for testing and is examined under a microscope by a doctor who can determine if this tissue is cancerous (malignant) or benign (not malignant). If the cells are cancerous, they may be studied further to detect the rate of growth and extent of the cancer.

### **Biomarker testing**

A biomarker is a naturally occurring molecule, gene, or characteristic by which a particular process, condition or disease can be identified. For example, by conducting biomarker testing, doctors can find out what genetic mutations are present in a tumour.

## **6. WHAT ARE THE AVAILABLE TREATMENT OPTIONS?**

There are various forms of treatment used in the management of lung cancer that can be used separately or in combination – surgery, radiation, chemotherapy and a newer form of treatment: targeted therapy. However, SCLC and NSCLC behave and respond to treatment quite differently. To determine the most appropriate treatment, cancers are ‘staged’ to determine the severity of a patient’s disease. The different stages and subtypes of NSCLC are treated in different ways; however, surgery offers the best patient outcome for those with early-stage NSCLC.

Targeted therapy is a newer form of treatment available to advanced NSCLC patients. It works by recognising specific targets in cancer cells and interfering with cancer cell growth and division in different ways and at various points during the development, growth and spread of cancer. Rather than having a broad effect, many of these therapies focus on specific proteins that are involved in signalling processes. By blocking the signals that tell cancer cells to grow and divide uncontrollably, targeted cancer therapies can help to stop the growth and division of cancer cells.

By focusing on molecular and cellular changes that are specific to the relevant subtype of lung cancer, these ‘targeted’ therapies may be more effective than current treatments and less harmful to normal cells, thereby reducing unwanted treatment side effects.

In order to determine how well a treatment is working, the following outcomes are sometimes monitored:

- Overall survival (OS) – the length of time patients are still alive for after the start of treatment
- Progression-free survival (PFS) – the length of time before the tumour begins to grow again after the start of treatment
- Patient reported outcomes (PRO) – a questionnaire is given to patients enrolled in a clinical study to assess the improvement in disease related symptoms whilst taking the medicine
- Quality of life (QoL) – how a patient’s life is impacted whilst taking the medicine. For example, the impact it has on their working life.

# LUNG CANCER

## B A C K G R O U N D E R

Stage	Extent	Treatment
Stage I	Cancer is present only in one part of the lung and has not spread to lymph nodes	The tumour can often be removed with surgery. Chemotherapy is sometimes used after surgery (adjuvant chemotherapy) to reduce recurrence. Chemotherapy may sometimes be given before surgery and/or radiotherapy to shrink the tumour. This is known as neo-adjuvant chemotherapy.
Stage II	Cancer has spread to nearby lymph nodes or nearby tissues, e.g. chest wall	It may also be possible to remove stage II NSCLC with surgery, and chemotherapy is often given following surgery or radiotherapy to reduce the risk of recurrence.
Stage III	Cancer has spread more extensively within the chest and, generally, to the major lymph nodes. Large tumours that have invaded surrounding organs and lymph nodes outside the chest	Although surgery may be considered as an option at this stage, this is often not possible because the cancer may have spread too far. Chemotherapy, on its own or combined with radiotherapy, may be given before an operation. If surgery is not possible, radiotherapy can be given instead. In some cases, chemotherapy given on its own, or in combination with radiotherapy, will be the only treatment used. For some patients with locally advanced or metastatic NSCLC, newer targeted treatments may also be used.

# LUNG CANCER

## BACKGROUND

Stage IV	Cancer has spread to distant parts of the body, e.g. to the liver or bones (metastases)	The aim is to control symptoms and maintain a good quality of life for as long as possible. Radiotherapy may be used to shrink the cancer and reduce symptoms such as pain. Chemotherapy may be given before or after radiotherapy and may shrink the cancer and improve quality of life for some people. For some patients with locally advanced or metastatic NSCLC, newer targeted treatments may also be used.
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