

LUNG CANCER

Facts and figures

In 2012, more than 1.8 million people were diagnosed with lung cancer, making it the most common form of cancer worldwide.¹

Leading cause of cancer deaths in men¹



Second most common cause of cancer deaths in women¹

Lung cancer claims **1.59 million lives each year**, and almost half of all cases are in developing countries.^{1,2} Only **one in ten patients** with lung cancer are alive five years after diagnosis.³ This high mortality is mainly due to the late manifestation of symptoms. Common symptoms at the time of diagnosis include new or persistent cough, breathlessness, chest pain, and coughing up blood.⁴

As a result:

- **The majority of patients** are diagnosed when lung cancer is already metastatic⁵
- **Only 15%** are diagnosed while the cancer is still localised in the lung⁶

More than one disease

Non-small cell lung cancer (NSCLC) accounts for **80-85% of all cases** of lung cancer,⁷ and **up to half of NSCLC cases** are associated with known mutations.⁸ Identification of mutations is now widely used when assessing treatment options.⁹ Common NSCLC mutations occur in:

EGFR

Epidermal growth factor receptor protein, thought to play a role in cancer cell growth. EGFR mutations occur in 10-15% of patients in Europe,⁹ 15% of patients in the US¹⁰ and 30-40% of patients in Asia.¹¹ Research has also shown that patients with EGFRm NSCLC may develop resistance to targeted treatments; nearly two-thirds who experience disease progression after treatment develop the T790M resistance mutation.¹²

KRAS

Kirsten rat sarcoma gene, involved in regulating cell division. KRAS mutations can cause cells to grow, divide and copy themselves in an uncontrolled manner and occur in about 15-25% of patients.^{13,14,15}

ALK

Anaplastic lymphoma kinase gene, also involved in cell growth and division. When rearranged, ALK genes can result in tumour growth, which occurs in roughly 3-7% of patients.^{16,17}

MET

Mesenchymal-epithelial transition gene, involved in protein creation. The MET gene can create problems for cells when it mutates and/or undergoes gene amplification, which occurs in 2-4% of patients.^{8,18}

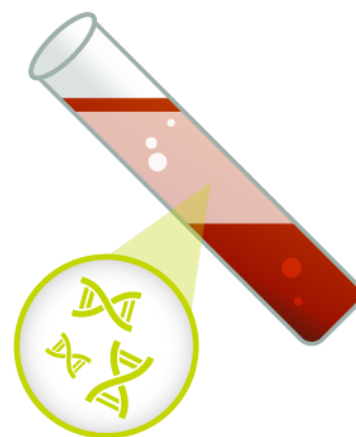
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Developments in tumour testing

Typically, physicians use tumour samples such as biopsies to diagnose advanced NSCLC, assess mutation status, and identify appropriate patients for targeted treatment.¹⁹ Obtaining a tumour tissue sample is not always feasible where patients are too ill or the tumour is too small or inaccessible.¹⁹ Circulating tumour DNA (ctDNA) tests are blood tests that detect fragmented tumour DNA circulating in the blood.^{20,21} As such, this method is emerging as a popular non-invasive, low-risk alternative to tumour biopsy.²⁰⁻²²

While detection rates can be influenced by various factors such as limitations in DNA extraction and mutation testing methods, recent studies indicate that EGFR mutations identified in ctDNA are highly predictive of EGFR mutation-positive tumours. This approach can be used to identify molecular mechanisms of acquired resistance to EGFR-TKIs and direct treatment approaches.^{19,21,23}

*It is important for physicians to note that ctDNA mutation testing is associated with a risk of false negative. Any negative results should be confirmed by testing a tumour sample, if it can be obtained.



Stages of disease and treatment

Lung cancer is staged on a scale of I to IV, according to the severity of disease.²⁴ Patients in stages (Stages I-III B) can be treated with surgical resection and/or a combination of radiotherapy and chemotherapy.^{25,26} Treatments in Stage III can include platinum-based chemotherapy regimens and agents that target specific gene mutations or alterations.^{25,26}

Recommended treatments for patients with Stage IV lung cancer include multiple cycles of a platinum-based chemotherapy regimen,^{27,28} and tyrosine kinase inhibitors (TKIs) for a proportion of patients whose tumours have EGFR-activating mutations with or without secondary T790M mutations, or for those with advanced, pre-treated ALK-positive NSCLC.²⁹⁻³² Immunotherapy agents are now also demonstrating increasingly promising response rates across certain groups of patients; however, even as targeted therapies and checkpoint inhibitors continue to improve outcomes, there are still limited therapeutic options for the majority of patients.^{32,33}

Complications

The prognosis is poor for patients whose cancer has spread to other areas of the body,^{4,5} especially for those who develop central nervous system (CNS) metastases such as brain metastases or leptomeningeal (LM) disease.^{34,35}

Brain metastases occur when tumour cells spread from their original site and grow in the brain. Lung cancer accounts for approximately 20% of cases.³⁶



LM disease is much rarer, and occurs when the cancer spreads to the meninges (membranes) surrounding the brain and spinal cord. Lung cancer is the second most common tumour associated with LM.³⁵

Lung cancer is more likely to spread to the CNS than many other types of cancer; brain metastases are found in 10% of patients at the time of diagnosis, and approximately **40% of all patients** will develop them over the course of their disease.³⁷

Both brain metastases and LM are difficult to treat.³⁴⁻³⁶ Radiotherapy, surgery and chemotherapy rarely have a durable effect on CNS metastases, and can cause serious side effects.^{35,36} Treatment with some EGFR-TKIs is challenging due to their poor penetration of the blood-brain barrier, which makes it difficult for them to reach the central nervous system.³⁸⁻⁴⁰

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