ABOUT LUNG CANCER

Global burden in 2020¹

2.2M



of all cancer deaths are caused by lung cancer

19% of patients are alive five years after diagnosis²

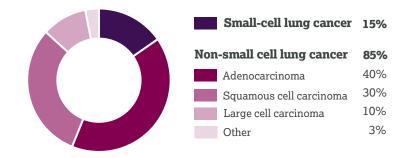
Types of lung cancer³

Non-small cell lung cancer (NSCLC)

NSCLC originates from the larger cells in the lungs. such as epithelial cells lining the lung airways or mucus-producing cells.4

Small cell lung cancer (SCLC)

SCLC is less common, and originates from small, hormone-releasing cells. SCLC is more aggressive and fast-growing compared to NSCLC.5



Stages of disease

Identifying the stage is important for doctors to determine patients' prognosis and help assess treatment options. NSCLC is staged on a **scale of I to IV***, according to the severity of disease. In addition to the traditional four stages, SCLC is divided into two groups: **limited stage (I-III)** and **extensive stage (IV)**.

Stage I NSCLC

Tumour has not spread beyond the lungs and is less than 5cm wide.8



Five-year survival rate: 68-92%8

Stage II NSCLC

Tumour can be between 5 and 7 cm, and is categorised as Stage IIB once it has reached the lymph nodes.8



Five-year survival rate: 53-60%8

Stage III NSCLC

Stage III lung cancer is often referred to as locally advanced disease. The tumour may have spread outside the lung and can be of any size.9



Divided into 3 sub-categories (IIIA, IIIB and IIIC), defined by how much the cancer has spread locally and the possibility of surgery.8

Five-year survival rate: 13-36%¹⁰

*Staging is more complex than the examples shown here

Stage IV NSCLC

The most advanced form of lung cancer, often referred to as metastatic disease. Tumour has metastasised (spread) beyond the lung throughout the body.6



Five-year survival rate: 0-10%11

Diagnosing and treating patients in earlier stages of disease can maximise the potential for long-term disease remission and the possibility of cure.



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The importance of biomarker testing

Lung cancer is a **diverse disease**, characterised by a variety of different genetic and molecular characteristics. 12 These characteristics, known as biomarkers, can serve as indicators of various types of cancer and many promote tumour growth. Some biomarkers arise as a result of **point mutations** (changes within genes), and some reflect altered expression. 12-14

Up to

of NSCLC cases are 50% associated with biomarkers¹²



Doctors use tumour samples to diagnose NSCLC, and test for biomarker mutation status and levels of biomarker expression. Biomarker testing is critical to learning more about each patient's tumour type and can be used to help determine treatment options. Based on the test results, patients may be matched with targeted therapies aimed at specific biomarkers present in their genetic profile. 15

Established biomarkers

EGFR mutations

The **epidermal growth factor receptor** is a protein that helps cells grow. EGFR mutations can cause higher than normal amounts of the protein on cancer cells, allowing them to grow more rapidly. 16

Approximately 10-15% of patients in the US and Europe, and 30-40% of patients in Asia have EGFR mutations. 17-19

10-40% of patients

MET gene alterations

The **MET** gene is involved in protein creation. The MET gene can drive growth of tumour cells when it mutates, is amplified or if overexpression occurs.²⁰

- Exon 14 mutations: 3-4% of patients²¹
- Amplification: 1-6% of patients²¹
- Overexpression: 15-70% of patients²²

Studies suggest that MET gene alterations are a key mechanism of acquired resistance to EGFR targeted therapies.22

1-70% of patients

BRAF mutations

The BRAF gene makes a protein that helps control cell growth. Mutations in the BRAF gene can cause uncontrolled cell growth, leading to cancer. 23,24

1.5-3.5% of patients

ALK mutations

The **anaplastic lymphoma kinase** gene is involved in cell growth and division. When rearranged, ALK genes can result in tumour growth. 25-27

4-7% of patients

KRAS mutations

The **kirsten rat sarcoma gene** is involved in regulating cell division. KRAS mutations can cause uncontrolled cell growth, division and duplication. KRAS mutations occur in **5-15% of patients in Asia** and 25-50% of patients in Western populations. 28,29

5-50% of patients

PD-L1 expression

Programmed death-ligand 1 is a protein expressed on the surface of cancer cells that helps them evade the immune system. For patients whose cancer is not associated with a known mutation, abnormal PD-L1 expression may help characterise their disease. 15,30

19-100% of tumours have abnormal PD-L1 expression

Exploratory targets

HER2 gene alterations

Human epidermal growth factor receptor 2 is a protein that regulates cell growth. HER gene alterations, such as mutations or overexpression, can facilitate excessive or uncontrolled growth that may promote the formation of tumours.31

TROP2 overexpression

Trophoblast cell-surface antigen 2 is a transmembrane glycoprotein involved in cell selfrenewal, proliferation, invasion and survival. TROP2 expression has been associated with poor overall and disease-free survival in several types of solid tumors.32,33



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References

- World Health Organization. Globocan Fact Sheet: All cancers. Available at https://gco.iarc.fr/today/data/factsheets/cancers/39-All-cancers-fact-sheet.pdf. Accessed May 2021.
- American Society of Clinical Oncology (ASCO). Lung Cancer Non-Small Cell: Statistics. Available at https://www.cancer.net/cancertypes/lung-cancer-non-small-cell/statistics. Accessed May 2021.
- 3. LUNGevity Foundation. Types of Lung Cancer. Available at https://lungevity.org/for-patients-caregivers/lung-cancer-101/types-of-lung-cancer. Accessed May 2021.
- 4. American Society of Clinical Oncology (ASCO). Lung Cancer Non-Small Cell: Introduction. Available at http://www.cancer.net/cancer-types/lung-cancer-non-small-cell/introduction. Accessed May 2021.
- 5. American Society of Clinical Oncology (ASCO). Lung Cancer Small Cell: Introduction. Available at https://www.cancer.net/cancer-types/lung-cancer-small-cell/introduction. Accessed May 2021.
- American Cancer Society. Non-Small Cell Lung Cancer Stages. Available at https://www.cancer.org/cancer/lung-cancer/detection-diagnosis-staging/staging-nsclc.html. Accessed May 2021.
- 7. Go2 Foundation for Lung Cancer. Types of Lung Cancer. Available at https://go2foundation.org/what-is-lung-cancer/types-of-lung-cancer/. Accessed May 2021.
- 8. Goldstraw P, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM. J Thorac Oncol. 2015; 11(1): 39-51.
- 9. Cancer Research UK. Stage 3. Available at https://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/stage-3. Accessed May 2021.
- 10. Provencio M, et al. Inoperable stage III non-small cell lung cancer: Current treatment and role of vinorelbine. J Thorac Oncol. 2011; 3: 197-204.
- GlobalData. Non-Small Cell Lung Cancer (NSCLC) Epidemiology Forecast to 2025. Available at https://store.globaldata.com/report/gdhcer132-16--epicast-report-non-small-cell-lung-cancer-nsclc-epidemiology-forecast-to-2025/. Accessed May 2021.
- 12. Korpanty G, et al. Biomarkers that currently affect clinical practice in lung cancer: EGFR, ALK, MET, ROS-1, and KRAS. Frontiers in Oncology. 2014(4).
- National Cancer Institute (NCI). NCI Dictionary of Cancer Terms Biomarker. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=45618. Accessed May 2021.
- 14. Encyclopaedia Britannica. Point mutation. Available at https://www.britannica.com/science/point-mutation. Accessed May 2021.
- 15. Awad M and Hammerman P. Durable Responses With PD-1 Inhibition in Lung and Kidney Cancer and the Ongoing Search for Predictive Biomarkers. *J Clin Oncol.* 2015; 33.
- National Cancer Institute. NCI Dictionary of Cancer Terms -- EGFR. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/search/EGFR/?searchMode=Begins. Accessed September 2020.
- 17. Szumera-Ciećkiewicz A, *et al.* EGFR Mutation Testing on Cytological and Histological Samples in Non-Small Cell Lung Cancer: a Polish, Single Institution Study and Systematic Review of European Incidence. *Int J Clin Exp Pathol.* 2013:6;2800-12.
- 18. Keedy VL, *et al.* American Society of Clinical Oncology Provisional Clinical Opinion: Epidermal Growth Factor Receptor (EGFR) Mutation Testing for Patients with Advanced Non-Small-Cell Lung Cancer Considering First-Line EGFR Tyrosine Kinase Inhibitor Therapy. *J Clin Oncol.* 2011:29;2121-27.
- 19. Ellison G, et al. EGFR Mutation Testing in Lung Cancer: a Review of Available Methods and Their Use for Analysis of Tumour Tissue and Cytology Samples. *J Clin Pathol.* 2013:66;79-89.
- 20. Landi L, et al. MET overexpression and gene amplification in NSCLC: a clinical perspective. Lung Cancer: Targets and Therapy. 2013;4:15-25.
- 21. Wolf J, et al. Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. NEJM. 2020: 383: 944-957.
- 22. Zhang Z, et al. Impact of MET alterations on targeted therapy with EGFR-tyrosine kinase inhibitors for EGFR-mutant lung cancer. Biomark Res. 2019: 7:27.
- National Cancer Institute (NCI). NCI Dictionary of Cancer Terms BRAF gene. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/braf-gene. Accessed May 2021.
- 24. Leonetti A, *et al.* BRAF in non-small cell lung cancer (NSCLC): Picklaxing another brick in the wall. *Cancer Treatment Reviews*. 2018; 66: 82-94.
- 25. National Cancer Institute (NCI). NCI Dictionary of Cancer Terms ALK gene. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/def/alk-gene. Accessed May 2021.
- 26. Chia P, et al. Prevalence and natural history of ALK positive non-small-cell lung cancer and the clinical impact of targeted therapy with ALK inhibitors. Clinical Epidemiology. 2014; 6: 423-432.
- 27. Zhao F, et al. Clinicopathological Characteristics of Patients with Non-Small-Cell Lung Cancer Who Harbor EML4-ALK Fusion Gene: A Meta-Analysis. PLOS ONE. 2015; 1-13.
- 28. Boch C, et al. The frequency of EGFR and KRAS mutations in non-small cell lung cancer (NSCLC): routine screening data for central Europe from a cohort study. BMJ Open. 2013;3(4).
- 29. Medscape. Genetics of Non-Small Cell Lung Cancer. Available at https://emedicine.medscape.com/article/1689988-overview. Accessed May 2021.
- 30. Mei J, et al. PD-1/PD-L1 expression in non-small-cell lung cancer and its correlation with EGFR/KRAS mutations. *Journal of Cancer Biology & Therapy*. 2015;17(4): 407-413.
- 31. National Cancer Institute (NCI). NCI Dictionary of Cancer Terms HER2 gene. Available at https://www.cancer.gov/publications/dictionaries/cancer-terms/search/her2/?searchMode=Begins. Accessed May 2021.
- 32. Shvartsur A, *et al.* Trop2 and its overexpression in cancers: regulation and clinical/therapeutic implications. *Genes Cancer.* 2015; 6(3-4): 84-105.
- 33. Inamura K, *et al* Association of tumor TROP2 expression with prognosis varies among lung cancer subtypes. *Oncotarget.* 2017; 8(17): 28725-28735.