

# Understanding EGFR Mutations in Non-Small Cell Lung Cancer (NSCLC)

## ABOUT METASTATIC LUNG CANCER

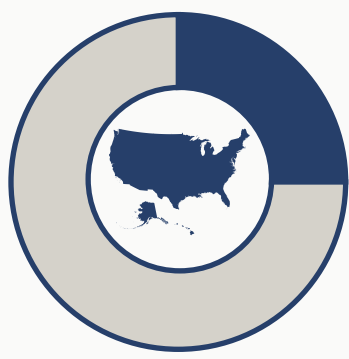
Lung cancer is a cancer that starts in a person's lungs. Metastatic cancer means cancer cells have spread to other parts of the body.

Lung cancer may spread to other parts of the body, including bones, adrenal glands, the brain, and the liver. People with lung cancer whose cancer cells have spread to these places have metastatic cancer.

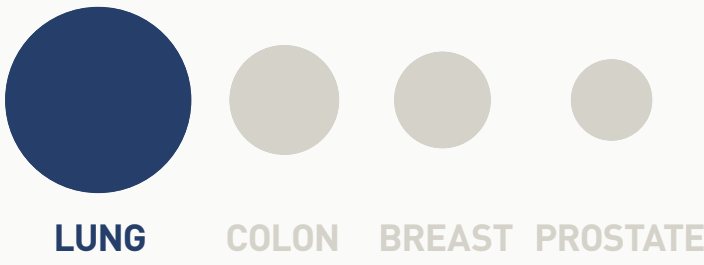
LUNG CANCER STATS AT A GLANCE



Globally, lung cancer is the **leading cause of cancer deaths**, killing nearly 1.8 million people worldwide each year.<sup>1</sup>



In the U.S., lung cancer is the **2nd most common cancer** (not counting skin cancer) and the leading cause of cancer death among both men and women, accounting for **almost 25% of all cancer deaths**.<sup>2</sup>



Every year, **more people die of lung cancer** than of **colorectal, breast, and prostate cancers combined**.<sup>2</sup>

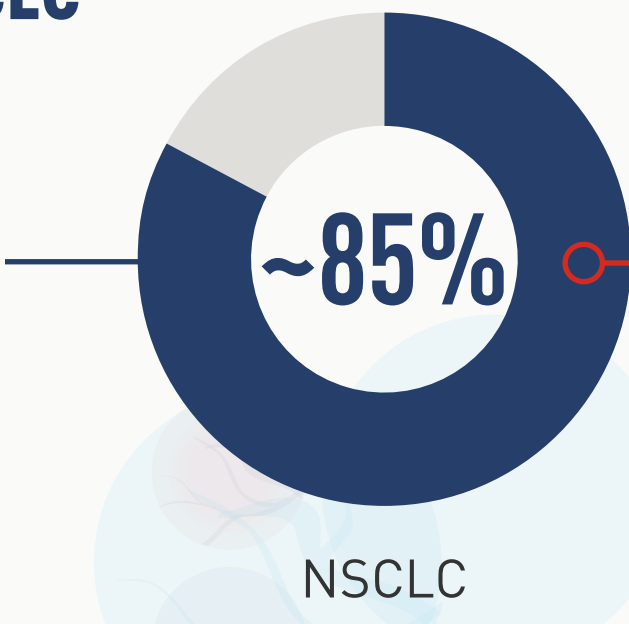


135,720 DEATHS

The American Cancer Society estimates that in 2020, there will be about **228,820 new cases** of lung cancer; about **135, 720 deaths** from lung cancer in the U.S.<sup>2</sup>

## ABOUT METASTATIC NSCLC

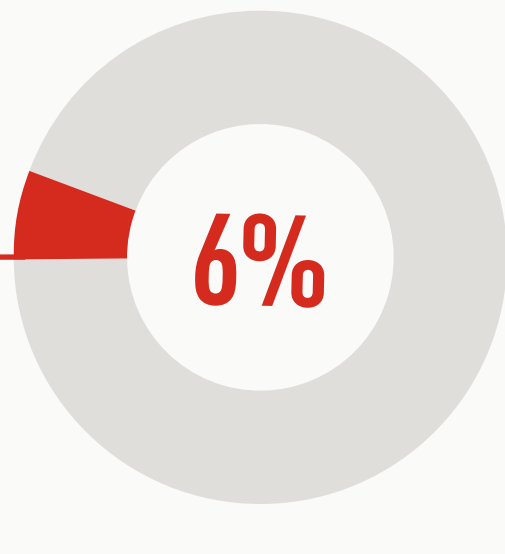
NSCLC is the most common type of lung cancer accounting for about 85% of all lung cancers.<sup>3</sup> Metastatic NSCLC is a very difficult-to-treat cancer with a poor prognosis.<sup>4</sup>



NSCLC



Those who present with advanced or metastatic disease at diagnosis of NSCLC<sup>5</sup>



The five-year survival rate for metastatic NSCLC<sup>6</sup>

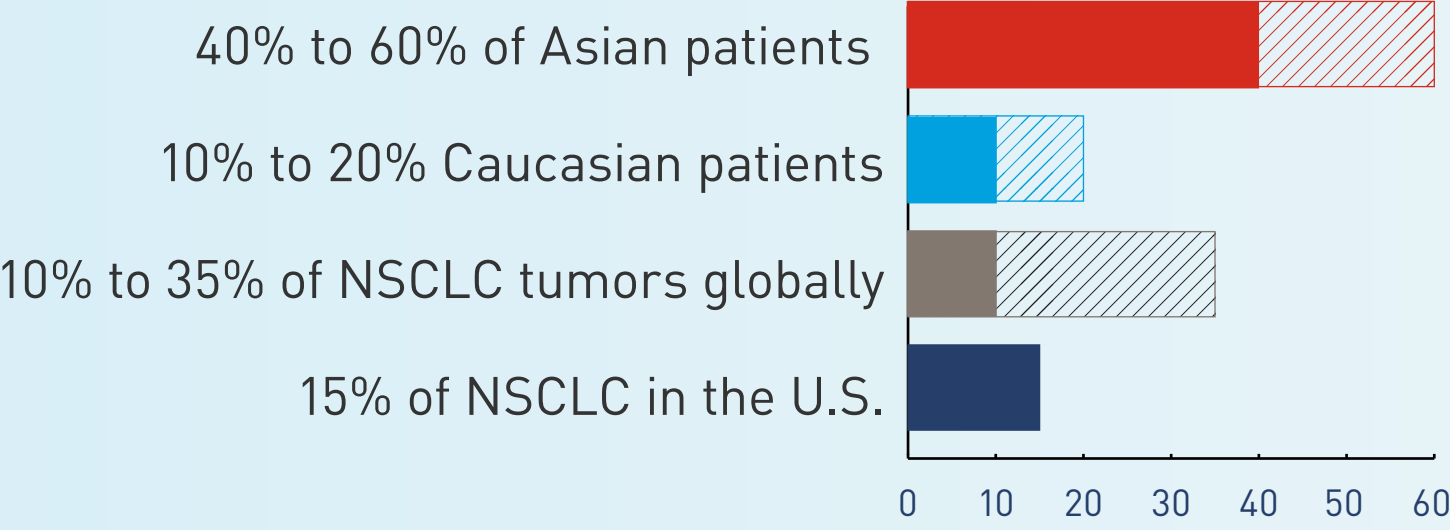
## WHAT IS EGFR?

**Epidermal Growth Factor Receptor**

EGFR is a protein that helps cells grow and divide.

When the EGFR gene is mutated it can cause the protein to be overactive, causing cells to grow and divide more quickly.

Activating EGFR mutations are found in:<sup>8, 9, 10, 11, 12</sup>



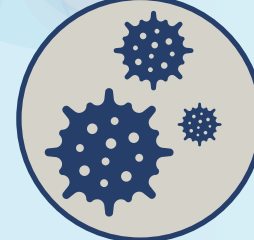
Regardless of ethnicity, these mutations are more commonly present in:<sup>13, 14</sup>



Females

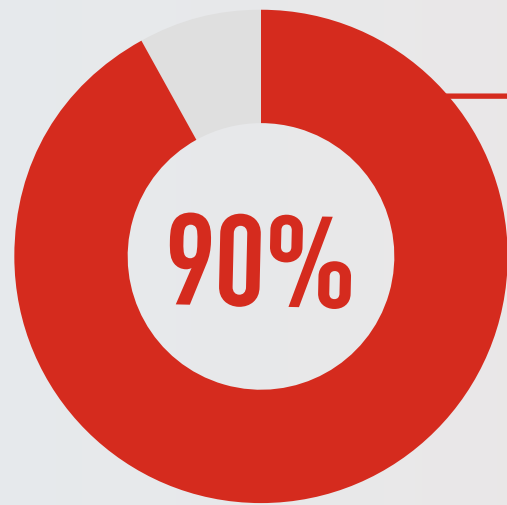


Non-smokers



Those who have adenocarcinoma histology

## MOST COMMON ACTIVATING EGFR MUTATION SUBTYPES

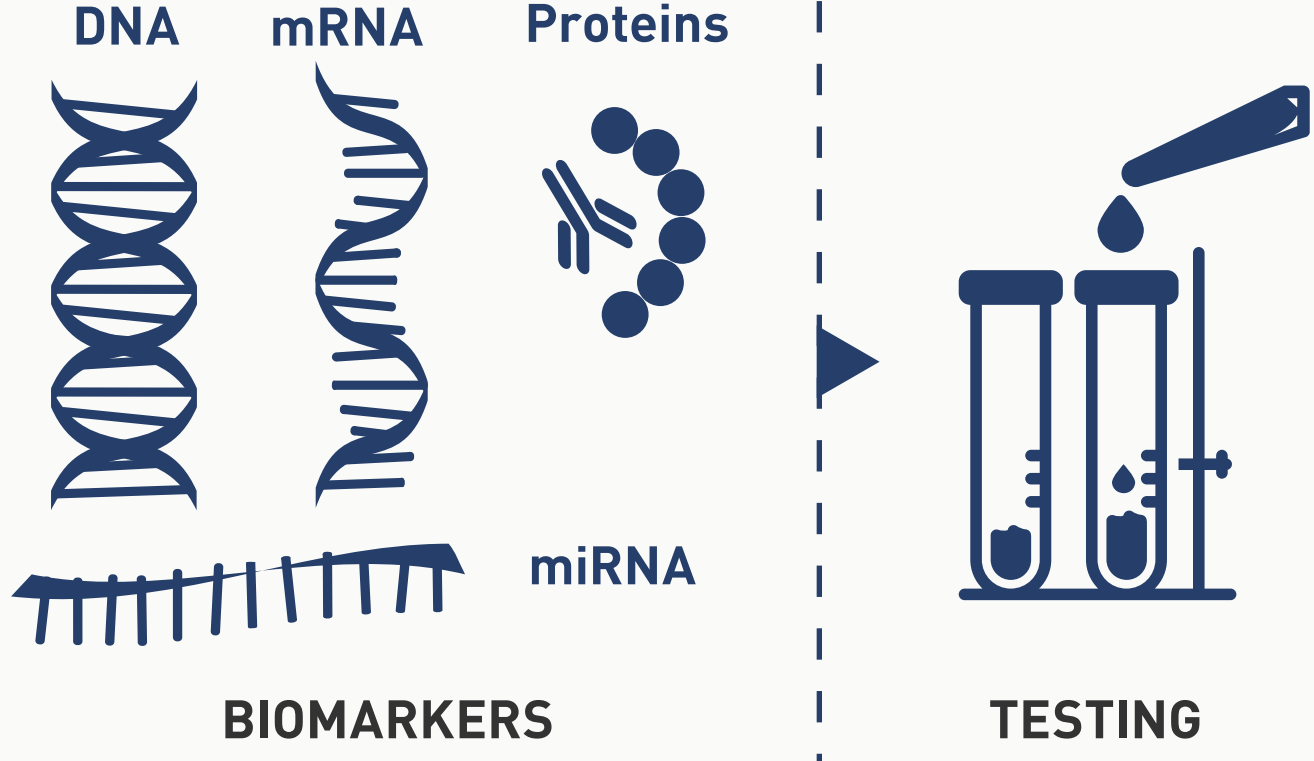


**19 & 21:** The most common activating EGFR mutations are deletions within exon 19 and a substitution in exon 21. These mutations are present in 90% of EGFR-mutated NSCLC tumors.<sup>15</sup>

## HOW ARE CERTAIN NSCLC MUTATIONS IDENTIFIED

The best way to know if a cancer has an alteration that can be treated is to **talk to a doctor about getting tested for all treatable biomarkers**.<sup>16</sup> A biomarker test is a type of genetic test that can tell the doctor a lot about the cancer's DNA.<sup>17, 18</sup> Certain biomarker tests require a doctor to biopsy the tumor, which means removing some tissue for testing.<sup>19, 20</sup> These tests help oncologists develop a treatment plan for their patients. Knowing what is driving the cancer can help the patient and his or her doctor choose the right treatment.<sup>16</sup>

\*If a tumor has been biopsied previously, some tissue may already be available for testing.



## AN IMPORTANT TREATMENT GOAL IS TO EXTEND THE TIME PATIENTS LIVE WITHOUT THEIR DISEASE GETTING WORSE.<sup>21</sup>

## TREATMENT OPTIONS FOR EGFR-MUTATED METASTATIC NSCLC<sup>7, 22</sup>

Treatment options depend on where the cancer has spread, the number of tumors, and overall health.



**Chemotherapy:** Reserved for when most options have been used, limited by its toxicity.



**Radiation therapy:** Uses high-energy rays or particles to kill cancer cells.



**Surgery:** Used to remove the cancer at an early stage and is the best chance for a cure. May be used for limited lesions in advanced or metastatic disease.

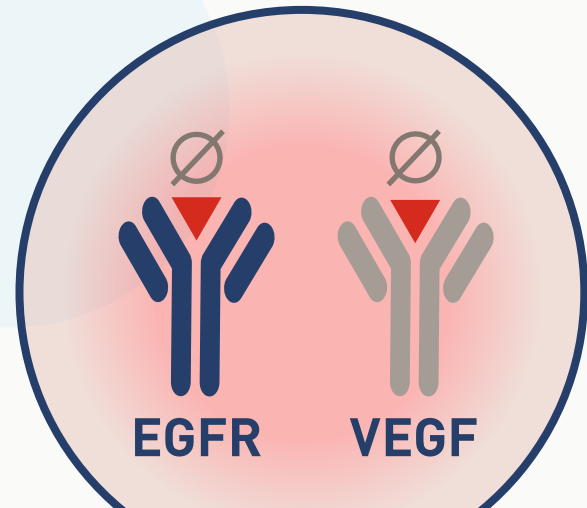


**EGFR tyrosine kinase inhibitors (TKIs):** Block the signal from EGFR that tells the cells to grow. EGFR is a protein on the surface of cells and helps cells grow and divide. When the EGFR gene is mutated, it can cause the protein to be overactive, causing cells to grow and divide more quickly.



**Angiogenesis inhibitors:** Block the formation of new blood vessels. Tumors need oxygen and nutrients, which are delivered through the blood, in order to grow. They get these nutrients through the development of new blood vessels, which is a process called angiogenesis.

**DYK:** Research has shown that blocking both the EGFR pathway and another pathway, known as VEGF, could lead to positive outcomes in patients with EGFR mutations.<sup>10, 23, 24</sup>



## METASTATIC EGFR-MUTATED NSCLC IS A SERIOUS AND LIFE-THREATENING DISEASE.

There is no cure for this disease and all patients will eventually develop disease progression on current therapy, which is why different treatment options are necessary. Although metastatic cancer is a more severe stage, there are treatment options available to help.

## TO LEARN MORE, VISIT:



## REFERENCES

1. International Agency for Research on Cancer. 2018 Lung Cancer Fact Sheet. Available at: <http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>. Accessed April 23, 2020.
2. American Cancer Society. Key Statistics for Lung Cancer. Available at: <https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html>. Accessed April 23, 2020.
3. American Cancer Society. What is non-small cell lung cancer? Available at: <http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer>. Accessed April 23, 2020.
4. American Cancer Society. Non-Small Cell Lung Cancer Survival Rates, by Stage. Available at: <http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-survival-rates>. Accessed April 23, 2020.
5. Riess, J. Shifting Paradigms in Non-Small Cell Lung Cancer: An Evolving Therapeutic Landscape Supplement. *Am J Manag Care*. 2013;19:S390-S397.
6. Cancer.Net. Lung Cancer – Non Small Cell: Statistics. Available at: <https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics>. Accessed April 23, 2020.
7. American Cancer Society. Targeted Therapy for Non-Small Cell Lung Cancer. Available at <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/targeted-therapies.html>. Accessed April 23, 2020.
8. Girard N. Optimizing outcomes in EGFR mutation-positive NSCLC: which tyrosine kinase inhibitor and when? *Future Oncol*. 2018 May;14(11):1117-1132. doi: 10.2217/fon-2017-0636.
9. Hirsh V. Turning EGFR mutation-positive non-small-cell lung cancer into a chronic disease: optimal sequential therapy with EGFR tyrosine kinase inhibitors. *Ther Adv Med Oncol*. 2018 Jan 22;10:1758834017753338. doi:10.1177/1758834017753338.
10. National Comprehensive Cancer Network. NCCN guidelines non-small cell lung cancer. Version 2. 2020. Available from: [https://www.nccn.org/professionals/physician\\_gls/pdf/nscl.pdf](https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf).
11. Dong L, Lei D, Zhang H. Clinical strategies for acquired epidermal growth factor receptor tyrosine kinase inhibitor resistance in non-small-cell lung cancer patients. *Oncotarget*. 2017 Sep 8; 8(38): 64600-64606.
12. Li Y, Appiari A, Pattipaka T, Feyereislova A, Cassidy A, Ganti AK. Real-world management of patients with epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer in the USA [published correction appears in *PLoS One*. 2019 Feb 20;14(2):e0212831]. *PLoS One*. 2019;14(1):e0209709. Published 2019 Jan 4. doi:10.1371/journal.pone.0209709.
13. Midha A, Dearden S, McCormack R. EGFR mutation incidence in non-small-cell lung cancer of adenocarcinoma histology: a systematic review and global map by ethnicity (mutMapII). *Am J Cancer Res*. 2015 Aug 15;5(9):2892-911.
14. Ladanyi M, Pao W. Lung adenocarcinoma: guiding EGFR-targeted therapy and beyond. *Mod Pathol*. 2008 May;21 Suppl 2:S16-22. doi: 10.1038/modpathol.3801018.
15. Murray S, Dahabreh IJ, Linardou H, Manoloukos M, Bafaloukos D, Kosmidis P. Somatic mutations of the tyrosine kinase domain of epidermal growth factor receptor and tyrosine kinase inhibitor response to TKIs in non-small cell lung cancer: an analytical database. *J Thorac Oncol*. 2008;3(8):832-839.
16. Gregg JP, Li T, Yoneda KY. Molecular testing strategies in non-small cell lung cancer: optimizing the diagnostic journey. *Transl Lung Cancer Res*. 2019;8(3):286-301.
17. Committee on Policy Issues in the Clinical Development and Use of Biomarkers for Molecularly Targeted Therapies; Board on Health Care Services; Institute of Medicine; National Academies of Sciences, Engineering, and Medicine.
18. Graig LA, Phillips JK, Moses HL, eds. Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine. Washington, DC: National Academies Press (US); 2016: 1-21. Accessed April 23, 2020.
19. Biopsy: what you need to know. Medical News Today. [https://www.medicalnewstoday.com/articles/174043.php#what\\_is\\_a\\_biopsy](https://www.medicalnewstoday.com/articles/174043.php#what_is_a_biopsy). Accessed February 6, 2020.
20. Cheung AHK, Chow C, To KF. Latest development of liquid biopsy. *J Thorac Dis*. 2018;10:S1645-S1651.
21. Fallowfield LJ, Fleissig A. The value of progression-free survival to patients with advanced stage cancer. *Nat Rev Clin Oncol*. 2012;9(1):41-47.
22. American Cancer Society. Treatment Choices for NSCLC By State. Available at <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/by-stage.html>. Accessed on April 15, 2020.
23. Naumov GN, Nilsson MB, Cascone T, Briggs A, Straume O, Akslen LA, et al. Combined vascular endothelial growth factor receptor and epidermal growth factor receptor (EGFR) blockade inhibits tumor growth in xenograft models of EGFR inhibitor resistance.  *Clin Cancer Res*. 2009;15(10):3484-3494.
24. Xu L, Nilsson MB, Saintigny P, Cascone T, Herynk MH, Du Z, et al. Epidermal growth factor receptor regulates MET levels and invasiveness through hypoxia-inducible factor-1alpha in nonsmall cell lung cancer cells. *Oncogene*. 2010;29(18):2616-2627.

