

NSCLC Disease State

LUNG CANCER

STATISTICS >



3rd
Most common cancer in the US

SIGNS, SYMPTOMS, AND RISK FACTORS >

80%–90%

of lung cancer deaths in the US are linked to cigarette smoking

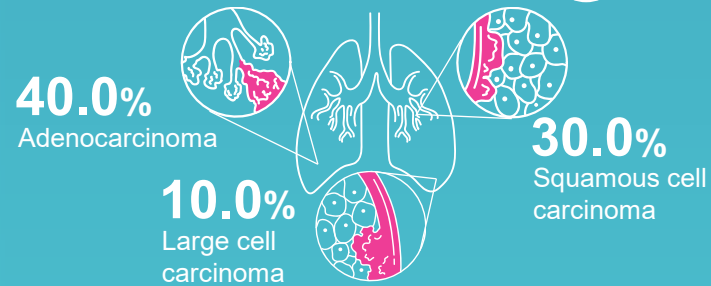


SUBTYPES >



NSCLC

SUBTYPES AND LOCATION >



DISEASE CLASSIFICATION AND SURVIVAL >

NSCLC is classified in stages **I to IV**

5-year relative survival rate **≈ 6.4%** at diagnosis for metastatic disease

METASTATIC DISEASE >



ONCOGENIC DRIVERS >

In adenocarcinoma, about

60%

of patients have 1 known oncogenic driver



In squamous cell carcinoma, about

50%–80%

of patients have 1 known oncogenic driver



NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®) – RECOMMENDED TREATMENT >



Surgery



Radiation



Systemic therapies

QUALITY OF LIFE >

Disease-related symptoms such as fatigue, pain, dyspnea, anorexia, and cough





Lung Cancer: Key Global and US Statistics



3rd most common cancer in the US¹

Estimated new cases in 2024
234,580

Estimated deaths in 2024
125,070

Median age at diagnosis
71 years



1st most common cancer globally²

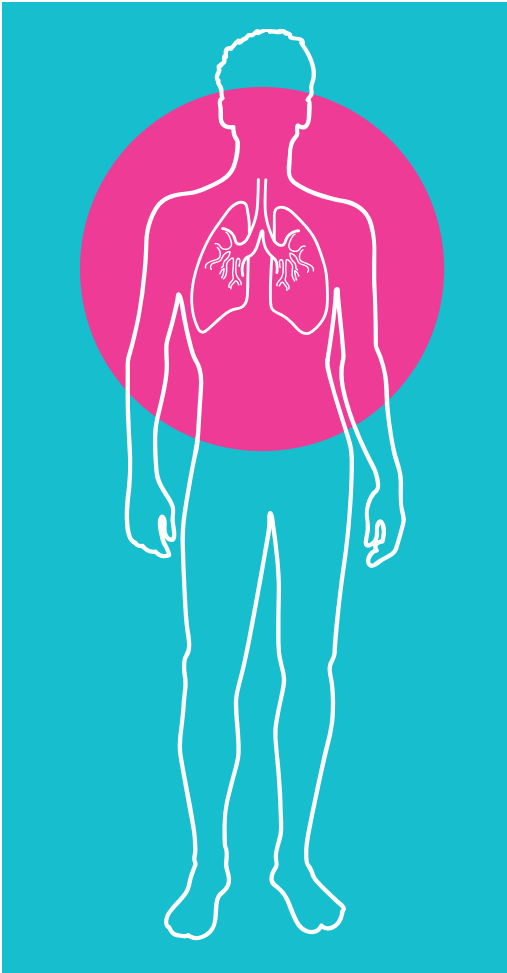
Estimated new cases in 2022
2,480,301

Estimated deaths in 2022
1,817,172

ESTIMATED NUMBER OF NEW CASES AND DEATHS BY CANCER TYPE, 2024¹

Common types of Cancer	Estimated new cases 2024	Estimated deaths 2024
Breast cancer (female)	310,720	42,250
Prostate cancer	299,010	35,250
Lung and bronchus cancer	234,580	125,070
Colorectal cancer	152,810	53,010
Melanoma of the skin	100,640	8,290
Bladder cancer	83,190	16,840
Non-Hodgkin lymphoma	80,620	20,140
Kidney and renal pelvis cancer	81,610	14,390
Uterine cancer	67,880	13,250
Pancreatic cancer	66,440	51,750

Lung Cancer: Signs & Symptoms



Symptoms of lung cancer are often linked to other conditions and are not specific to lung cancer, making early detection challenging. However, symptoms might become apparent in the later stages of the disease¹

EARLY LUNG CANCER SYMPTOMS MAY INCLUDE¹:

- Persistent cough
- New onset of wheezing
- Rust-colored sputum
- Chest pain
- Shortness of breath
- Persistent bronchitis and pneumonia
- Hoarseness
- Loss of appetite
- Unexplained weight loss
- Feeling tired or weak

LUNG CANCER METASTASES SYMPTOMS MAY INCLUDE¹:

- Bone pain (pain in the back or hips)
- Nervous system changes (headache, weakness or numbness of an arm or leg, dizziness, balance problems, or seizures)
- Jaundice
- Swelling of lymph nodes, such as those in the neck or above the collarbone

Lung Cancer: Key Risk Factors



INTRINSIC RISK FACTORS¹⁻⁷



AGE

- The median age of people at diagnosis is 71 years
- Age 65 and older



GENDER

Women have a higher risk for developing lung cancer



RACE

African Americans have highest incidence of lung cancer than other races



GENETICS

- People with a family history of lung cancer have an increased risk
- Inherited and acquired gene changes



LUNG DISEASE

- People with a prior history of lung disease such as COPD or pulmonary fibrosis
- Previous radiation therapy to lungs

ENVIRONMENTAL RISK FACTORS^{1-4,8-9}



SMOKING

- 80%-90% of lung cancer deaths are linked to cigarette smoking in the US; quitting smoking at any age can lower the risk of lung cancer
- Secondhand smoke: >7000 deaths/ year in the US
- Beta carotene supplements in heavy smokers
- 3–4-fold higher lung cancer risk for vaping and smoking



CHEMICALS

Exposure to certain chemicals



POLLUTION

- Radon: Second leading cause of lung cancer in the US
- Air pollution



WORKPLACE EXPOSURES

Exposure to asbestos, arsenic, chromium, nickel, soot, tar, and other substances can cause lung cancer

COPD, chronic obstructive pulmonary disease.

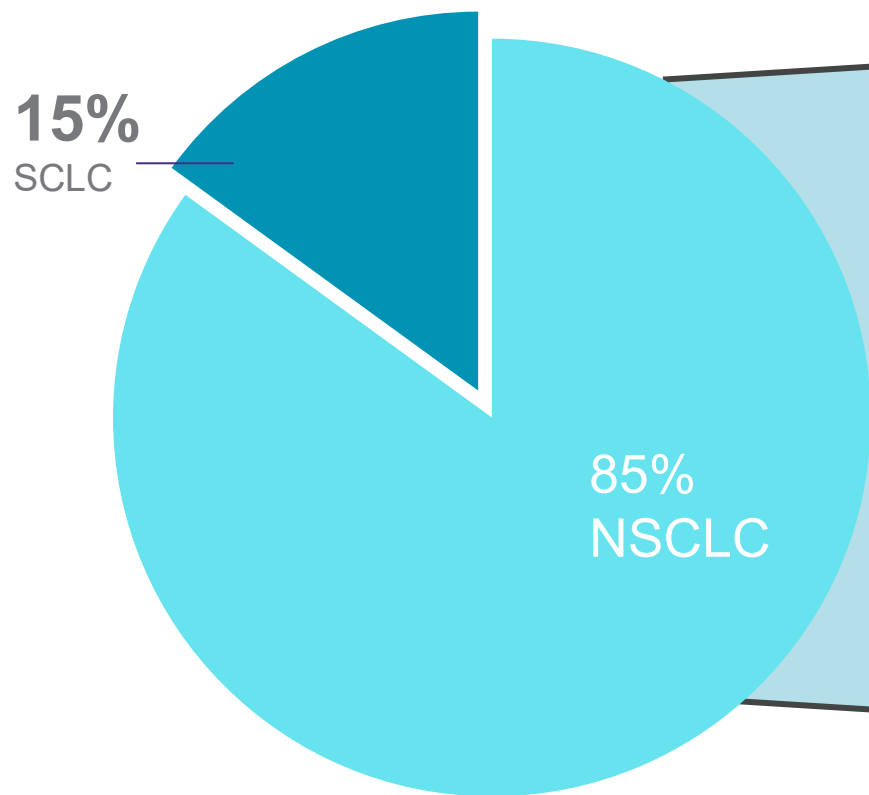
1. Reducing Your Risk. Lungevity. [Reducing Your Risk | LUNgevity Foundation](#) (accessed August 2024); 2. Lung Cancer Risk Factors. American Cancer Society. [Lung Cancer Risk Factors | Smoking & Lung Cancer | American Cancer Society](#) (accessed August 2024); 3. What Causes Lung Cancer? American Cancer Society. [Lung Cancer Causes | Lung Cancer in Non-Smokers | American Cancer Society](#) (accessed August 2024); 4. Non-Small Cell Lung Cancer Treatment (PDQ®)–Health Professional Version. National Cancer Institute. [Non-Small Cell Lung Cancer Treatment \(PDQ®\) - NCI](#) (accessed August 2024); 5. Cancer Stat Facts: Lung and Bronchus Cancer. SEER Program, National Cancer Institute. [Lung and Bronchus Cancer — Cancer Stat Facts](#) (accessed August 2024). 6. Gasperino J Med Hypotheses. 2013; 76: 328-331 7. Race and ethnicity as cancer risk factors. MD Anderson Cancer Centre. <https://www.mdanderson.org/cancerwise/race-and-ethnicity-as-cancer-risk-factors.h00-158592156.html> (accessed August 2024). 8. Bittoni MA, et al. J Oncol Res Ther. 2024;9(3):10229; 9. CDC. [Lung cancer risk factors](#) (accessed September 2024).



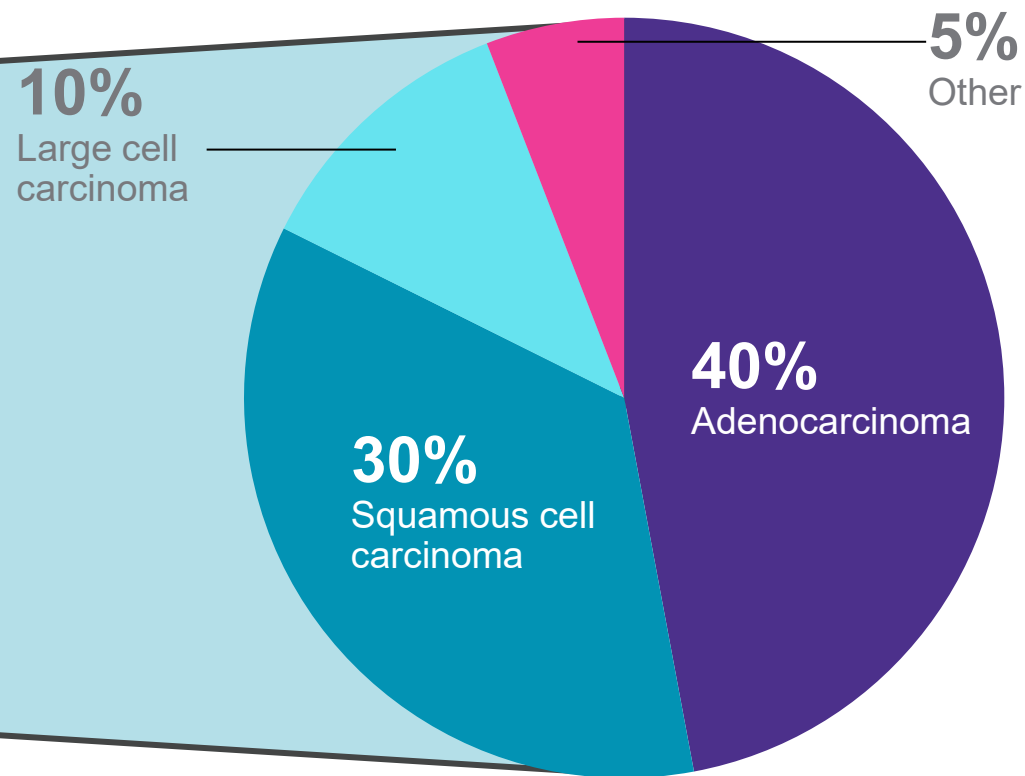
Lung Cancer: Subtypes



LUNG CANCER DISTRIBUTION



NSCLC SUBTYPES BY HISTOLOGY





NSCLC: Subtypes and Location



LOCATION OF HISTOLOGICAL SUBTYPES WITHIN THE LUNGS¹⁻⁴

40%

Adenocarcinoma

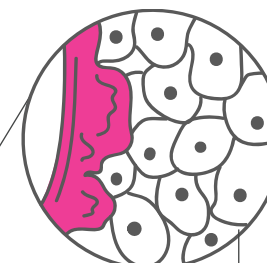
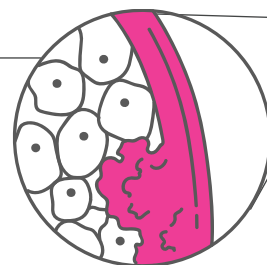
- Glandular cells secreting mucus and alveoli
- Outer edges of lungs



10%

Large cell carcinoma

- Mostly found in lung periphery



30%

Squamous cell carcinoma

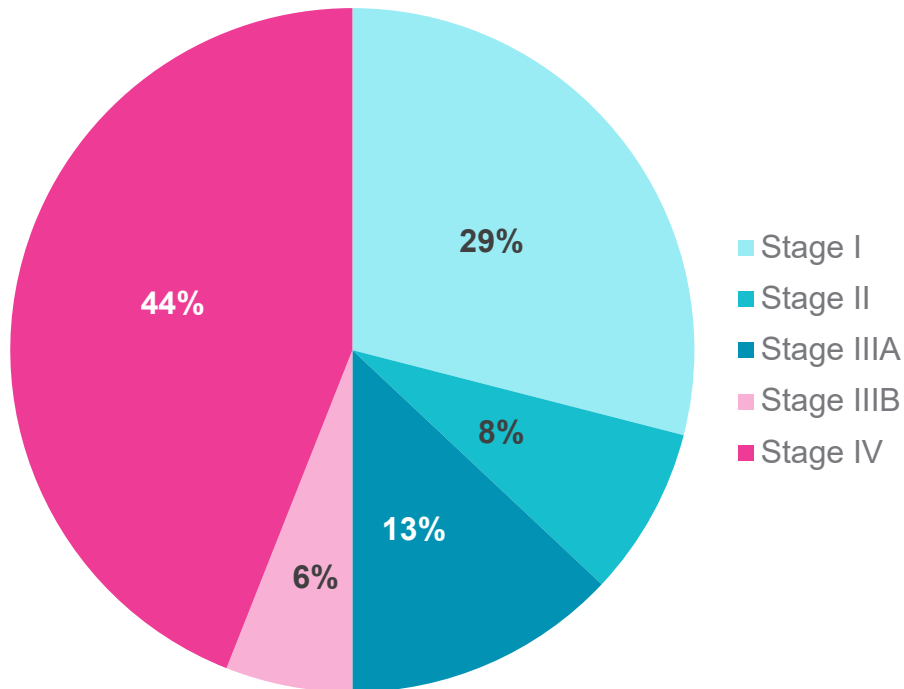
- Squamous cells lining the inside of airways
- Central part of the lung or 1 of the main airways (left or right bronchus)



NSCLC: Disease Classification



NSCLC STAGE AT DIAGNOSIS^{1,2,*}



STAGES OF NSCLC³:

- **0:** Primary tumor restricted to the superficial cell layers (localized)
- **I:** Minimally invasive, small tumor ≤ 4 cm across that has not yet spread
- **II:** Tumor has reached the inner or outer membranes of the lungs or airways, or may have entered lymph nodes within the lung or surrounding area (regional)
- **III:** Partial clogging of the airways and has entered nearby lymph nodes (regional)
- **IV:** Cancer that has spread beyond the point of origin (metastatic)

* Based on 2017 data from the SEER-18 registry.

AJCC, American Joint Committee on Cancer; NSCLC, non-small cell lung cancer; SEER, Surveillance, Epidemiology, and End Results; TNM, tumor, nodes, and metastasis.

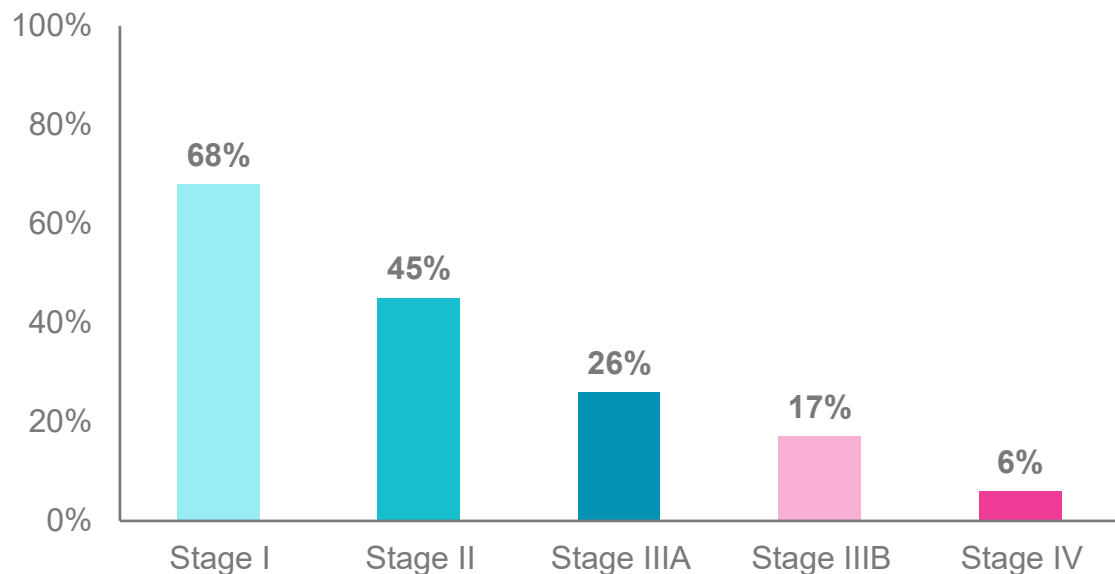
1. Ganti AK, et al. JAMA Oncol. 2021; 7(12):1824-1832; 2. Ganti AK, et al. JAMA Oncol. 2021; 7(12):1824-1832, Supplemental Content; 3. Non-Small Cell Lung Cancer Stages. American Cancer Society [NSCLC Staging | American Cancer Society](#) (accessed August 2024).



NSCLC: Disease Survival



FIVE-YEAR RELATIVE SURVIVAL BY NSCLC STAGE AT DIAGNOSIS, 2010–2017¹



THE COMMONLY USED STAGING SYSTEM FOR NSCLC IS THE AJCC TNM SYSTEM OF CLASSIFICATION, WHICH IS BASED ON²:

Category	Description
Tumor (T)	Size and extent of the main tumor
Nodes (N)	Spread to nearby lymph nodes
Metastasis (M)	Spread of cancer to distant organs

* Based on 2017 data from the SEER-18 registry.

AJCC, American Joint Committee on Cancer; NSCLC, non-small cell lung cancer; SEER, Surveillance, Epidemiology, and End Results; TNM, tumor, nodes, and metastasis.

1. Ganti AK, et al. JAMA Oncol. 2021; 7(12):1824-1832; 2. Non-Small Cell Lung Cancer Stages. American Cancer Society [NSCLC Staging | American Cancer Society](#) (accessed August 2024).



NSCLC: Metastatic Disease



COMMON METASTATIC SITES OF NSCLC^{1,2}:



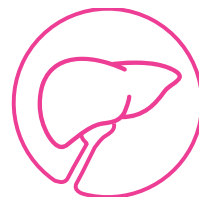
38.8%

Pleural/
pericardial fluid



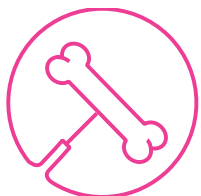
**13.3–
28.4%**

Brain



**12.2–
13.4%**

Liver



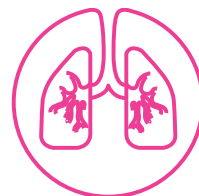
**19.2–
34.3%**

Bone



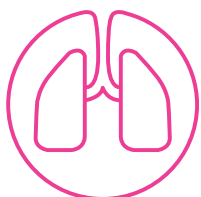
16.7%

Adrenal glands



5.6%

Pleura



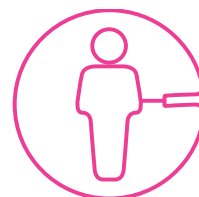
32.1%

Lungs



6.5–9.5%

Extrathoracic
lymph nodes



5.5%

Others

Approximately

50%

of patients have metastatic NSCLC at diagnosis¹

More than

70%

of patients with metastatic NSCLC are current or former smokers¹

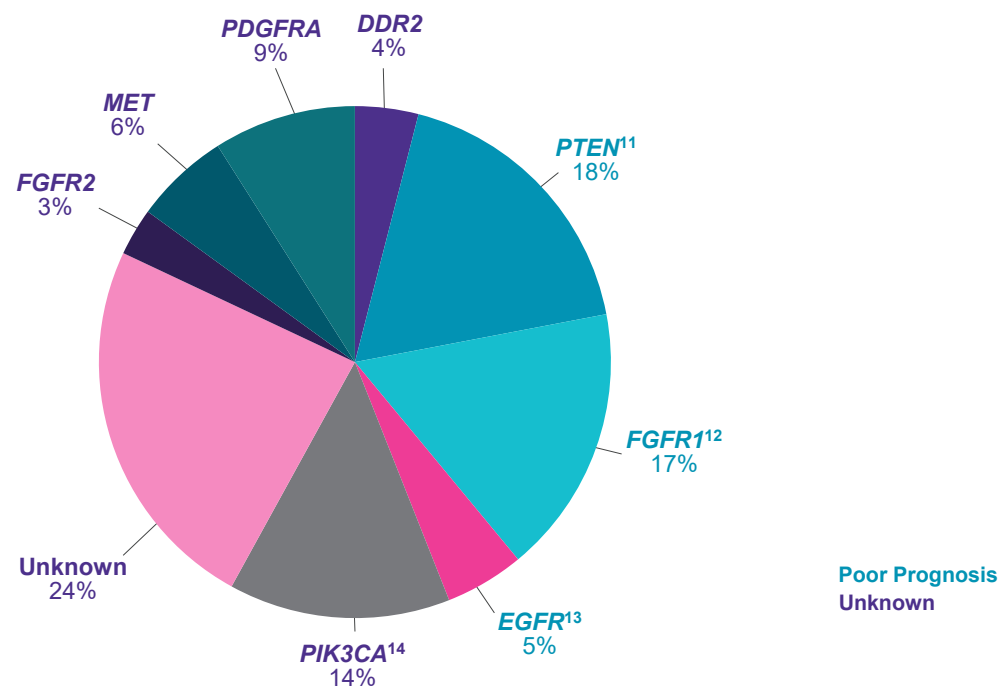
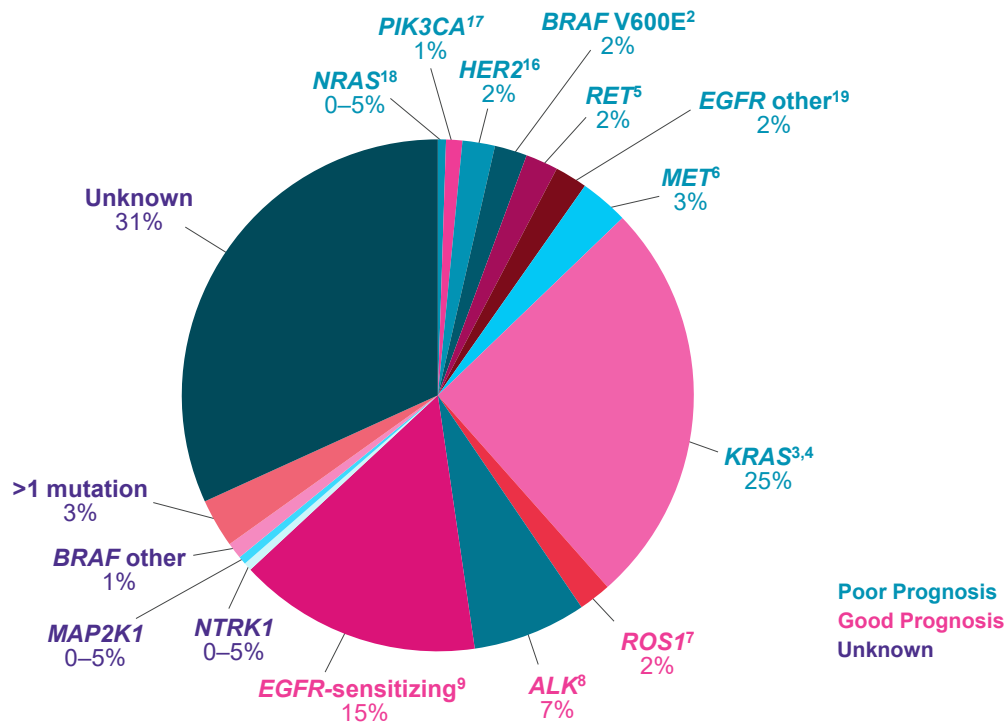


NSCLC: Oncogenic Drivers



ONCOGENIC DRIVERS IN ADENOCARCINOMA¹

ONCOGENIC DRIVERS IN SQUAMOUS CELL CARCINOMA¹



About 60% of patients with adenocarcinoma have 1 known oncogenic driver¹⁰

About 50–80% of patients with squamous cell carcinoma have 1 known oncogenic driver¹⁰

Oncogenic drivers may serve as prognostic or predictive biomarkers to help guide patient management¹⁵



NSCLC, non-small cell lung cancer.

¹Types of Lung Cancer. Lungevity. [Types of Lung Cancer | LUNGevity Foundation](https://www.lungevity.org/types-of-lung-cancer) (accessed August 2024); ² O'Leary CG, et al. Transl Lung Cancer Res. 2019;8(6):1119-24; ³ Svaton M, et al. Anticancer Res. 2016;36(3):1077-82; ⁴ Finn SP, et al. J Thorac Oncol. 2021;16(6):990-1002; ⁵ Qiu Z, et al. Sci Rep. 2020 Jun 25;10(1):10387; ⁶ Tong JH, et al. Clin Cancer Res. 2016;22(12):3048-56; ⁷ Park S, et al. J Thorac Oncol. 2018;13(9):1373-82; ⁸ Christopoulos P, et al. Oncotarget. 2019;10(33):3093-103; ⁹ Li WY, et al. BMC Cancer. 2019;19(1):145; ¹⁰ Chan BA, et al. Transl Lung Cancer Res. 2015;4:36-54; ¹¹ Fischer T, et al. Cell Biosci. 2022;12(1):50; ¹² Kim HR, et al. J Clin Oncol. 2013;31(6):731-7; ¹³ Jin R, et al. Front Oncol. 2021;11:680804; ¹⁴ Qiu X, et al. Am J Cancer Res. 2021;11(6):3189-200; ¹⁵ Ballman KV. J Clin Oncol. 2015;33:3968-71; ¹⁶ Wu R, et al. J Thorac Dis. 2021;13(6):3708-3720; ¹⁷ Wang L, et al. PLoS One. 2014;9(2):e88291; ¹⁸ Zhao J, et al. Onco Targets Ther. 2021;14:1113-1116; ¹⁹ Remon J, et al. Cancer Treat Rev. 2020;90:102105.



NSCLC: Actionable biomarkers according to NCCN Guidelines^{®1}



PREDICTIVE BIOMARKERS ASSOCIATED WITH RESPONSIVENESS TO TARGETED THERAPY

- *EGFR*[†] mutations such as exon 19 indels, exon 20 mutations (eg, p.T790M), or exon 21 mutations (eg, p.L858R)
- *ALK*[†] rearrangements
- *ROS1*[†] gene fusions
- *BRAF* V600E point mutations
- *ERBB2* (*HER2*) mutations
- *KRAS* G12C point mutations
- *MET*ex14 skipping mutations
- *RET* gene rearrangements
- *NTRK1/2/3* gene fusions

PREDICTIVE BIOMARKERS ASSOCIATED WITH RESPONSIVENESS TO IMMUNOTHERAPY

- PD-L1 protein expression level

EMERGING BIOMARKERS

- High-level *MET* amplification[‡]



NSCLC: NCCN Guidelines Treatment Recommendations and Unmet Need¹



Treatment modalities can be used alone or in combination depending on NSCLC disease status

Stage	Surgery	Radiation therapy	Chemoradiation	Chemotherapy	Targeted therapy	Immunotherapy*
IA	✓	✓ (definitive) [†]				
IB	✓	✓ (definitive) [†]		✓ (neoadjuvant; adjuvant therapy)	✓ [§]	
II	✓ (additional evaluation may be needed for pathologic disease)	✓ (definitive) [†]	✓ (neoadjuvant or alone, excluding IIA)	✓ (neoadjuvant; adjuvant therapy)	✓ [§]	✓ (neoadjuvant; adjuvant therapy)
IIIA N2	✓ (select patients with resectable disease)		✓ (neoadjuvant or alone)	✓ (neoadjuvant; adjuvant therapy)	✓ [§]	✓ (neoadjuvant; adjuvant therapy)
IIIB N3 and IIIC disease			✓			
IV (extensive metastases)		✓ (palliative) [‡]		✓	✓ [¶] (anti-VEGF inhibitors are also options)	✓
IV (limited brain metastasis)	✓	✓ (SRS alone or following surgery)		✓	✓ [¶] (anti-VEGF inhibitors are also options)	✓
IV (metastases; ECOG PS 0–1; negative for actionable mutations)				✓	✓ [¶] (anti-VEGF inhibitors are also options)	✓
IV (ECOG PS 2)				✓	✓ [¶] (anti-VEGF inhibitors are also options)	✓

The NCCN Guidelines recommend molecular testing, but strongly advises broader molecular profiling, to identify driver mutations for which targeted therapies may be available to ensure that patients receive the most appropriate treatment¹

*As first-line therapy. [†]Patients that are medically inoperable or those that decline surgery. In patients upstaged to N2+ after surgery, postoperative chemotherapy is an option followed by postoperative radiation therapy. [‡]Symptom relief and potentially for prophylaxis at primary or distant sites (such as pain, bleeding, or obstruction). [§]Select EGFR inhibitors are recommended for patients with completely resected stage IB–IIIA EGFR (exon 19 deletion, L858R) NSCLC who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy. [¶]Suitable targeted therapy following NCCN[®] recommended molecular testing.

ECOG PS, Eastern Cooperative Oncology Group Performance Status; EGFR, epidermal growth factor receptor; NCCN, National Comprehensive Cancer Network[®] (NCCN[®]); NSCLC, non-small cell lung cancer; QoL, quality of life; SRS, stereotactic radiosurgery.

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NSCLC: Quality of Life



- Late detection of the disease results in poor life expectancy¹
- Factors such as stage IV disease, line of treatment, and progressive disease significantly impact HRQoL²
- Psychological distress, associated comorbidities, older age, and living alone significantly impact the HRQoL, wellbeing, and family functioning of people with NSCLC³
- Patients experience disease-related symptoms, such as fatigue, pain, dyspnea, anorexia, and cough⁴
- Palliative care plays a major role in treatment strategy for patients with advanced disease, who often have significant disease-related symptoms and poor quality of life⁵