NON-SMALL CELL LUNG CANCER

FACT SHEET

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NON-SMALL CELL LUNG CANCER (NSCLC)

KEY STATISTICS[1,2]

- Lung cancer is the second most common type of cancer in the United States.
- The two main types of lung cancer are non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).
  - **~85% lung cancers are NSCLC**

In 2020, it is estimated that there will be:

- 228,820 new cases of lung and bronchus cancer in the United States, accounting for 12.7% of all new cancers.
- 135,720 deaths due to lung and bronchus cancer, accounting for 22.4% of all cancer deaths in the United States.

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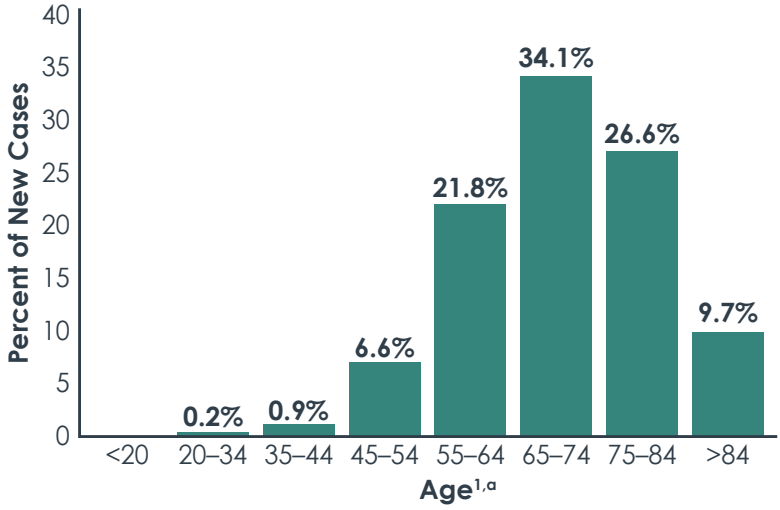
Who Is Most Likely to Get Lung and Bronchus Cancer?

- Lung and bronchus cancer is more common in men than women, particularly African American men.[1]
- The majority of new cases are diagnosed between 65 and 74 years of age.[1,a]

[a]Based on data for 2013-2017 from the NIH Surveillance Epidemiology and End Results Program (SEER) 21.



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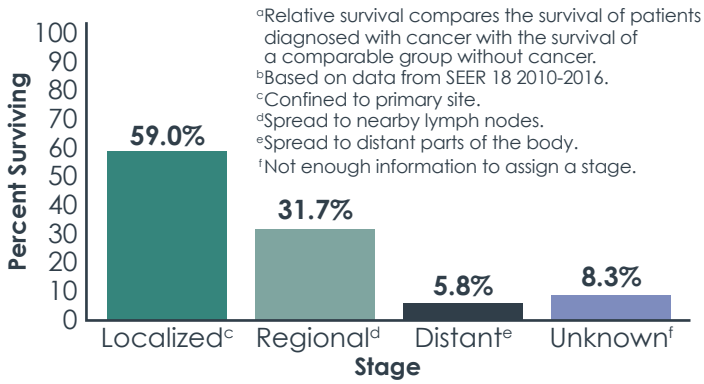
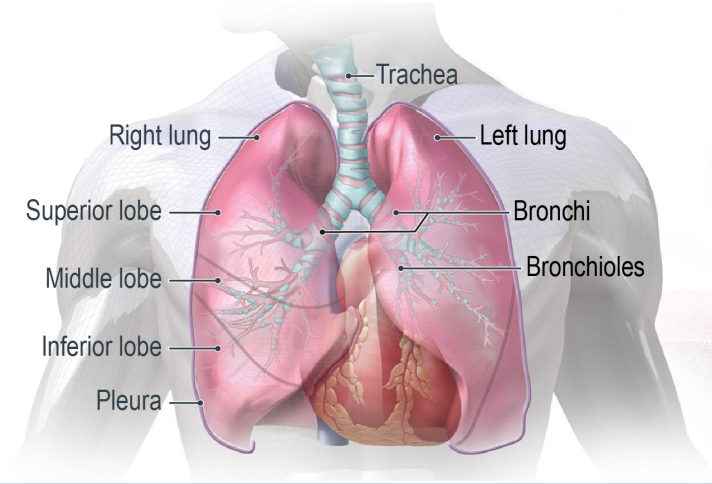
LUNG CANCER SURVIVAL[1]

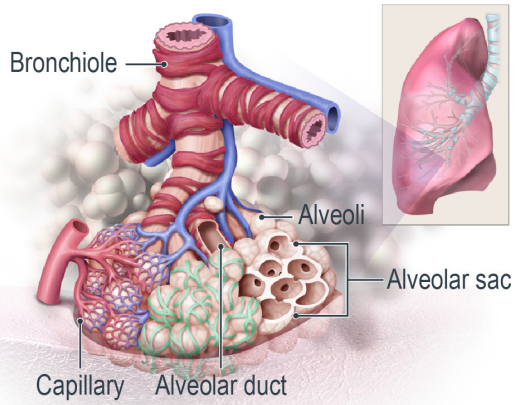
- Lung cancer is the leading cause of cancer death in the United States.
- The 5-year relative survival between 2010 and 2016 for people diagnosed with lung cancer was 20.5%.
- The majority of cases (57%) are diagnosed after the disease has distantly spread (metastasized).
- Survival is poor among people diagnosed with metastatic disease.

5-year Relative[a] Survival by Stage[b]



KEY ANATOMY AND PHYSIOLOGY





Macroscopic Anatomy[3]

- The lungs are two sponge-like organs located within the thoracic cavity and protected by the rib cage. The lungs are part of the respiratory system, whose primary function is to take in oxygen from the atmosphere and eliminate carbon dioxide that is released by the body's cells as they perform their metabolic functions.
- The lungs are separated from each other by the heart and other structures of the mediastinum (not shown), which divides the thoracic cavity into two anatomically distinct chambers.
- Each lung is surrounded by a thin, two-layered membrane called the pleura. Between the two layers is a small, fluid-filled space called the pleural cavity.
- The right lung has three sections, or lobes. The left lung, which has two lobes, is slightly smaller than the right to allow room for the heart.

Macroscopic and Microscopic Airways[3,4]

- When a person inhales air, it travels through the trachea (windpipe), and reaches the lungs through a series of extensively branching airways.
- The trachea divides into passageways called bronchi, which enter the lungs and divide into smaller bronchi. These divide to form smaller branches called bronchioles. Bronchioles in turn subdivide into alveolar ducts, which end in tiny alveolar sacs composed of alveoli.
- Alveoli are surrounded by tiny blood vessels called capillaries; gas exchange between the air and blood occurs across the alveolar and capillary walls.
- The types of cells that comprise the respiratory epithelial lining varies depending on their location. This is an important point because the different histologic subtypes of NSCLC are largely based on their site of origin.

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LUNG CANCER RISK FACTORS

- Smoking is the leading cause of lung cancer, accounting for approximately 80% of cases.[1,2]

Risk Factors for Lung Cancer Include[3]

- Smoking (primary risk factor)
- Exposure to secondhand smoke
- Increasing age
- Occupational exposure to asbestos and other agents
- Radiation exposure
- Air pollution
- Family history of lung cancer
- Human immunodeficiency virus (HIV) infection
- Beta carotene supplements in heavy smokers

LUNG CANCER SCREENING[5]

- Screening with a low-dose computed tomography (LDCT) scan is recommended for people with a higher risk of getting lung cancer.
- The National Comprehensive Cancer Network (NCCN) Screening Guidelines identify two high risk groups:

Group 1

- Age 55 to 77 years ***and***
- ≥30 pack-year smoking history ***and***
- Smoking cessation <15 years

Group 2

- Age ≥50 years ***and***
- ≥20 pack-year smoking history ***and***
- Additional risk factors (other than secondhand smoke exposure) that increase the risk of lung cancer to ≥1.3%

What is a Pack-Year?

A pack-year of smoking history is defined as the number of packs of cigarettes smoked every day multiplied by the number of years of smoking. For example, a person could have a 30 pack-year history by smoking one pack per day for 30 years or two packs per day for 15 years.

DIAGNOSIS OF NSCLC

- NSCLC symptoms may result from the location of the primary tumor, compression of structures adjacent to the lung, or from distant metastases.[4]

Symptoms of NSCLC Include[4,6]

- Cough is the most common symptom, occurring in 50% to 75% of patients
- Chest pain
- Hemoptysis (coughing up blood)
- Malaise
- Dyspnea
- Weight loss
- Hoarseness

Diagnostic Methods

- Tumor biopsy is needed to confirm diagnosis, determine histologic subtype and staging, and identify molecular features of the tumor that help to guide treatment strategy.[5]

Initial Diagnostic Evaluation Typically Includes[4]:	Additional Testing Options[7]:
• Patient history • Physical examination • Laboratory testing • Chest x-ray • Chest CT	• Sputum cytology • Magnetic resonance imaging(MRI) • Positron emission tomography (PET) scan • Bone scan

Possible Biopsy Methods[8]:

- Bronchoscopy with biopsy and transbronchial needle aspiration (TBNA)
- Image-guided transthoracic needle biopsy or fine needle aspiration (FNA)
- Thoracentesis
- Mediastinoscopy
- Open surgical biopsy
- Endobronchial ultrasound (EBUS)

DIAGNOSIS OF NSCLC (cont.)

Staging

- The American Joint Committee on Cancer (AJCC) TNM (tumor, node, metastasis) classification system is used to stage NSCLC.
- TNM stages for NSCLC range from 0 to IV, with IV being the most advanced, described below.

TNM Stage IV NSCLC[8]	
IV	• Presence of distant metastasis • Any T (i.e., size), any N (i.e., may or may not affect nearby lymph node), M1a[a] and M1b[b] for IVA, M1c for IVB[c] **AND**
IVA	• Cancer has spread to the opposite lung (i.e., contralateral lobe) • Nodules (cancer cells) are present in the pleura or membrane surrounding the heart, which is called the pericardium • Cancer cells are present in pleural or pericardial fluid **OR** • Single metastasis outside the lung, to a distant lymph node or organ • Any T, any N, any M1a[a] and M1b[b]
IVB	• Multiple metastases outside the lung • Any T, any N, any M1c[c]

[a]M1a = Separate tumor nodule(s) in a contralateral lobe; tumor with pleural or pericardial nodules or malignant pleural or pericardial effusion.
[b]M1b = Single extrathoracic metastasis in a single organ (including involvement of a single nonregional node).
[c]M1c = Multiple extrathoracic metastases in a single organ or in multiple organs.

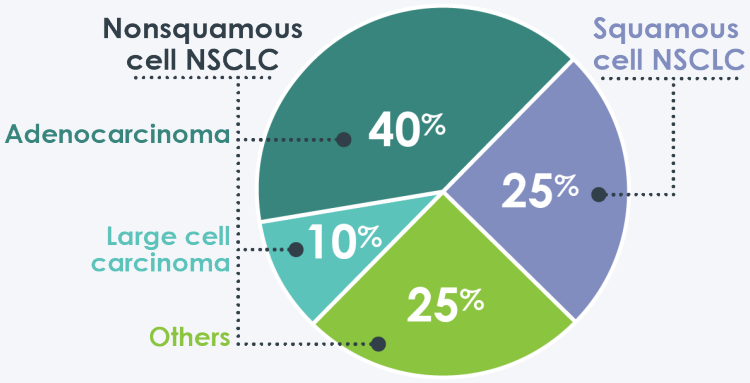
TREATMENT OF NSCLC

Factors Affecting NSCLC Treatment Planning

Treatment options for patients with NSCLC are determined by histology (subtype), stage, and patient considerations.[4]

NSCLC Histologic Subtypes[4,6,8]

- NSCLC arises within the epithelial cells that line lung structures.
- There are three main histological subtypes of NSCLC (see figure) that are primarily classified according to their site of origin; this reflects the variation in respiratory tract epithelium from the bronchi to the alveoli.
- Several other, less common subtypes and variants also exist; combinations of different types may occur within the same tumor.



Molecular Testing[8]

National Comprehensive Cancer Center (NCCN) guidelines recommend that all appropriate patients with metastatic NSCLC (mNSCLC) receive molecular testing to identify specific biomarkers that guide systemic treatment planning.

Predictive Biomarkers in NSCLC[8]

Genetic Alterations[a]	Protein Expression[b]
• ***EGFR (epidermal growth factor receptor)*** gene mutations • ***ALK (anaplastic lymphoma kinase)*** gene rearrangements • ***ROS1 (ROS proto-oncogene 1)*** gene rearrangements • ***BRAF (B-Raf proto-oncogene)*** point mutations • ***NTRK (Neurotrophic tyrosine receptor kinase)*** gene fusions	• PD-L1 (programmed death ligand 1) expression levels **NOTE: PD-L1 expression levels are categorized as:** • PD-L1 negative • PD-L1 ≥50% • PD-L1 ≥1% to ≥49%
Patients with these biomarkers are more likely to benefit from treatment with targeted therapy or immunotherapy than from traditional chemotherapy regimens.[8]	**Targeted therapy:** Treatment that targets specific types of cancer cells with less harm to normal cells.[9] **Immunotherapy:** Treatment with agents that stimulate or suppress the immune system.[9]

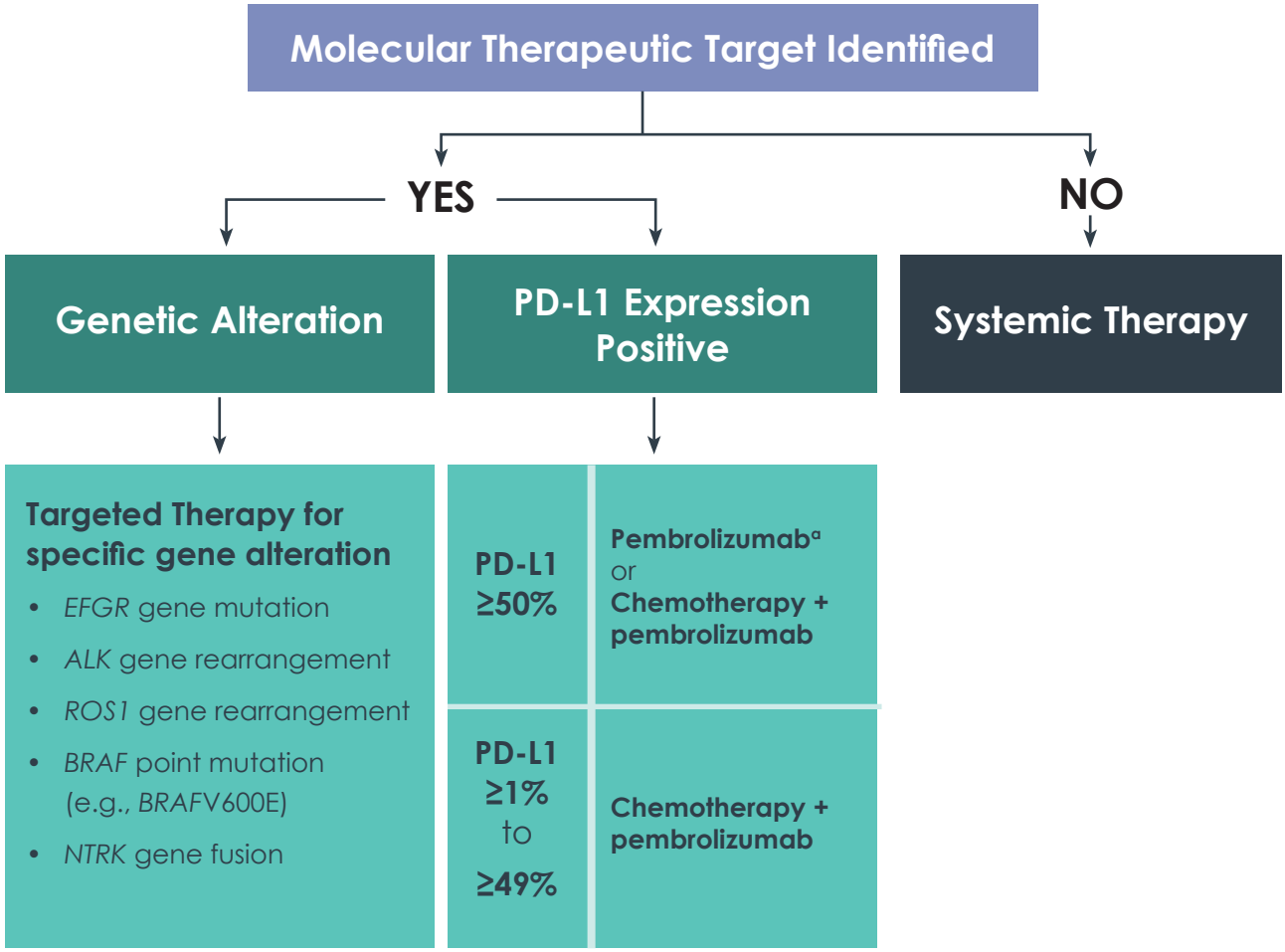
[a]Appropriate for all patients with non-squamous mNSCLC and certain patients with squamous mNSCLC (e.g., never smokers).
[b]Appropriate for all patients with mNSCLC, regardless of histology.

TREATMENT OF NSCLC (cont.)

Systemic Therapy for Advanced or Metastatic (Stage IV) NSCLC

- Over the past 20 years treatment has evolved because targeted therapy options are now available.[2]
- Platinum-based doublet chemotherapy had been the standard of care for patients with advanced NSCLC.[2]
- Now, many patients with advanced NSCLC receive first-line treatment with targeted therapies or immunotherapy.[10]

NCCN Guidelines for Choosing First-line Systemic Therapy for Patients With Metastatic NSCLC[8,10]



[a]Pembrolizumab, an immune checkpoint inhibitor (ICI), is currently the only ICI FDA-approved for first-line monotherapy in patients with PD-L1 ≥1%.[11]

NCCN RECOMMENDATIONS FOR FIRST-LINE TREATMENT OF ADVANCED OR METASTATIC DISEASE

Initial Targeted Therapy Options[8]

Genetic Alteration	Preferred	Other Recommended	Useful In Certain Circumstances
Sensitizing *EGFR* mutation positive	• Osimertinib	• Afatinib • Erlotinib • Dacomitinib • Gefitinib • Erlotinib + ramucirumab	• Erlotinib + bevacizumab[a] (nsq)
***ALK* rearrangement positive**	• Alectinib	• Brigatinib • Ceritinib	• Crizotinib
***ROS1* rearrangement positive**	• Crizotinib • Entrectinib	• Ceritinib	
***BRAF* V600E mutation positive**	• Dabrafenib + trametinib	• Dabrafenib • Vemurafenib	
***NTRK* gene fusion positive**	• Larotrectinib • Entrectinib		
***PD-L1* expression positive (≥1%-49%)**	• (Carboplatin or cisplatin) + pemetrexed + pembrolizumab	• Carboplatin + paclitaxel + bevacizumab[a] + atezolizumab • Carboplatin + albumin-bound paclitaxel + atezolizumab	• Nivolumab + ipilimumab • Pembrolizumab
***PD-L1* expression positive (≥50%)**	• Pembrolizumab • (Carboplatin or cisplatin) + pemetrexed + pembrolizumab	• Carboplatin + paclitaxel + bevacizumab[a] + atezolizumab • Carboplatin + albumin-bound paclitaxel + atezolizumab	• Nivolumab + ipilimumab

Nsq: nonsquamous.
[a]An FDA-approved biosimilar is an appropriate substitute for bevacizumab.

NCCN RECOMMENDATIONS FOR FIRST-LINE TREATMENT OF ADVANCED OR METASTATIC DISEASE (cont.)

Initial Systemic Therapy Options[8,a]

	Non-squamous Cell Carcinoma	Squamous Cell Carcinoma
No contraindications to PD-1 or PD-L1 inhibitors		
Preferred	• Pembrolizumab + (carboplatin or cisplatin) + pemetrexed	• Pembrolizumab + carboplatin + (paclitaxel or albumin-bound paclitaxel)
Other recommended	• Atezolizumab + carboplatin + paclitaxel + bevacizumab • Atezolizumab + carboplatin + albumin-bound paclitaxel • Nivolumab + ipilimumab	• Nivolumab + ipilimumab
Contraindications to PD-1 or PD-L1 inhibitors		
Useful in certain circumstances	• Bevacizumab[b] + carboplatin + paclitaxel • Bevacizumab[b] +(carboplatin or cisplatin) + pemetrexed • Carboplatin + (albumin-bound paclitaxel or docetaxel or etoposide or gemcitabine or paclitaxel or pemetrexed) • Cisplatin + (docetaxel or etoposide or gemcitabine or paclitaxel or pemetrexed) • Gemcitabine +(docetaxel or vinorelbine)	• Carboplatin + (albumin-bound paclitaxel or docetaxel or gemcitabine or paclitaxel) • Cisplatin + (docetaxel or etoposide or gemcitabine or paclitaxel) • Gemcitabine + (docetaxel or vinorelbine)

[a]For patients with good performance status.
[b]Or FDA-approved biosimilar.

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