

Lung Cancer, a cancer that forms in tissues of the lung, usually in the cells lining air passages,¹ has traditionally been classified into two major types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).^{1,2} About 85 percent of all lung cancers are identified as non-small cell, and approximately 75 percent of these are metastatic, or advanced, at diagnosis.³ Recent findings have changed our understanding of the disease, and today lung cancer is known to be made up of many distinct subsets of cancer that can be classified by the genetic makeup of a person's tumor.

Facts and Figures

- An estimated 1.6 million new cases of lung cancer were diagnosed worldwide in 2008, accounting for about 13 percent of total cancer diagnoses.⁴ In Europe, lung cancer represents 12 percent, or 386,000, of an estimated 3.2 million cancer cases.⁵ An estimated 221,130 new cases of lung cancer are expected to be diagnosed in the U.S. in 2011, accounting for 14 percent of all cancer diagnoses.²
- Lung cancer is the leading cause of cancer death worldwide in both men and women,⁴ with an estimated 1.4 million deaths each year.⁶
 - An estimated 156,940 deaths, accounting for about 27 percent of all cancer deaths, are expected to occur in the U.S. in 2011.²
- Lung cancer accounts for 20 percent of all cancer-related deaths in Europe, the highest of any cancer.⁷ There are more deaths due to lung cancer among men (28 percent) than among women (10 percent).⁷
 - In both the United States and in some European countries like the United Kingdom, more women die each year from lung cancer than from breast cancer.^{2,6}
- The U.S. incidence of lung cancer is 62.5 of every 100,000 patients; mortality is 52.5 of every 100,000 patients.⁸

Risk Factors

- Lung cancer affects a diverse group of people, including the young and non-smokers.
- Some lung cancer risk factors may include:⁹
 - Smoking cigarettes or cigars
 - Exposure to second-hand smoke, asbestos, radon, chromium, arsenic, soot or tar
 - Treatment with radiation therapy to the breast or chest
 - Personal or family history of the disease
- Historically, smoking was seen as the major risk factor in developing lung cancer. Recent figures show that in the U.S., while smoking is a significant factor, about 13 percent of lung cancers are unrelated to smoking.²
- Most lung cancers do not cause any symptoms until the disease has already reached an advanced stage. Even when symptoms do appear, they are often mistaken for other health problems.⁶

Non-Small Cell Lung Cancer

- NSCLC is a disease in which malignant cells form in the tissues of the lung. Historically, NSCLC has been categorized by histology to include adenocarcinoma, squamous cell carcinoma and large cell carcinoma.³
 - Adenocarcinoma, which accounts for about 40 percent of NSCLC cases, is usually found in the outer region of the lung.⁹
 - Squamous cell carcinoma, which accounts for about 25 to 30 percent of all NSCLC cases, tends to be located in the middle of the lungs, and is more often linked to a history of smoking.⁹
 - Large cell carcinoma, which accounts for about 10 to 15 percent of NSCLC cases, may appear in any part of the lung, and tends to grow and spread quickly.⁹
 - Several less common histologies are classified as NSCLC, including pleomorphic, carcinoid tumor, salivary gland carcinoma, unclassified carcinoma, mixed histology, and not otherwise specified (NOS) due to small specimen size or poorly differentiated histology.¹⁰
- In recent years, it has become clear that beyond a histology level, some patients also have a combination of tumor-driving genetic mutations or alterations, with distinct molecular characteristics that allow them to be further classified into subsets of disease, such as epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK).^{3,6}
 - Mutations in the EGFR occur in 10 to 20 percent of NSCLC tumors,¹¹ and as high as 60 percent in Asian patients.¹²

- Preliminary epidemiology suggests that approximately 3-5 percent of NSCLC tumors are ALK-positive.¹³
- NSCLC is a difficult disease to treat, particularly in the metastatic or advanced setting (Stage IIIB/IV). In these patients, the five-year survival rate is only 6 percent.¹⁴
- The current standard of care with chemotherapy based regimens for advanced NSCLC demonstrates a response rate of about 15-35 percent, with a median progression free survival (PFS) of 4.5 to 6.2 months.¹⁵

NSCLC Treatment

- Current treatment options for NSCLC include surgery, radiation therapy, chemotherapy, targeted therapy, or some combination of these, depending on the type of cancer, stage of the disease and overall health and age of the patient.³
- With the identification and increased understanding of molecular abnormalities in lung cancer, research efforts have focused on identifying molecular targets and using this knowledge to develop molecular-targeted therapies and guide treatment decisions. Targets currently being investigated in the treatment of NSCLC include the HER (human epidermal growth factor receptor) family of receptors, EGFR, KRAS, ALK, PI3K/AKT/mTOR, IGF-1R and MET.¹⁶

¹ National Cancer Institute. Lung Cancer. 2009. Available at: <http://www.cancer.gov/cancertopics/types/lung>. Accessed September 14, 2010.

² American Cancer Society. Cancer Facts and Figures 2011. Available at:

<http://www.cancer.org/Research/CancerFactsFigures/CancerFactsFigures/cancer-facts-figures-2011>. Accessed July 12, 2011.

³ Reade CA, Ganti AK. EGFR targeted therapy in non-small cell lung cancer: potential role of cetuximab. *Biologics*. 2009; 3: 215–224.

⁴ American Cancer Society. Global Cancer Facts and Figures; 2nd Edition 2008. Available at:

<http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspsc-027766.pdf>. Pg 15. Accessed February 18, 2011.

⁵ Wilking N et al. Karolinska Institutet/i3 Innovus Benchmarking Report of Lung Cancer Care in Selected European Countries. 2008. Available at: http://www.comparatorreports.se/Lung_cancer_benchmarking_080526.pdf. Accessed September 14, 2010.

⁶ World Health Organization. Cancer fact sheet. <http://www.who.int/mediacentre/factsheets/fs297/en/>. Accessed February 8, 2011.

⁷ European Lung Foundation. What is Lung Cancer? Available at: <http://www.european-lung-foundation.org/index.php?id=65>. Accessed September 14, 2010.

⁸ Surveillance Epidemiology and End Results. SEER stat fact sheets: lung and bronchus. <http://seer.cancer.gov/statfacts/html/lungb.html>. Accessed February 23, 2011.

⁹ American Cancer Society. Detailed Guide: Lung Cancer (Non-Small Cell). Available at:

<http://www.cancer.org/acs/groups/cid/documents/webcontent/003115-pdf.pdf>. Accessed September 14, 2010.

¹⁰ National Cancer Institute. General Information About Non-Small Cell Lung Cancer. Available at:

<http://www.cancer.gov/CANCERTOPICS/PDQ/TREATMENT/NON-SMALL-CELL-LUNG/PATIENT>. Accessed March 11, 2011.

¹¹ Pao W, Miller VA. Epidermal growth factor receptor mutations, small-molecule kinase inhibitors, and non-small-cell lung cancer: current knowledge and future directions. *J Clin Oncol* 2005;23:2556-2568.

¹² Mok T et al. Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma. *N Engl J Med* 2009; 361:947-957.

¹³ Chiarle R, Voena C, Ambrogio C et al. The anaplastic lymphoma kinase in the pathogenesis of cancer. *Nat Rev Cancer*. 2008;8(1): 11-23.

¹⁴ American Cancer Society. Detailed guide: lung cancer – non-small cell. Non-small cell lung cancer survival rates by stage. <http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/index>. Accessed February 8, 2011.

¹⁵ Sandler A, Gray R, Perry MC, et al. Paclitaxel–carboplatin alone or with bevacizumab for non–small-cell lung cancer. *New England Journal of Medicine*. 2006;355:2542-50. [Erratum, *N Engl J Med* 2007;356:318.]

¹⁶ Janku F et al. Targeted therapy in non-small-cell lung cancer- is it becoming a reality? *Nature Reviews Clinical Oncology*. 2010; 7: 401-414.