

**Lung Cancer**, a cancer that forms in tissues of the lung, usually in the cells lining air passages,<sup>1</sup> has traditionally been classified into two major types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).<sup>1,2</sup> 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.<sup>3</sup> Recent findings have changed our understanding of the disease, and today distinct molecular subsets of lung cancer have been identified that can be classified by a biomarker profile of a patient's tumor.<sup>4</sup>

### Facts and Figures

- Worldwide in 2010, an estimated 1.7 million new cases of lung cancer were expected to be diagnosed,<sup>5</sup> accounting for approximately 13 percent of total cancer diagnoses.<sup>5,6</sup> Lung cancer is the leading cause of cancer death worldwide,<sup>7</sup> with an estimated 1.4 million deaths each year.<sup>8</sup>
- In Europe in 2010, an estimated 400,000 new cases of lung cancer were expected to be diagnosed,<sup>9</sup> representing 12 percent of an estimated 3.3 million cancer cases.<sup>9,10</sup> Lung cancer accounts for 20 percent (more than 350,000<sup>11</sup>) of all cancer-related deaths in Europe, the highest of any cancer.<sup>11,12</sup>
  - There are more deaths each year due to lung cancer among men (almost 262,400) than among women (almost 89,400).<sup>11</sup>
- Lung cancer is typically a disease of the elderly and in most cases is related to smoking, although it can also affect the young and non-smokers.<sup>13,14</sup>

### Risk Factors

- Lung cancer risk factors include:<sup>13</sup>
  - 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
- Most lung cancers do not cause any symptoms until the disease has already reached an advanced stage. Even when symptoms do appear, they can be mistaken for other health problems.<sup>13</sup>

### 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 or large cell carcinoma.<sup>3</sup>
  - Adenocarcinoma, which accounts for about 40 percent of NSCLC cases, is usually found in the outer region of the lung.<sup>13</sup>
  - 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.<sup>13</sup>
  - 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.<sup>13</sup>
  - Less common histologies include pleomorphic, carcinoid tumor, salivary gland carcinoma, unclassified carcinoma and not otherwise specified (NOS) due to small specimen size or poorly differentiated histology.<sup>15,16</sup>
- Recently, it became clear that beyond a histology level, some patients' tumors also have distinct molecular characteristics that allow them to be further classified into subsets of disease, such as activating mutations in the epidermal growth factor receptor (EGFR) gene and alterations of the anaplastic lymphoma kinase (ALK).<sup>3,13</sup>
  - EGFR mutations occur in 10 to 20 percent of NSCLC tumors,<sup>17</sup> and as high as 60 percent in NSCLC tumors in Asian populations.<sup>18</sup>
  - Preliminary epidemiological data suggests that approximately 3-5 percent of NSCLC tumors are ALK-positive.<sup>19,20</sup>

## NSCLC Treatment

- Despite treatment, the outlook for patients with NSCLC, particularly in the metastatic or locally advanced setting (Stage IIIB/IV), is generally poor. In this group of patients, the five-year survival rate is only 6 percent.<sup>13</sup>
- 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.<sup>13</sup>
- The current first line standard of care with chemotherapy-based regimens for advanced NSCLC demonstrates a response rate of about 24-30 percent,<sup>21</sup> with a median survival of 10.3 to 12.3 months<sup>21,22</sup> and a progression free survival (PFS) of 4.8 to 5.1 months.<sup>23</sup>
- 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. Targets currently being investigated for 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.<sup>24</sup>

## References

- <sup>1</sup> National Cancer Institute. Lung Cancer. 2009. Available at: <http://www.cancer.gov/cancertopics/types/lung>. Accessed June 26, 2012.
- <sup>2</sup> American Cancer Society. Cancer Facts and Figures 2011. Available at: <http://www.cancer.org/Research/CancerFactsFigures/CancerFactsFigures/cancer-facts-figures-2011>. Accessed June 26, 2012.
- <sup>3</sup> Reade CA, Ganti AK. EGFR targeted therapy in non-small cell lung cancer: potential role of cetuximab. *Biologics*. 2009; 3: 215–224.
- <sup>4</sup> Schein PS, Scheffler B. Barriers to efficient development of cancer therapies. *Clin Cancer Res*. 2006;12:3243-3248.
- <sup>5</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=220900&Text-p=World&selection\\_cancer=14110&Text-c=Lung&pYear=2&type=0&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=220900&Text-p=World&selection_cancer=14110&Text-c=Lung&pYear=2&type=0&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>6</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=220900&Text-p=World&selection\\_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=0&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=220900&Text-p=World&selection_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=0&window=1&submit=%A0Execute%A0). Accessed June 6, 2012.
- <sup>7</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008, Available at: <http://globocan.iarc.fr/> (select 'World' from the drop down menu under 'Fact Sheets'). Accessed June 26, 2012.
- <sup>8</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=220900&Text-p=World&selection\\_cancer=14110&Text-c=Lung&pYear=2&type=1&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=220900&Text-p=World&selection_cancer=14110&Text-c=Lung&pYear=2&type=1&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>9</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=63968&Text-p=Europe&selection\\_cancer=14110&Text-c=Lung&pYear=2&type=0&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=63968&Text-p=Europe&selection_cancer=14110&Text-c=Lung&pYear=2&type=0&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>10</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=63968&Text-p=Europe&selection\\_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=0&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=63968&Text-p=Europe&selection_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=0&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>11</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=63968&Text-p=Europe&selection\\_cancer=14110&Text-c=Lung&pYear=2&type=1&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=63968&Text-p=Europe&selection_cancer=14110&Text-c=Lung&pYear=2&type=1&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>12</sup> The International Agency for Research on Cancer, the World Health Organization, GLOBOCAN 2008. Available at: [http://globocan.iarc.fr/burden.asp?selection\\_pop=63968&Text-p=Europe&selection\\_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=1&window=1&submit=%A0Execute%A0](http://globocan.iarc.fr/burden.asp?selection_pop=63968&Text-p=Europe&selection_cancer=280&Text-c=All+cancers+excl.+non-melanoma+skin+cancer&pYear=2&type=1&window=1&submit=%A0Execute%A0). Accessed June 26, 2012.
- <sup>13</sup> 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 June 26, 2012.
- <sup>14</sup> Consonni D, et al. Lung Cancer and Occupation in a Population-based Case-Control Study. *Am J Epidemiol*. 2010;171:323–333.
- <sup>15</sup> 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 June 26, 2012.
- <sup>16</sup> Oncology Pro. Metastatic non small cell lung cancer. Available at: <http://oncologypro.esmo.org/guidelines/clinical-practice-guidelines/metastatic-non-small-cell-lung-cancer.aspx>. Accessed June 26, 2012.
- <sup>17</sup> 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 Onc*. 2005;23:2556-2568.
- <sup>18</sup> Mok T, et al. Gefitinib or Carboplatin–Paclitaxel in Pulmonary Adenocarcinoma. *N Engl J Med*, 2009; 361:947-957.
- <sup>19</sup> Garber K. ALK, lung cancer, and personalized therapy: portent of the future? *JNCI*. 19 May, 2010; 102:10:672-675.
- <sup>20</sup> Sasaki T, et al. The biology and treatment of EML4-ALK non-small cell lung cancer. *Euro J of Cancer*. 2010 46:1773–1780.
- <sup>21</sup> Vilmar AC, et al. Customising chemotherapy in advanced nonsmall cell lung cancer: daily practice and perspectives. *Eur Respir Rev*. March 1, 2011 vol. 20 no.119 045-052.

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<sup>22</sup> Sandler A, et al. Crino` Treatment Outcomes by Tumor Histology in Eastern Cooperative Group Study E4599 of Bevacizumab with Paclitaxel/Carboplatin for Advanced Non-small Cell Lung Cancer. *J of Thor Onc*. September, 2010. 5:9:1416–1423.

<sup>23</sup> Scagliotti GV et al. Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naïve Patients With Advanced-Stage Non–Small-Cell Lung Cancer. *J of Clin Onc*. 20 July, 2008 26:21:3543-3551.

<sup>24</sup> 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.