Evolution of Lung Cancer
Overview

Objectives

• To provide an overview of the evolution of lung cancer, including developments in patient classification, treatment innovation, and unmet need

Executive Summary

• Lung cancer remains a challenge in the United States
• Lung cancer is complex and fragmented; many tumor and patient types exist
• While available treatments have improved outcomes, an unmet need still remains
• Collaboration across FDA, physicians, manufacturers, and payers may help to improve survival
• Genentech is committed to the fight against lung cancer
Lung Cancer Remains a Challenge in the United States

- **Second most frequent cancer diagnosis:** ~221,000 new cases are expected in 2015\(^1\)
- **Largest cause of cancer-related mortality:** ~158,000 deaths are expected in 2015\(^1\)
- **Lung cancer treatment has required significant financial investment:** Approximately $12.1 billion was spent in 2010 (fourth highest spend among cancers)\(^2\)

<table>
<thead>
<tr>
<th>Leading Sites of New Cancer Cases (2015)(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (female)</td>
</tr>
<tr>
<td>Lung and bronchus</td>
</tr>
<tr>
<td>Prostate</td>
</tr>
<tr>
<td>Colon and rectum</td>
</tr>
<tr>
<td>Bladder</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
</tr>
</tbody>
</table>

Lung cancer patient classification has evolved.

- Lung cancer is now understood as heterogeneous [1,2]

<table>
<thead>
<tr>
<th>Year</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Lung cancer</td>
</tr>
<tr>
<td>2000</td>
<td>Non-small cell lung cancer (85% to 90% of all lung cancers)</td>
</tr>
<tr>
<td>2008</td>
<td>Non-squamous Adenocarcinoma (about 40% of all lung cancers)</td>
</tr>
</tbody>
</table>

**Sources:**
Within NSCLC, Tumor Classification Is Further Segmented\(^1,^2\)

- NSCLC tumors can be **classified by the presence of key biomarkers**
- **Targeted treatments are available** for NSCLC patients
- Genentech continues to **identify specific biomarkers** important in lung cancer

*Adenocarcinoma NSCLC used as an example. Other forms of lung cancer may vary in the incidence of these biomarkers.

\(^1\)Incidence data for PD-L1 overexpression are still maturing; PD-L1 overexpression may be higher in different patient populations.


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**Incidence of Biomarkers in NSCLC\(^1-^3,^*\)**

- **NONE (36%)**
- **KRAS (25%)**
- **EGFR (21%)**
- **ALK (8%)**
- **PD-L1\(^*\) (~23%)\(^3,^†\): Tumors expressing PD-L1 may have genetic mutations in other pathways important in NSCLC (e.g., EGFR).\(^4\)**
- **AKT1 (<1%)**
- **MEK1 (<1%)**
- **NRAS (<1%)**
- **MET (<1%)**
- **PIK3CA (<1%)**
- **BRAF (2%)**
- **HER2 (3%)**

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\(^*\)Incidence of Lung Cancer Biomarkers

\(^†\)Adenocarcinoma NSCLC used as an example. Other forms of lung cancer may vary in the incidence of these biomarkers.
Outcomes Have Increased Through Treatment Innovation

U.S. Mean Overall Survival in Advanced NSCLC (1990–2015)

<table>
<thead>
<tr>
<th>Year</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Best supportive care (BSC)</td>
</tr>
<tr>
<td>1995</td>
<td>Single-agent chemotherapy</td>
</tr>
<tr>
<td>2000</td>
<td>Platinum-doublet chemotherapy</td>
</tr>
<tr>
<td>2005</td>
<td>Next-generation platinum-doublet chemotherapy</td>
</tr>
<tr>
<td>2010</td>
<td>Biologic agents</td>
</tr>
<tr>
<td>2015</td>
<td>Targeted therapies</td>
</tr>
</tbody>
</table>

While Available Treatments Have Improved Outcomes, an Unmet Need Still Remains

- Lung cancer accounts for more deaths than any other cancer (approximately 27% of all cancer deaths)\(^1\)
- Survival rates are low: the 5-year survival rate for patients with metastatic disease is 4.2%\(^2\)
- Genentech is committed to the fight against lung cancer and to improving the lives of patients by focusing on these 3 key areas:
  - Medicines, screening and testing, and access to care

Expanded Therapy Options Are Needed for All NSCLC Patient Types

- NSCLC is comprised of many unique tumor types that need specific and targeted treatments
- Genentech is focused on addressing unmet needs in NSCLC, including
  - The development of more efficacious and more tolerable therapeutics
  - Treatment for squamous NSCLC
  - Adjuvant treatment for early-stage lung cancer
  - Later-line treatment for advanced NSCLC
  - Treatment targeting tumors with unique genetic or expression profiles
Late-Stage Diagnosis and Tumor Misclassification Have Contributed to Poor Survival in Lung Cancer

- Majority of cases (~60%) diagnosed at a late stage\(^1\)
- Inconsistent use of diagnostics
  - According to 2 recent surveys, U.S. testing rates for common biomarkers ranged from 67% to 81% in 2014\(^2,3\)

**Sources:**
Social and Clinical Factors Contribute to Suboptimal Access to Lung Cancer Care

- Many people with advanced cancer do not receive therapy. Approximately 55% of those patients have lung cancer¹
- Many patients are not seen by a cancer specialist, which may cause delays in optimal treatment²-⁴
- There are negative attitudes toward lung cancer⁵,⁶
- High out-of-pocket patient cost may lead to nontreatment

**Sources:**

Collaboration Across FDA, Physicians, Manufacturers, and Payers May Help to Improve Survival

Examples of collaborative initiatives that may help to improve survival

- Use of surrogate clinical trial endpoints (e.g., objective response rate [ORR])
  - Increase patient access
  - Screen earlier for lung cancer
  - Provide novel therapeutics to patients
  - Improve use of diagnostics
  - Expand personalized treatment options

Screen earlier for lung cancer

Use of surrogate clinical trial endpoints (e.g., objective response rate [ORR])

Provide novel therapeutics to patients

Increase patient access

Improve use of diagnostics

Expand personalized treatment options

Demonstrating the Value of Innovation
Genentech Is Committed to the Fight Against Lung Cancer

Medicines
Develop treatments for patients where there is a significant unmet need

Screening & Testing
Advance comprehensive lung cancer screening and testing

Access to Care
Increase access to therapies for appropriate patients with lung cancer

Genentech
A Member of the Roche Group

Demonstrating the Value of Innovation