Lung Cancer in Non-Smokers

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Outline

Changing lung cancer epidemiology and demographics
EGFR-mutant lung cancer diagnosis and treatment
Lung cancer screening guidelines

Disclosures

Revolution Medicines  Consulting
AstraZeneca  Research Funding
Novartis  Research Funding
Roche  Research Funding
Mirati  Research Funding
Takeda  Research Funding
Spectrum  Research Funding
MedImmune  Research Funding

Lung Cancer in the U.S.

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2018</th>
<th>Estimated Deaths 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Cancer (Female)</td>
<td>260,220</td>
<td>40,950</td>
</tr>
<tr>
<td>2. Lung and Bronchus Cancer</td>
<td>234,290</td>
<td>154,220</td>
</tr>
<tr>
<td>3. Prostate Cancer</td>
<td>144,660</td>
<td>28,440</td>
</tr>
<tr>
<td>4. Colorectal Cancer</td>
<td>140,250</td>
<td>59,520</td>
</tr>
<tr>
<td>5. Melanoma of the Skin</td>
<td>11,270</td>
<td>8,320</td>
</tr>
<tr>
<td>6. Bladder Cancer</td>
<td>11,170</td>
<td>17,240</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>7,480</td>
<td>10,640</td>
</tr>
<tr>
<td>8. Kidney and Renal Pelvis Cancer</td>
<td>6,040</td>
<td>34,910</td>
</tr>
<tr>
<td>9. Uterine Cancer</td>
<td>6,020</td>
<td>11,360</td>
</tr>
<tr>
<td>10. Leukemia</td>
<td>5,280</td>
<td>24,570</td>
</tr>
</tbody>
</table>

Lung and bronchus cancer represents 12.5% of all new cancer cases in the U.S.
### Relationship of lung cancer to smoking

**Tobacco Use in the US, 1900-2006**

<table>
<thead>
<tr>
<th>Year</th>
<th>Per Capita Cigarette Consumption</th>
<th>Male Lung Cancer Rate</th>
<th>Female Lung Cancer Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1900</td>
<td>500</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>1950</td>
<td>1000</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>2000</td>
<td>2000</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*Data source: American Lung Association.*

### Non-smoking related lung cancer on the rise

**Estimated Incidence and Mortality Rates, 1999-2019**

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Incidence</th>
<th>Estimated Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999</td>
<td>100,000</td>
<td>50,000</td>
</tr>
<tr>
<td>2009</td>
<td>120,000</td>
<td>60,000</td>
</tr>
<tr>
<td>2019</td>
<td>140,000</td>
<td>70,000</td>
</tr>
</tbody>
</table>

*Data source: American Cancer Society.*
Shifting Subtypes of Lung Cancer

Male
- USA Black
- USA White
- Male

Female
- USA Black
- USA White
- Female

Lung cancer is the leading cause of cancer mortality in China for both Men and Women.

In 2015, a total of 733,300 new lung cancer cases and 610,200 lung cancer deaths were estimated in China.

Summary of lung cancer demographics

- Lung cancer is the leading cause of cancer deaths in the U.S. and China for both men and women.
- Lung cancer incidence and mortality in the U.S. is decreasing overall, but more for men than women.
- Lung cancer rates in never smokers are increasing.

EGFR-mutant lung cancer
Oncogenic driver mutations identified in NSCLC

Current breakdown of oncogenic driver mutations in lung adenocarcinoma in the U.S.


Spectrum of oncogenic driver mutations in lung adenocarcinomas from Asian never smokers.
Why did I get this?

Genetic association of EGFR-mutant lung cancer in never smoking Asian women

Constitutively active mutant-EGFR drives a subset of lung cancers

Landmark IPASS study performed in Asia

EGFR TKIs for the treatment of advanced EGFR-mutant lung cancer are effective but not curative

Resistance invariably occurs
Mechanisms of acquired resistance to EGFR TKI therapy

- ~40% EGFR Bypass Pathways
- SCLC, BRAF mut, PK3CA mut, HER2 amp, MET amp, EGFR amp, Other EGFR mut

Osimertinib is Active Against EGFR Sensitizing Mutations and T790M

Mutant-specific EGFR TKIs

Relative CS (x)

- T790M
- WT
- EGFRwt
- WT EGFR wt
- T790M EGFR wt
- Gefitinib
- Afatinib
- Osimertinib

Osimertinib Improves OS Compared to Standard EGFR TKI Treatment

1st vs 3rd Generation EGFR TKI Progression Free Survival


Less benefit observed for Asian patients

Summary of EGFR-mutant lung cancer

- 75% frequency of EGFR mutations in lung cancers from Asian never smokers
- Likely a genetic component to EGFR-mutant lung cancer, but poorly understood
- Targeted therapy with tyrosine kinase inhibitors are very effective, but non-curative treatments for EGFR-mutant lung cancer
20% reduction in lung cancer deaths in LDCT screening group

- 1060 lung cancers in LDCT group
- 941 lung cancers in CXR group

- 443 deaths from lung cancer in CXR group
- 356 deaths from lung cancer in LDCT group

Number needed to screen = 307 per death prevented

Asians were underrepresented in the study

<table>
<thead>
<tr>
<th>Race or ethnic group</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>11,712</td>
<td>11,352</td>
</tr>
<tr>
<td>Female</td>
<td>28,752</td>
<td>26,030</td>
</tr>
<tr>
<td>Total</td>
<td>40,464</td>
<td>37,382</td>
</tr>
</tbody>
</table>

Role of LDCT for screening high risk never smokers is unknown and not currently recommended.

Lung Cancer Screening Recommendations

- Risk assessment
- Risk stratification
- Screening

Number needed to screen = 307 per death prevented
The leading cause of cancer mortality for women in the U.S. is?
A. Breast Cancer
B. Lung Cancer
C. Ovarian Cancer
D. Cervical Cancer

LDCT is recommended for lung cancer screening in the following patient:
A. 65 year old male non-smoker with 10 years of second hand smoke exposure.
B. 45 year old male, current 20 pack year smoking history and radon exposure.
C. 55 year old Asian female, never smoker.
D. 60 year old female with 30 pack year smoking history, but quit 10 years ago.

Which diagnosis should NOT be considered in a never smoker with a chronic cough?
A. Lung cancer, never smokers cannot get lung cancer.
B. Asthma
C. ILD
D. Chronic infection
E. None of the above (anyone with lungs can get lung cancer).

Thank you!