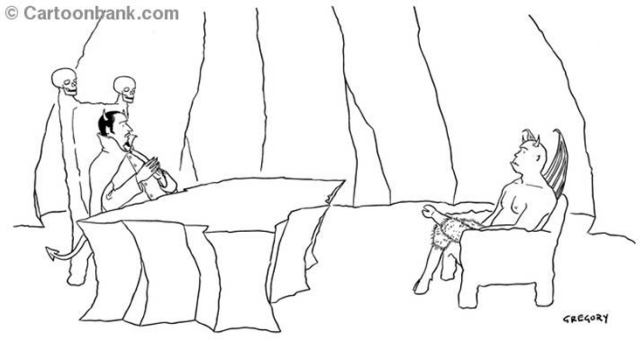
Lung Cancer: Overview and Updates

Peter H. Johnson, M.D.

Medical Oncologist & Hematologist, Columbia-St. Mary's Hospital

February 1, 2018



"I need someone well versed in the art of torture—do you know PowerPoint?"

Disclosures

No financial interests to disclose
No conflicts of interest to disclose

Overview and Objectives

1. Relevance of lung cancer to medical practice

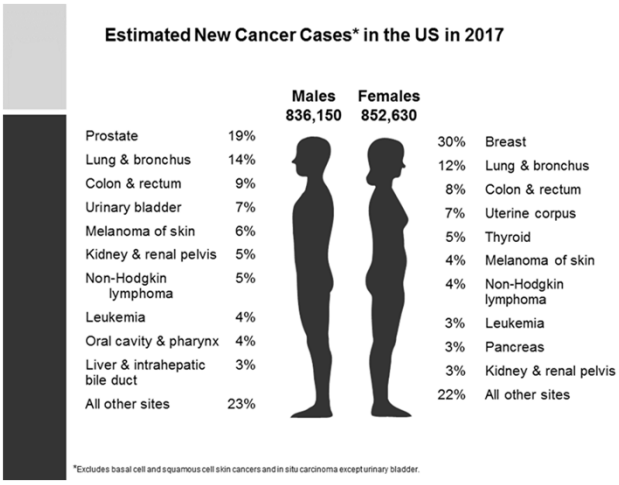
2. Screening and Staging

3. Overall Approach to Treatment

4. Targeted and Immune-Modulating Therapy

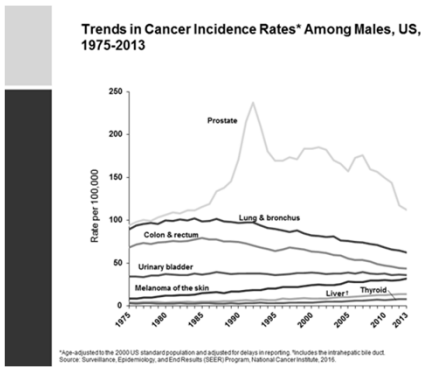
Bottom Line Goal: To be useful to primary care and midlevel providers

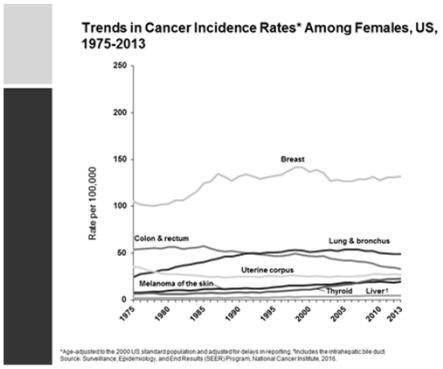
Relevance Of Lung Cancer: High Incidence



From American Cancer Society, Cancer Statistics 2017, at www.cancer.org

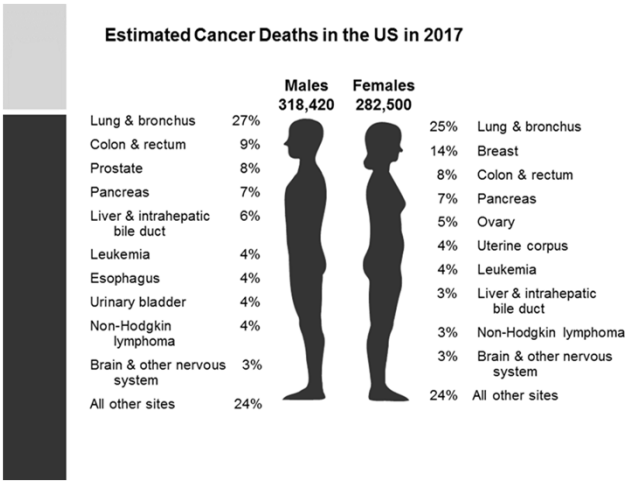
Relevance of Lung Cancer: Waning, Kind Of





From American Cancer Society, Cancer Statistics 2017, at www.cancer.org

Relevance of Lung Cancer: High Mortality



From American Cancer Society, Cancer Statistics 2017, at www.cancer.org

Relevance of Lung Cancer: Increasingly Curable

"Unfortunately, there's no cure—there's not even a race for a cure."

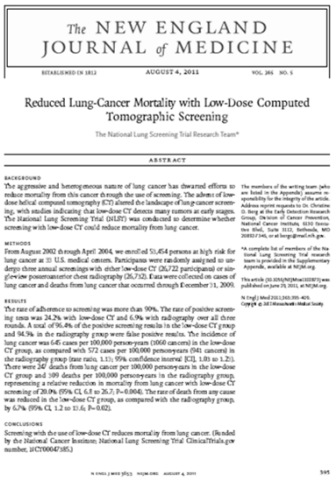
Trends in Five-year Relative Survival Rates (%), 1975-2012

Site	1975-1977	1987-1989	2006-2012
All sites	49	55	69
Breast (female)	75	84	91
Colorectum	50	60	66
Leukemia	34	43	63
Lung & bronchus	12	13	19
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	73
Ovary	36	38	46
Pancreas	3	4	9
Prostate	68	83	99
Urinary bladder	72	79	79

5-year relative survival rates based on patients diagnosed in the 9 oldest SEER registries from 1975-1977, 1987-1989, and 2006-2012, all followed through 2013.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2016.

From American Cancer Society, Cancer Statistics 2017, at www.cancer.org

Screening & Staging: Screening Saves Lives



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

ABSTRACT

BACKGROUND

The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

METHODS

From August 2002 through April 2004, we enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers. Participants were randomly assigned to undergo three annual screenings with either low-dose CT (26,722 participants) or standard chest posteroanterior chest radiography (26,732). Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

RESULTS

The rate of adherence to screening was more than 90%. The rate of positive screening tests was 24.2% with low-dose CT and 6.9% with radiography over all three rounds. A total of 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false positive results. The incidence of lung cancer was 645 cases per 100,000 person-years (1060 cancers) in the low-dose CT group, as compared with 572 cases per 100,000 person-years (941 cancers) in the radiography group (rate ratio, 1.13; 95% confidence interval [CI], 1.03 to 1.23). There were 247 deaths from lung cancer per 100,000 person-years in the low-dose CT group and 309 deaths per 100,000 person-years in the radiography group, representing a relative reduction in mortality from lung cancer with low-dose CT screening of 20.0% (95% CI, 6.8 to 26.7; P=0.004). The rate of death from any cause was reduced in the low-dose CT group, as compared with the radiography group, by 6.7% (95% CI, 1.2 to 13.6; P=0.02).

CONCLUSIONS

Screening with the use of low-dose CT reduces mortality from lung cancer. (Funded by the National Cancer Institute; National Lung Screening Trial ClinicalTrials.gov number, NCT00047385.)

- Ages 55 – 74 years
- Smoked at least 30 pack-years
- If former, quit within 15 years
- 3 annual CTs or 3 CXRs
- CTs reduced lung-cancer mortality by 20% (P = 0.004)*
- CTs reduced death from any cause by 6.7% (P = 0.02)*
- 2/2015: Medicare covers this
- BTW, Mammograms reduce relative risk of breast cancer death by ~15%, depending upon the population screened**

* The National Lung Screening Trial Research Team, in NEJM 8/4/2011 ** Krishnaiah et al, AmFamPhysician 2012 Jan 15;85(2): 176-183

Screening & Staging…Dx: Histology Matters

Small Cell: ~25% of U.S. Cases

- Limited Stage: Chemo-XRT…?Cure
- Extensive Stage: Chemo in 1st-line
- Extensive Stage: 2nd line ? Immune-Modulating Therapy (PD1-inibitor, with or without CTLA4-inhibitor)
- Prophylactic WBRT decreases brain mets and improves survival

NSCLC: ~75% of U.S. Cases

- Take incidental findings seriously:
- 1990-2013: Proportion of never-smokers with lung cancer increased from 8 to 14.9%--women predominated (their rate rose from ~10% to 22%).*
- Remainder of today's talk: NSCLC
- Specifically: Adeno vs Squamous
- (Not large cell or neuroendocrine)
- Type of chemo informed by histo
- Check mutations, re targeted Tx

* Pelosof et al, in JNCI 2017 Jul;109

Staging: Informs Prognosis and Treatment

- 4 Stages by ~random decree; point is to succinctly convey Px & Tx
- Novel Concept: Basically, cancer is bad; the less of it, the better
- TNM Staging Matrix: Know of it (e.g., www.nccn.org); do NOT memorize it
- Multidisciplinary collaboration is critical: Surgery, Rad Onc, Med Onc, etc.
- Staging often requires surgery, e.g., assessment of mediastinal nodes.
- Don't forget the most important organ in the body: MRI Head for Stage 2+

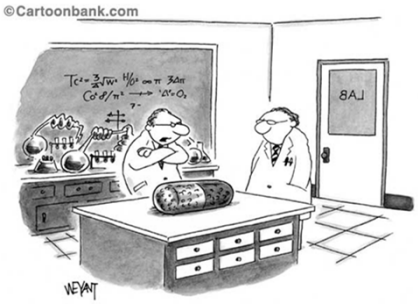
Overall Approach to Treatment

- With recent advances, the Px and Tx targets are moving faster and faster…Very Broadly:
- If <4 cm, with negative margins and no nodal involvement: Surgery only
- > golf ball, nodal involvement, + margins, or other badness: multimodality Tx
- **Stage I**: Likely Surgery Only, then surveillance (for, like, forever, or @least 5 years)
- **Stage II**: Surgery --> Adjuvant Chemo, +/- Radiation (e.g., for + margins)
- **Stage III**: Concurrent Chemo-Radiation --> Surgery, if possible
- **Stage IV**: Systemic Therapy (as opposed to chemo) +/- Radiation, Surgery

See nccn.org section on non-small cell lung cancer

Overall Approach to (Systemic) Treatment

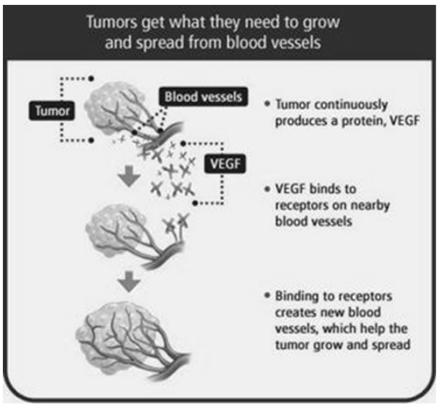
- Golden Oldies: Platinum-based doublets; taxane-based doublets
- Used in pre-operative, adjuvant, and metastatic settings
- Carboplatin-Paclitaxel, Cisplatin-Pemetrexed, Gemcitabine-Docetaxel, "blah blah blah…"
- Can be tough on the kidneys
- Can be tough on the nerves
- Can be tough on the blood cells
- Can be tough on the patient… and the oncologist…



"That's just great. I discover the cure for the common cold and all you can do is criticize."

Targeted Therapy

Bevacizumab is a VEGF Inhibitor,* used w/ chemotherapy in Stage 4 Adenocarcinoma



Specific Genetic Alterations Targeted by Therapies for Stage 4**

- EGFR Mutation (4 agents!)
- ALK Rearrangement (4 agents)
- ROS1 Rearrangement (2 agents)
- BRAF V600 Mutation (1 agent)
- PD-L1 Expression (3 agents)
- More targets are on the horizon
- Most alterations are rare; look for them all with multi-gene testing
- Most treatment agents are oral (TKIs), well-tolerated (e.g., no hair loss).

* www.colorectal-cancer.ca

** www.nccn.org

Immune-Modulating Therapy

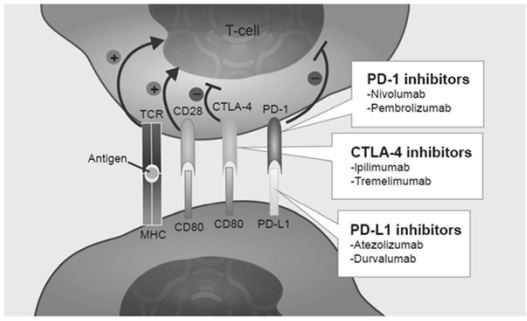


Figure 2 Mechanism of action of immune checkpoint inhibitors.
Notes: T_{reg} depend on the activity of CTLA-4, PD-1, and PD-L1 to induce immunosuppression. Ipilimumab and tremelimumab are monoclonal antibodies that inhibit CTLA-4, while nivolumab, pembrolizumab, atezolizumab, and durvalumab inhibit PD-1 and PD-L1. These drugs act by reducing immuno checkpoint activity on a T_{reg}-rich microenvironment, thus diminishing tumor evasion.
Abbreviations: T_{reg}, regulatory T-cells; TCR, T-cell receptor; MHC, major histocompatibility complex.

- These agents turn on the immune system, to help the body fight the cancer
- Toxicities often stem from autoimmune problems, e.g., colitis, pneumonitis, and endocrine problems

From de Mello et al, in OncoTargets and Therapy, 2017, Volume 10

Summary & Recap

1. Relevance of lung cancer to medical practice

- Lung Cancer is the leading cause of cancer death in both M&W in the US
- Rates are declining overall, but increasing among never-smokers
- Lung cancer cure rates are improving

2. Screening and Staging

- Screening current or ex-smokers w/ 30+ pk yrs, ages 55-74, saves lives
- Staging helps convey prognosis and treatment; both are moving targets, given advances
- Staging often requires surgical eval of the mediastinum, and MR imaging of the brain

3. Overall Approach to Treatment

- Histology matters (small cell vs NSCLC; adeno vs squamous, etc.)
- Multidisciplinary approach to treatment is critical to optimizing outcomes
- Classic chemotherapy doublets (platinums, taxanes) remain important in stages II-IV

4. Targeted and Immune-Modulating Therapies

- Currently these agents are confined to use in the stage 4 setting
- We have an increasing # of treatments for an increasing number of targets (each is rare)
- These agents are generally better tolerated and more effective than chemo, but they still have side effects

Bottom Line: To be useful! Questions?