Lung Cancer: Overview and Updates

Peter H. Johnson, M.D.

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

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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

![Estimated New Cancer Cases in the US in 2017](image)

Relevance of Lung Cancer: Waning, Kind Of


Relevance of Lung Cancer: High Mortality

Relevance of Lung Cancer: Increasingly Curable


Screening & Staging: Screening Saves Lives

- 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**

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-inhibitor, 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...
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

- 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?