Treating Invisible Disease:
How the Probability of Disease We Can’t See Changes Our Treatment Strategy in Lung Cancer

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Why should we care about cancer we can’t see?

• Cancer risk is a combination of that from visible disease and potential/presumed risk posed by disease we cannot see.

• The balance of our focus on visible vs. invisible disease shapes a huge amount of our treatment recommendations for different settings in lung cancer (and other cancers).

• The main threat of recurrence in early stage, and the reason metastatic disease is considered incurable, is a product of invisible, micrometastatic cancer.
Assessing Risk of Invisible/Micrometastatic Disease

**Lower risk**
- Squamous cell, bronchiololalveolar carcinoma
- Lower metabolic uptake (SUV) on PET
- Lower grade/well differentiated cancer
- Minimal progression over scans prior to diagnosis
- Lower stage
  - Smaller primary tumor
  - Lower nodal stage
  - Few nodes involved

**Higher risk**
- Significant progression over scans prior to diagnosis
- Adenocarcinoma, small cell lung cancer
- Higher metabolic uptake (SUV) on PET
- Higher grade/more poorly differentiated cancer
- Higher stage
  - Larger primary tumor
  - Higher nodal stage
  - Larger number of nodes involved
Local Therapy is Leading Treatment for Limited Visible Cancer

- Surgery is the cornerstone of treatment for early stage NSCLC.
- Radiation is favored for early stage NSCLC in patients who cannot tolerate surgery.
- Traditionally, surgery has been favored for disease that is felt most likely to be limited to what you can see (if tolerable for patient).
- As risk of invisible disease relative to visible disease increases, radiation becomes more favored over surgery because radiation “casts a wider net” to treat regional invisible disease than surgery.
Systemic therapy can treat both visible and invisible/micrometastatic disease

- Systemic (whole body) treatments like chemotherapy (usually IV) or targeted therapies (oral or IV) go throughout the bloodstream to treat cancer everywhere*

- It is used in many lung cancer settings.
  - For potentially curable lung cancer, it is given to reduce risk of micrometastatic disease causing recurrence after surgery and/or radiation given to eradicate localized disease.
  - In locally advanced (stage III) NSCLC, it is given to make radiation more effective within the radiation field, and also to treat invisible disease outside of the radiation field.
  - For advanced lung cancer (NSCLC or SCLC), it is given to simultaneously shrink visible disease and to inhibit progression with new areas of disease caused by invisible micrometastases.

*systemic therapies often don’t get into the central nervous system (CNS) very well because of the blood-brain barrier
Why We Can’t Consider Advanced NSCLC Cured Even if We Can’t See it

- Once someone has metastatic disease (including spread to fluid outside of the lungs), this indicates that cancer can spread throughout the body and will almost invariably recur, even if all of the visible disease is removed.

- Having metastatic lung cancer (or many other cancers) is like having a lawn full of dandelions. Just as pulling each dandelion won’t eradicate the problem, treating every individual lesion in the body is not a cure.

- The invisible cancer, like dandelion seeds, are destined to cause new areas to pop up.

- The goal is to control invisible disease along with visible disease simultaneously.
Getting to NED: The Goals of Treatment for Advanced Lung Cancer

• Because we can’t feasibly eradicate all invisible disease, our goals for patients with advanced lung cancer involve balancing several factors.

  – We want to shrink the visible cancer as much as possible, with the ideal case being “NED”: No Evidence of Disease

  – We want to prevent both existing lesions from growing and from invisible, micrometastatic disease progressing into new visible lesions. This boils down to maximizing time before disease shows evidence of progression.

  – We want to do control the visible and invisible disease for as long as possible and with the best tolerated treatment possible.

A normal chest CT. Even if we can’t realistically expect “NED” status to last forever in someone with advanced lung cancer, it’s great to see and associated with a very favorable prognosis.