Genetic Testing: Who and Why?

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Objective

To understand the populations in whom genetic testing is performed and why

Agenda

Clinical vs. Molecular Dx

Types of testing

Who to test

Agenda

Clinical vs. Molecular Dx

Types of testing

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Clinical Utility

- Can the diagnosis be made on clinical features alone?

- How will molecular testing aid in prognosis or treatment?

Clinical vs. Molecular Diagnosis

Achondroplasia

Typically diagnosed by characteristic clinical and radiographic findings

Down syndrome

Physical features may be present, but a molecular test is often needed for confirmation

Agenda

Clinical vs. Molecular Dx

Types of testing

Who to test

Types of testing

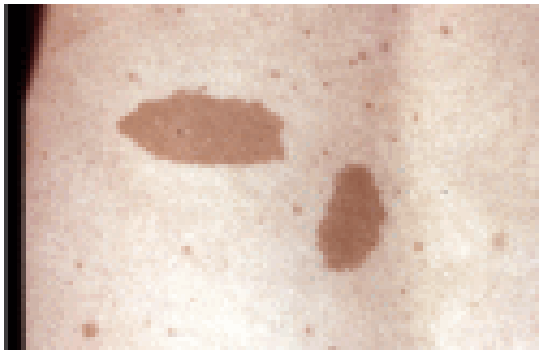
- Testing an affected (symptomatic) individual's germline
  - Diagnostic, Prognostic, Therapeutic
- Testing an asymptomatic individual to determine future risk
- Testing an individual's germline to benefit family
- Testing of DNA from cancer cells
  - Diagnostic, Prognostic, Treatment response

1. Germline testing in affected individuals

Diagnostic

Neurofibromatosis Type 1?

Risk for neurofibromas and optic glioma



Legius?

No risk for tumors

Constitutional Mismatch Repair Deficiency?

Risk for colon and brain cancer in childhood

1. Germline testing in affected individuals

Prognostic

- Long QT syndrome
  - Syncope
  - Sudden cardiac death

- LQT1 – exercise, emotion
  - Avoidance of strenuous exercise

- LQT2 – emotional stress and auditory stimuli
  - Avoidance of loud noises, e.g. alarm clocks

1. Germline testing in affected individuals

Therapeutic

Plavix

CYP2C19

2. Germline testing to benefit family

FAP

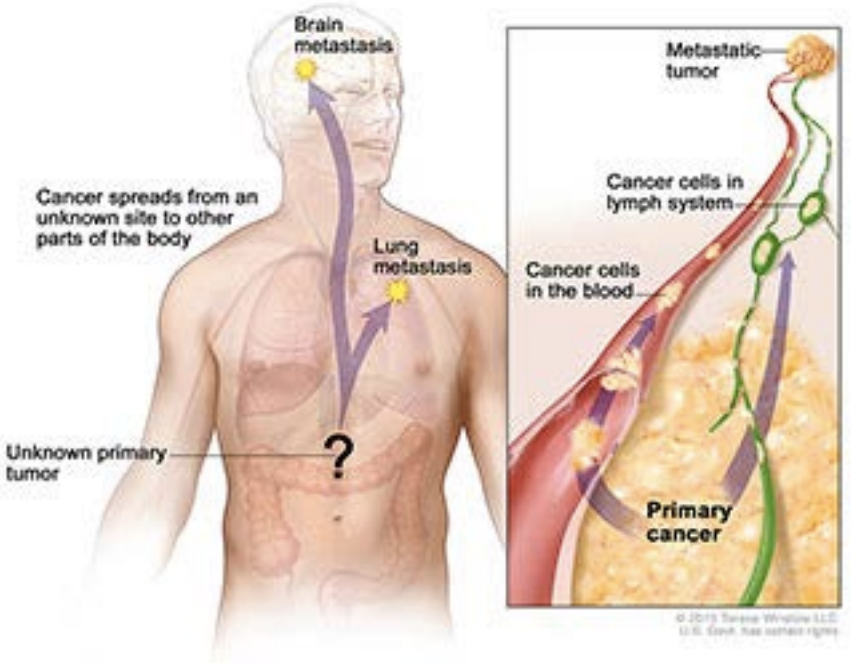
Often a clinical diagnosis, BUT...

3. Germline testing in UNaffected individuals

- No personal history/features
- Family history
- Clinical Utility

4. DNA testing of cancer cells

Diagnostic



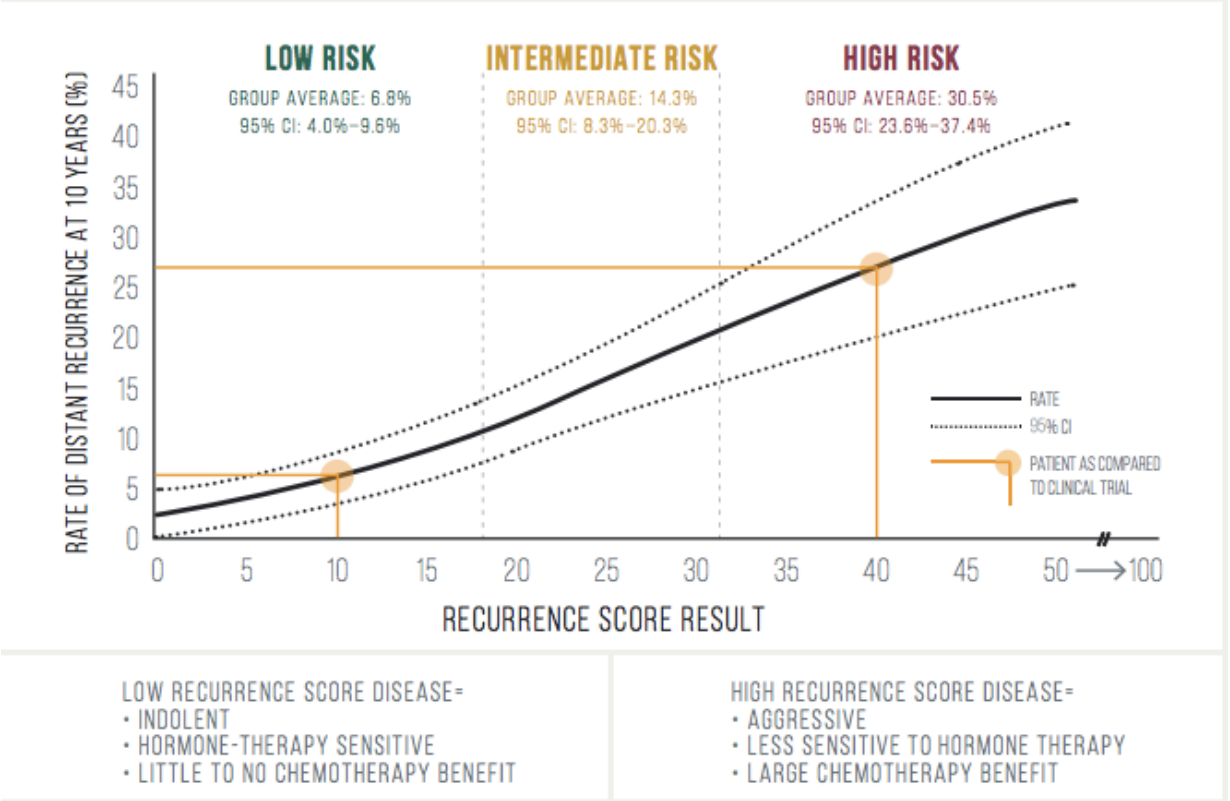
Cancer of Unknown Primary

http://www.cancer.gov/types/unknown-primary

4. DNA testing of cancer cells

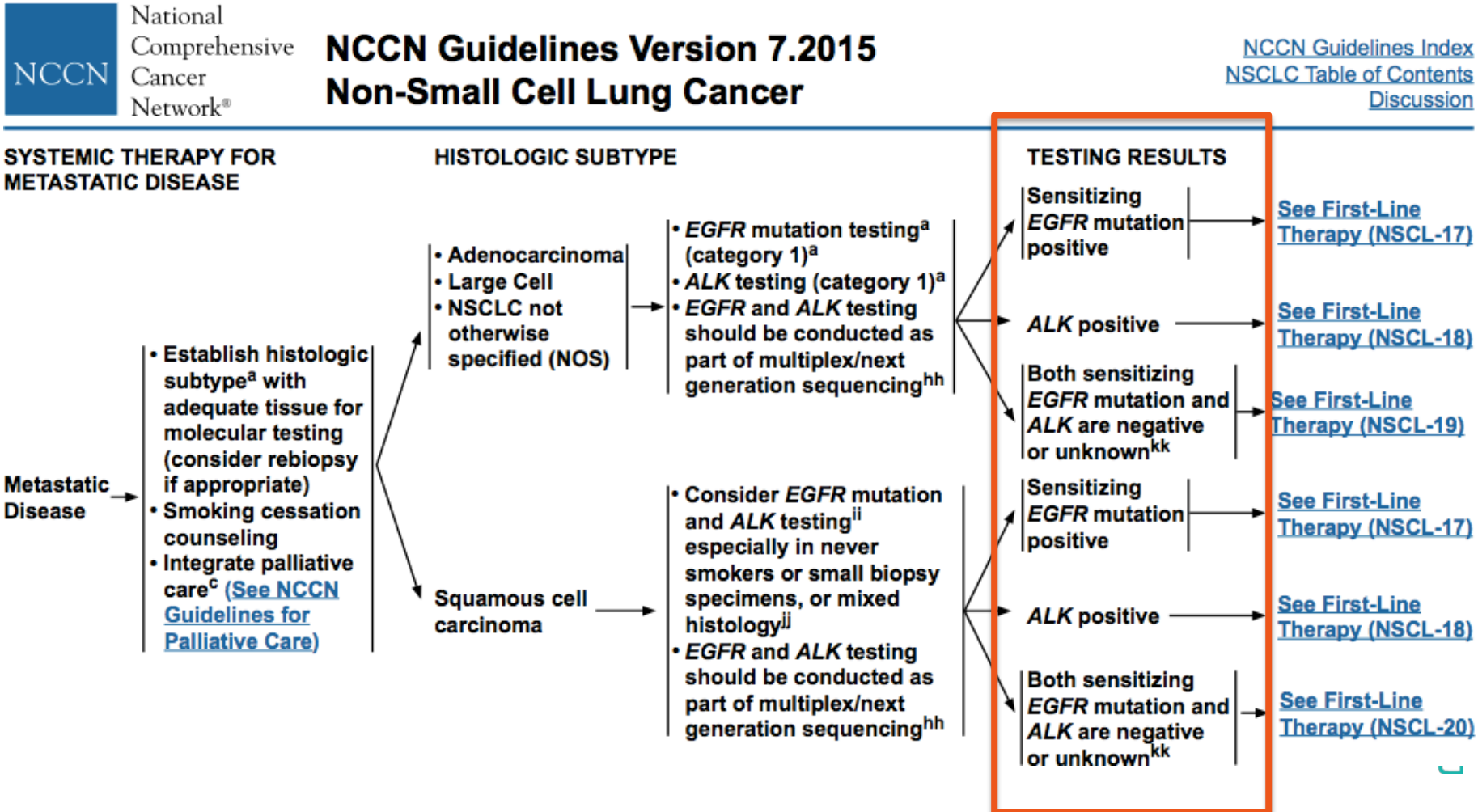
Prognostic

oncotype DX® Breast Cancer Assay



4. DNA testing of cancer cells

Therapeutic



Agenda

Clinical vs. Molecular Dx

Types of testing

Who to test

Who to test

- Proband

- At risk-relatives
  - Mode of inheritance (AR, AD, X-linked)
  - De-novo mutation rate
  - Degree of penetrance

Who to test

- Li-Fraumeni syndrome
  - AD
  - Highly penetrant
  - Management guidelines available
- Rett syndrome
  - X-linked dominant
  - >99% de-novo rate

Clinical Utility

Thank you