Molecular In My Pocket™

ONCOLOGY: Molecular Testing in NSCLC – Clinical Aspects in Small Specimen Processing

Pre-Procedural Evaluation

• Choose the best biopsy method to optimize yield (EBUS-TBNA for large mediastinal adenopathy, TTNA for peripheral nodule, etc.)
• Identify reason for biopsy
  • Initial diagnosis
  • Known diagnosis but need additional tissue for molecular testing
• Optimize pre-procedural imaging to maximize procedural yield

Specimen Collection

• Image guidance to improve sample acquisition
• Utilize ROSE to confirm adequate tissue for testing needs
• Needle gauge (procedure dependent)
• Number of passes
• Operator skill and technique

Specimen Handling

• Utilizing ROSE to triage specimen
• Collection of specimen within appropriate media (formalin/non-formalin fixatives)
• Perform additional passes for cell block
• Communicate case details with pathology to optimize specimen triage

Request for molecular studies and follow up on the biopsy results

Initial biopsy reveals adenocarcinoma
  PD-L1 immunohistochemistry
  Test for actionable mutations (NGS panel testing favored over individual tests)

Initial biopsy reveals adenocarcinoma, but limited tissue remains after diagnostic workup
  Communicate presence of limited testing material to the ordering provider and prioritize testing based on discussion
  Consider ordering cell-free DNA test (informative, if positive)
  Consider repeat biopsy, communicate “molecular priority” protocol for known diagnosis

Patients progressing on initial EGFR TKI
  Test for actionable mutations such as T790M, MET amplification, ERBB2/Her-2 amplification
  Cell-free DNA test (informative, if positive), otherwise repeat tissue biopsy

Patient progressing after immunotherapy: biopsies remain experimental in this situation.

See online supplement for references and abbreviations: www.amp.org/PocketGuides

See Reverse
**Biopsy/FNA Procedure**

- **Additional NFC Specifically for Molecular**
  - **Fine Needle Aspiration**
    - EBUS TBNA
    - Transthoracic (lung)
    - Metastatic sites
  - **Other Cytology**
    - Brushing/Washing
    - Bronchial Lavage
    - Effusion
  - **Needle Biopsy**
    - Transthoracic (lung)
    - Metastatic sites
  - **Forceps Biopsy**
    - Transbronchial

**FFPE**
- Biopsy
- Cytology cell block

**FFPE Histology Processing**
- 10% neutral buffered formalin
- Volume of fixative (10:1)
- Fixation Time (6-72 h)
- Avoid acid/heavy metal fixatives
- Avoid decal with harsh acids
- Separate soft tissue before decal
- Use EDTA/formic acid for decal

**Non-FFPE Cytology**
- Smears
- Cytospin preparations
- Touch preparations (TP)
- Liquid based cytology (LBC)

**Diagnostic Workup**

**Molecular Testing**

**Transfer directly to molecular**

**Tissue Preserving Processing**
- Minimize IHC use (TTF-1 & p40 as first line IHC)
- Sectioning protocols with designated upfront sections for potential IHC, FISH, and molecular
- Special tissue preserving techniques for molecular priority cases
- Use paired FNA as non-decal source
- Use paired NFC (smear, TP, LBC) as alternate source for molecular testing

**Non-FFPE Cytology (NFC)**
- Additional smear/TP for molecular**
- LBC residual needle rinse**

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