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

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*

* if the sample is too small to do mutation testing, reflex to fluorescence *in situ* hybridization (FISH) for rearrangements of *ALK*, *ROS1*, *RET*, and *MET* amplification.

See Reverse

Prepared by the Association for Molecular Pathology Training and Education Committee
For more educational resources, see: *www.amp.org/AMPEducation*

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Biopsy/FNA Procedure

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 (NFC)
- Smears
- Cytospin preparations
- Touch preparations (TP)
- Liquid based cytology (LBC)

Diagnostic Workup

Molecular Testing

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

Transfer directly to molecular

**Assay specific validation required

Additional NFC Specifically for Molecular

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

See Reverse

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