Testing Solutions

Overcome common biomarker testing challenges with actionable solutions.

Reading time: **15 min**

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Adopt a Collaborative, Multidisciplinary Approach to Help Reduce Barriers to Biomarker Testing

To order the right test at the right time, MDT collaboration is crucial. Consistent reporting and interpretation of results can open opportunity for pathologists within their MDT to work closely together and optimize the biomarker testing process.[1]

Here, you will find a range of practical solutions to overcome common challenges across the biomarker testing journey.

MDT, multidisciplinary team.

Sample Collection

Challenge: To test patients we need enough tissue

- Patients may miss out on biomarker tests if an initial biopsy is not performed or there is insufficient tissue or tumor cell content due to tumor inaccessibility[2]

Solutions:

Rapid on-site evaluation (ROSE):
May help increase the number of passes, slides, and cell blocks[3]

Liquid biopsy:
Can supplement tissue biopsy in the advanced or metastatic setting to increase detection of actionable mutations[4,5]

Next-generation sequencing (NGS):
May help identify diagnostic and prognostic indicators, while minimizing tissue use and wastage[6,7]

NGS, next-generation sequencing; ROSE, rapid on-site evaluation.

Helpful Resources for Sample Collection

3.74 MB

FOR HCPS

Best practices in implementing biomarker testing for metastatic

Read about complete biomarker profiling for informing treatment in metastatic non-small cell lung cancer (mNSCLC), and best practices for performing biomarker testing.

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Sample Processing

Challenge: Suboptimal preanalytical factors resulting in lab testing errors

- As many as 70% of lab testing errors are caused by suboptimal preanalytical factors related to sample mishandling, transport, processing, and storage[8]

Solutions[8]:

- **Time to fixation/cold ischemia time**: ≤1 hour
- **Fixative type**: Standardized and quality-controlled 10% pH neutral phosphate-buffered formalin
- **Total fixation time**[a]: 6–36 hours
  - 24 hours (protein)
  - 6–48 hours (high fat content e.g., skin/breast)
- **Specimen thickness**: ≤4–5 mm
- **Ratio of fixative volume to tissue mass**: At least 4:1 (preferably 10:1)
- **Paraffin type**: Pure low-melt paraffin (melts at <60°C)
- **Block storage**: Dry, pest-free, room temperature (25°C) conditions

[a]Your surgeon can advise on the proper time to fixation.

Helpful Resources for Sample Processing

3.18 MB

FOR HCPS

Controlling preanalytical variables in blood specimens to help

Download this resource to understand the College of American Pathologists' (CAP) recommendations for controlling preanalytic variables in blood specimens for reliable biomarker testing results.

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FOR HCPS

Controlling preanalytical variables in tissue specimen variables to

Download this resource to understand the College of American Pathologists' (CAP) recommendations for controlling preanalytic variables in tissue specimens for reliable biomarker testing results.

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Diagnosis & Staging

Challenge: Estimation errors in tumor cell count leading to misclassification

- Even with proper sample processing, tumor cell content (TCC) can still be under- or over-estimated, impairing valid testing and possibly contributing to tumor misclassification informing the treatment decision[9]

Potential Solutions:

- Digital pathology:
  By creating magnified, high-resolution images similar to standard microscopy for pathologist examination, this technology may improve the accuracy of TCC estimates[9–12]
- Digitally guided microdissection:
  By aiding mutation detection in difficult to dissect tumors, this technique offers significant improvement in TCC through increased resolutions compared with manual microdissection[13,14]

TCC, tumor cell content.

Test Ordering

Challenge: Not ordering all recommended tests

- People can miss out on biomarker testing due to not having all their recommended tests ordered; this can happen through varying awareness of guidelines, low confidence in testing value, and test accessibility.[2] Lack of access to genetic counseling may also result in eligible people missing out on guideline-recommended genetic testing[15]

Solutions:

- **Next-generation sequencing (NGS)**:
  A comprehensive biomarker testing method of detecting genomic alterations, with more timely results compared to sequential or exclusionary testing[16,17]
- **Guidelines**:
  Access quick-reference flowcharts summarizing NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) for biomarker testing:

  Lung biomarker testing[a] → | **Ovarian biomarker testing** →
  Breast biomarker testing → | **Prostate biomarker testing** →

- **Approved tests**:
  Access a list of FDA-approved diagnostic assays for each biomarker:

  Lung Cancer
  EGFR →
  ERBB2 (HER2) →
  Ovarian Cancer
  HRD →
  Breast Cancer
  HER2 →
  BRCA1/2 →
  PIK3CA/AKT1/PTEN →
  Prostate Cancer
  HRRm, including *BRCA1/2* →

- **Genetic counseling:**
  Broaden access to genetic counseling services via telegenetics[15]

[a]This page contains content pertaining to non-small cell lung cancer (NSCLC) only

AKT1, serine/threonine protein kinase 1; *BRCA1/2*, BReast CAncer susceptibility gene 1/2; *EGFR*, epidermal growth factor receptor; *ERBB2*, erb-b2 receptor tyrosine kinase 2; FDA, US Food and Drug Administration; *HER2*, human epidermal growth factor receptor 2; HRD, homologous recombination deficiency; HRRm, homologous recombination repair mutation; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*, phosphatase and tensin homolog.

Testing & Interpretation

Challenge: Suboptimal test turnaround times impacting treatment decisions

- While test turnaround times (TATs) vary based on the type of test and batching of samples, suboptimal TATs can lead to premature initiation of treatment or untargeted therapy without consideration of test results[1]

Challenge: Lack of standardized testing protocols

- A lack of standardized testing protocols in place for the MDT that are clinically validated and reliably reproducible can contribute to incomplete testing[1]

Solutions:

- **Reflexive testing**:
  Can reduce biomarker TAT by an average of 15–37 days in lung cancer[18–20] and a nearly 34-day average reduction in melanoma vs. standard testing[21]
- **Liquid biopsy**:
  While tissue-based testing is typically performed for most biomarkers, liquid biopsies for plasma ctDNA NGS can support complementary (concurrent) testing along with a tissue sample, and may mitigate TAT or tissue insufficiency.[4–6,22] Although not recommended in all cancers, such as resectable NSCLC, plasma ctDNA biopsies are an option in others, such as metastatic NSCLC and metastatic prostate cancer, in situations where a tissue biopsy is unsafe or unfeasible.[6,23]

ctDNA, circulating tumor deoxyribonucleic acid; MDT, multidisciplinary team; NGS, next-generation sequencing; NSCLC, non-small cell lung cancer; TAT, test turnaround time.

Reporting & Results Delivery

Challenge: Delivering standardized reporting for greater clarity

- Unclear and inconsistent reporting can prevent the initiation of appropriate targeted therapy[24]

Solutions:

- **Synoptic reporting**:
  Adhere to regulatory guidelines using standard terminology to avoid ambiguities and misunderstandings[24–27]
- **Report mutations consistently**:
  Access sample reports for your practice below in Helpful Resources
- **Reporting guidance**:
  Navigate to guidance on interpreting and reporting biomarker test results

  Lung Cancer
  EGFR →
  ERBB2 (HER2) →
  Ovarian Cancer
  HRD →
  Breast Cancer
  HER2 →
  BRCA1/2 →
  PIK3CA/AKT1/PTEN →
  Prostate Cancer
  HRRm, including *BRCA1/2* →

AKT1, serine/threonine protein kinase 1; *BRCA1/2*, BReast CAncer susceptibility gene 1/2; *EGFR*, epidermal growth factor receptor; *ERBB2*, erb-b2 receptor tyrosine kinase 2; *HER2*, human epidermal growth factor receptor 2; HRD, homologous recombination deficiency; HRRm, homologous recombination repair mutation; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; *PTEN*, phosphatase and tensin homolog.

Considerations for Your Practice

Overcome biomarker testing challenges with a combined MDT process:

- Obtain initial biopsy and ensure tissue sufficiency
- Calibrate preanalytical factors
- Define appropriate diagnostic methods
- Identify and routinely order recommended tests
- Communicate TATs
- Standardize reporting for improved consistency and interpretation

Putting these protocols in place can reduce the risk of eligible people with cancer missing out on potential targeted therapeutic opportunities.

MDT, multidisciplinary team; TAT, test turnaround time.

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