Improving the Timeliness of Biomarker Testing by Using Liquid Biopsy When Tissue Samples are Insufficient for Testing

<table>
<thead>
<tr>
<th>Problem Statement</th>
<th>Root Causes</th>
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<tbody>
<tr>
<td>Biomarker testing may be delayed when tissue samples are inadequate for testing.</td>
<td>● The current process is to send biopsy tissue samples to an outside reference lab for biomarker testing. When the lab determines that the samples are inadequate for testing, then a report is generated and sent to pathology. The oncologist may then order a liquid biopsy test.</td>
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<tr>
<td>This may lead to delays in definite treatment planning for patients who have actionable molecular biomarkers (eg, ALK, EGFR, ROS1, etc.)</td>
<td>● There is no current workflow that triggers a reflex blood biopsy test if the tissue test is not adequate for testing.</td>
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</table>

As of June 2020, the following actionable molecular biomarkers (genomic alterations) have FDA-approved targeted therapies for patients with advanced NSCLC: *

<table>
<thead>
<tr>
<th>Molecular Biomarker</th>
<th>Targeted Therapy (Generic Drug Name)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>osimertinib, gefitinib, erlotinib, afatinib</td>
</tr>
<tr>
<td>ALK</td>
<td>alectinib, crizotinib, ceritinib, brigatinib, lorlatinib</td>
</tr>
<tr>
<td>ROS1</td>
<td>entrectinib, crizotinib</td>
</tr>
<tr>
<td>BRAF V600E</td>
<td>dabrafenib/trametinib</td>
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<tr>
<td>NTRK</td>
<td>larotrectinib, entrectinib</td>
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<tr>
<td>MET</td>
<td>capmatinib</td>
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<tr>
<td>RET</td>
<td>selpercatinib</td>
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*For this project, PD-L1 is not being included.
Baseline Measurement:

- Identify a cohort of patients with stage IV NSCLC who are being treated with one of the targeted agents listed above
  - Positive molecular biomarker:
  - Type of biomarker testing performed (tissue vs. blood testing)
  - Treatment drug name(s):
- Create a spreadsheet that includes the following dates (these are suggested dates and your team may choose to collect additional data):
  - [date1: date of biopsy]
  - [date2: date when molecular biomarker testing was ordered]
  - [date3: date when biomarker test results were available]
  - [date4: date when the targeted therapy was started]
- Calculate the intervals from [date1] to [date2], [date1] to [date3], and [date1] to [date4].
- Look for patterns or trends in the data: Are there any outliers? What factors may impact these time intervals?

Discuss causes and effects:
**Aim Statement (example):**

- When treating patients with advanced NSCLC who have positive actionable molecular biomarkers, we will work over the next <xx> months to reduce the time from diagnosis to treatment by <xx> days.

**Potential Solution:** New workflow that includes up-front liquid biopsy testing when the biopsy tissue samples are suspected to be inadequate for molecular biomarker testing

**Biopsy information sheet:**

- The team will develop a biopsy information sheet that includes essential information (e.g., the suspected disease stage, the performance status of the patient, etc.)
- Prior to performing a biopsy, the pulmonologist will review the biopsy information sheet

**At the time of biopsy:**

- At the time of biopsy, the nursing staff will draw blood and hold the sample for possible liquid biopsy testing
  - This blood sample will be sent if pathology reviews the biopsy tissue material and determines that the sample may not be adequate for molecular biomarker testing
- If pathology suspects that the biopsy tissue material is inadequate for molecular biomarker testing, then:
  - Pathology will send the tissue for PD-L1 testing
  - Pathology will notify pulmonology to send the blood for liquid biopsy testing
  - Pulmonology will send communication to pathology to confirm that the liquid biopsy test was ordered

**Measurement:**

- After implementing the new workflow, the project team will measure the following dates in patients with advanced NSCLC who have positive actionable molecular biomarkers:
  - [date1: date of biopsy]
  - [date2: date when molecular biomarker testing was ordered]
  - [Date3: date when liquid biopsy test was ordered]
  - [date4: date when biomarker test results were available]
  - [date5: date when the targeted therapy was started]
- Calculate the intervals from [date1] to [date2], [date1] to [date3], [date1] to [date4], and [date1] to [date5].
- Look for patterns or trends in the data: Are there any outliers? What factors may impact these time intervals?

This data collection sheet is a resource from the ACCC educational initiative, Fostering Excellence in Care and Outcomes in Patients with Stage III/IV NSCLC.