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

Problem Statement	Root Causes
Biomarker testing may be delayed when tissue samples are inadequate for testing. This may lead to delays in definite treatment planning for patients who have actionable molecular biomarkers (eg, ALK, EGFR, ROS1, etc.)	● 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. ● There is no current workflow that triggers a reflex blood biopsy test if the tissue test is not adequate for testing.

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

Molecular Biomarker	Targeted Therapy (Generic Drug Name)
EGFR	osimertinib, gefitinib, erlotinib, afatinib
ALK	alectinib, crizotinib, ceritinib, brigatinib, lorlatinib
ROS1	entrectinib, crizotinib
BRAF V600E	dabrafenib/trametinib
NTRK	larotrectinib, entrectinib
MET	capmatinib
RET	selpercatinib

https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq

*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
  - o Positive molecular biomarker:
  - o Type of biomarker testing performed (tissue vs. blood testing)
  - o 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):
  - o [date1: date of biopsy]
  - o [date2: date when molecular biomarker testing was ordered]
  - o [date3: date when biomarker test results were available]
  - o [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:
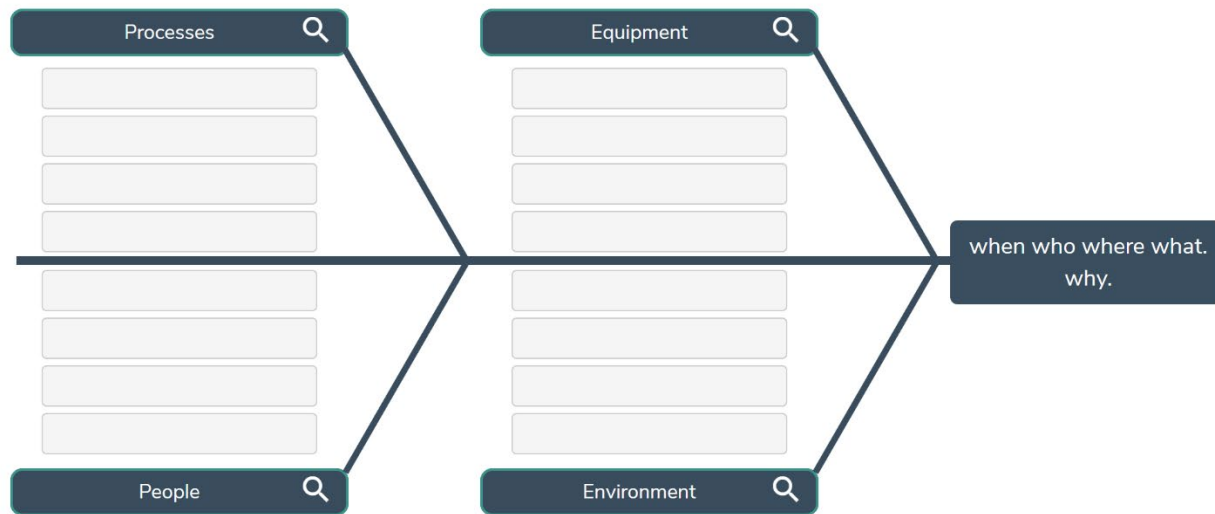
Aim Statement (example):

- 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

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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.