Addressing Lung Cancer Biomarker Testing Through Project ECHO

Case Presentation Form

Instructions

This case presentation form is intended to be completed and submitted electronically. Please email completed forms along with any optional supplemental information to Kelly.durden@cancer.org and carbon copy your regional ACS staff partner. We request that you submit your case presentation form **at least three business days** prior to your scheduled case presentation. Please do NOT submit a scan of a printed version of this form.

This form includes four sections: **Section 1: Presenter Information & Case Presentation Summary**, **Section 2: System-Level Case Presentation**, **Section 3: Patient-Level Case Presentation** and **Section 4: Faculty Recommendations**. You need to complete Section 1 and then, choose **either** Section 2 or Section 3. We recommend that each case presentation will range from **three minutes to five minutes**. Please do not include patient identifiers on this form or use any identifiers during the presentation. Please note, for patient-level case presentations, the faculty will provide guidance that should NOT be interpreted as direct medical advice.

Project ECHO Data Usage Statement

Project ECHO® collects registration, participation, questions/answers, chat comments, and poll responses for some teleECHO® programs. Your individual data will be kept confidential. These data may be used for reports, maps, communications, surveys, quality assurance, evaluation, research, and to inform new initiatives.

Section 1: Presenter Information and Case Presentation Summary

1. **Presentation Date:** 8/9/2021
2. **Presenter Name(s):** Swaty Arora
3. **Presenter Title(s):** Medical Oncologist
4. **Organization/Health System:** ARH Highlands
5. **Please summarize the case you are presenting to the group:** 69 y.o. female with RLL adenocarcinoma s/p VATS RLL lobectomy on 6/23/21. Final pathology was pT2aN0 but had two foci of adenocarcinoma in situ. Foundation-1 testing was negative for actionable mutation in EGFR. Incidental finding of BRAF V600E
6. **Which specific questions are you asking the faculty and the other participating spoke sites?**

Based on recent trials, the guidelines are clear on the role of biomarker testing and EGFR as a therapeutic target in early stage lung cancer. However, there is data to show that early stage BRAF mutant lung cancers are at an increased risk of developing second primary lung cancers harboring KRAS mutations. (Ref: J Thorac Oncol. 2014 Nov; 9(11): 1669–1674.). How does this change the management of the patient in our case? In the event of progressive disease, can I rely on the results of initial NGS and assume she has BRAF mutated disease or would I need to retest her markers? If we assume that the landscape of her tumor will change at the time of progression, should we stick to "single gene tests" for EGFR in early stage disease? In other words, are we "overtesting" with multi gene panels in early stage disease ?

Section 2: System-Level Case Presentation

1. **Describe your current system or workflow:** *If available, feel free to provide workflow charts separately.*
   Click or tap here to enter text.

2. **What are the primary challenges/barriers:** *Include specifics on identified gaps and quality improvement methods used to clarify the root causes.*
   Click or tap here to enter text.

3. **Describe what you are trying to improve and any other relevant background information:**
   Click or tap here to enter text.

4. **Briefly describe your vision of what it will look like when it is working well:**
   Click or tap here to enter text.

5. **Describe any recent changes (less than 6 months) made to this system or workflow, including when they were made and their impact:**
   Click or tap here to enter text.

6. **If applicable, what data (quantitative, qualitative) do you have to augment your observations:**
   Click or tap here to enter text.

Section 3: Patient-Level Case Presentation

DEMOGRAPHIC INFORMATION			
1. **Age**	2. **Gender (*Choose One*)**	3. **Race/Ethnicity *(Choose All that Apply)***	
69	Female☒ Male☐ Non-Binary/Third gender☐ Transgender female☐ Transgender male ☐	American Indian/Alaska Native ☐ Asian ☐ Black/African American ☐	Hispanic/Latino ☐ White ☒ More than One Race ☐ Other ☐
NON-SMALL CELL LUNG CANCER (NSCLC) HISTOLOGY & STAGE			
4. **Diagnosis**	5. **Histology**	6. **Stage**	
Initial Diagnosis ☒ Recurred and or Progressed ☐	Adenocarcinoma ☒ Squamous Cell ☐ Large Cell ☐	IB (T2aN0)	
BIOMARKER TESTING			
7. **Has biomarker testing been ordered for this patient (or will it be ordered)?**		8. **If biomarker testing was not ordered, please elaborate on the factors that precluded it:**	
Yes ☒ No ☐ Will be ordered ☐		Click or tap here to enter text.	
The next section is ONLY for those patients who HAVE received or WILL receive biomarker testing			
9. **Which technique was used (or will be used) to obtain specimen for pathologic diagnosis? *(Choose One)***			
Bronchoscopic biopsy ☐ Endobronchial ultrasound-guided transbronchial lymph node aspiration (EBUS-TBNA) ☐ Image-guided percutaneous biopsy ☒ Liquid biopsy ☐		Mediastinoscopy ☐ Surgical specimen ☒ Thoracentesis/pericardiocentesis ☐ Unsure ☐	
10. **Which platform was/will be used for lung biomarker testing? *(Choose One)***		11. **If single-gene test or short-cluster panel, please identify which genes were tested:**	

Single-Gene Test ☐ Short-Cluster Panel ☐ Multi-Gene Panel (next generation sequencing (NGS) ☒	ALK ☐ BRAF ☐ EGFR ☐	HER2 ☐ KRAS ☐ NTRK ☐ MET ☐	PD-L1 ☐ ROS1 ☐ RET ☐
ADDITIONAL INFORMATION			
12. **Please include any other information you would like to share with the group:** Foundation One testing showed BRAF V600E mutation. No actionable mutation in EGFR was detected.			

Section 4: Faculty Recommendations

This section will be completed by the ACS ECHO Coordinator. Recommendations from our faculty will be documented below.

From Susanne Arnold, MD (Guest Faculty)

- Spectacular set of questions; really hard questions, and an impressive case presentation
- Currently, not enough evidence for BRAF mutant targeted therapy adjuvantaly. However, recommend knowing this information as we really do not know when something may change. Would still recommend broad panel testing versus solely testing for EGFR or PDL-1 in the adjuvant setting. Not sure what others will recommend and will be excited to hear what Dr. Zinner and Dr. Kolesar recommendations may be.
- Time of progression: Serves as the perfect time to do either a liquid biopsy or repeat biopsy for NGS again, because as you rightly recognize, this patient could develop KRAS mutant lung cancer or still have fully BRAF mutated disease and develop recurrence and then, you are treating something completely different
- Repeat testing at the time of recurrence is an important concept
- Some individuals may suggest monitoring with liquid biopsy (Note from Dr. Arnold that this may not be as well established for BRAF as it is established for EGFR or other common mutations)

From Ralph Zinner, MD (Faculty)

- Agreed with Dr. Arnold regarding the utilization of NGS in this situation

From Jill Kolesar, PharmD, MS, BCPS, FCCP

- Looked up clinical trials; she (this patient) is not quite eligible for certain trials and is on the edge for several options. NGS is incredibly important especially if this patient is interested in clinical trial options.
- Written remarks provided by Dr. Kolesar:

  Dabrafenib + trametinib in BRAF mutant untreated metastatic NSCLC is associated with an ORR of 64% (CI: 46-79), with 2 CR and 21 with a partial responses. (Planchard, 2017; Lancet Oncol). If patient progresses to metastatic disease recommend this regimen.

  If patient progresses to Stage II disease, recommend the following clinical trial.

  NCT04302025. A Study of Alectinib, Entrectinib, Vemurafenib Plus Cobimetinib, or Pralsetinib in Patients With Resectable Stages II-III Non-Small Cell Lung Cancer With ALK, ROS1, NTRK, BRAF V600, or RET Molecular Alterations

From Swaty Arora, MD

- Will continue to monitor and utilize NGS while being mindful of the more we look, the more we find.

Susanne Arnold, MD (Guest Faculty) to Swaty Arora, MD

- (Dr. Arnold) What else will you be doing to monitor this patient, i.e., scans every 3 to 6 months? How did you answer these questions in your mind, outside of the broad panel?
- (Dr. Arora) Continue to follow the NCCN Surveillance guidelines in terms of CT surveillance every 4 to 6 months; this patient has formerly used tobacco and thus, we will continue to encourage her to maintain this behavior.
- Continue to scan her and ensure she is not progressing
- (Dr. Arnold): It is sort of strange when you know there is an actionable mutation
- (Dr. Arora) Yes, this the trigger for this case and if I should scan this every 3 months or every 6 months. Based on this conversation, and I believe that I may shorten the frequency
- Tim Mullett, MD, MBA:
    - As a surgeon, I would agree with the 3-month scan and continued surveillance. This case is really a perfect demonstration of some of the challenges in biomarker testing. For example, how do we not treat someone when we find something and how do we avoid the risk of potentially over-examining a patient? I really appreciate your reference of following the NCCN guidelines and the guidance of the Molecular Tumor Board. The NCCN and or the Molecular Tumor Board are resources when these sorts of questions emerge. We will continue to go deeper into the challenges in the next few sessions. It is imperative that we do not let ourselves drift too far outside of the current guidelines. In addition to the cost, these tests can be cumbersome for patients.
    - We will sometimes find out information that we do not know what to do with yet
- (Dr. Arnold): Sometimes, you will come across the presence of mutation that indicates germline mutations in this setting of the tumor; BRCA1 or BRCA2 are somewhat common, and we seem to see many in Kentucky. So often, there may be a need to refer to the genetic counselor. At the Molecular Tumor Board, we often end our review discussions with thoughts of familial risk or underlying risks to the patients; BRAF is not necessarily one of those. Genetic counseling in the proper setting is a reasonable thing to offer.
- (Dr. Kolesar): Want to remind everyone and put in a plug for the Molecular Tumor Board. No charge to the patient or for the patient's facility. For more information about the Molecular Tumor Board or to present a case, contact Dr. Kolesar at jill.kolesar@uky.edu
- (Dr. Zinner): Adding to what Dr. Kolesar and others have shared, the standard of care after you have exhausted the non-standards of care are Phase 1 clinical trials and for those trials, you will increasingly need markers. Emphasizes the merits of NGS and why it is so important.
- (Dr. Tim Mullett): With Stage I disease, one of the things that we are trying to change, is that it is only stage 1 if we have identified enough lymphatic tissue and the different lymph node stations that need to be evaluated at the time of surgery; surgical standards exist to ensure we capture at least the hilar lymph node and at three separate stations at the drainage pass of the particular tumor with any operative with curative intent. We need to ensure that we are staging patients properly. In the future, this may be an opportunity for us to understand NGS in early-stage disease.

Assigned Case Presentation Number: 892021