# 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:** 7/21/2021
2. **Presenter Name(s):** Daniel Gwan-Nulla, M.D.
3. **Presenter Title(s):** Thoracic surgeon
4. **Organization/Health System:** Piedmont Healthcare
5. **Please summarize the case you are presenting to the group:** 78 year old male who underwent surgical resection for a 6 cm left upper central mass which was adherent to the pulmonary artery. Surgical path T3N1 adenosquamous ca with microscopic positive bronchial margin
6. **Which specific questions are you asking the faculty and the other participating spoke sites?** Role and benefit for molecular testing?

## 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

<table>
<tr><td colspan="4">DEMOGRAPHIC INFORMATION</td></tr>
<tr><td>1. Age</td><td>2. Gender (Choose One)</td><td colspan="2">3. Race/Ethnicity (Choose All that Apply)</td></tr>
<tr><td>78</td><td>Female☐<br>Male☒<br>Non-Binary/Third gender☐<br>Transgender female☐<br>Transgender male ☐</td><td>American Indian/Alaska Native ☐<br>Asian ☐<br>Black/African American ☐</td><td>Hispanic/Latino ☐<br>White ☒<br>More than One Race ☐<br>Other ☐</td></tr>
<tr><td colspan="4">NON-SMALL CELL LUNG CANCER (NSCLC) HISTOLOGY & STAGE</td></tr>
<tr><td>4. Diagnosis</td><td>5. Histology</td><td colspan="2">6. Stage</td></tr>
<tr><td>Initial Diagnosis ☒<br>Recurred and or Progressed ☐</td><td>Adenocarcinoma ☒<br>Squamous Cell ☒<br>Large Cell ☐</td><td colspan="2">Stage IIIA</td></tr>
<tr><td colspan="4">BIOMARKER TESTING</td></tr>
<tr><td colspan="2">7. Has biomarker testing been ordered for this patient (or will it be ordered)?</td><td colspan="2">8. If biomarker testing was not ordered, please elaborate on the factors that precluded it:</td></tr>
<tr><td colspan="2">Yes ☐<br>No ☒<br>Will be ordered ☒</td><td colspan="2">Recent diagnosis</td></tr>
<tr><td colspan="4">The next section is ONLY for those patients who HAVE received or WILL receive biomarker testing</td></tr>
<tr><td colspan="4">9. Which technique was used (or will be used) to obtain specimen for pathologic diagnosis? (Choose One)</td></tr>
<tr><td colspan="2">Bronchoscopic biopsy ☐<br>Endobronchial ultrasound-guided transbronchial lymph node aspiration (EBUS-TBNA) ☐<br>Image-guided percutaneous biopsy ☐<br>Liquid biopsy ☐</td><td colspan="2">Mediastinoscopy ☐<br>Surgical specimen ☒<br>Thoracentesis/pericardiocentesis ☐<br>Unsure ☐</td></tr>
<tr><td colspan="2">10. Which platform was/will be used for lung biomarker testing? (Choose One)</td><td colspan="2">11. If single-gene test or short-cluster panel, please identify which genes were tested:</td></tr>
<tr><td colspan="2">Single-Gene Test ☐<br>Short-Cluster Panel ☐<br>Multi-Gene Panel (next generation sequencing (NGS) ☒</td><td>ALK ☐<br>BRAF ☐<br>EGFR ☐</td><td>HER2 ☐<br>KRAS ☐<br>NTRK ☐<br>MET ☐</td><td>PD-L1 ☐<br>ROS1 ☐<br>RET ☐</td></tr>
<tr><td colspan="4">ADDITIONAL INFORMATION</td></tr>
<tr><td colspan="4">12. Please include any other information you would like to share with the group:<br>Click or tap here to enter text.</td></tr>
</table>

## Section 4: Faculty Recommendations

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

**Question from Dr. Gwan-Nulla: Would anyone do anything different for treatment (chemotherapy, followed by sequential radiotherapy)?**

*Dr. Pierre de Delva (UMMC)*

Agree. In our practice, in an elderly patient like this case, sequential radiotherapy is favored, to minimize the impact. This would be indicated based on NCCN Guidelines and considering the patient's stage and R1 resection. An interesting question may be where would PD-L1 and immunotherapy factor for this patient?

**Dr. de Delva asked Dr. Wistuba (didactic presenter) what pathology work up would you want to see in this case, e.g., adenosquamous that will likely need adjuvant therapy?**

*Dr. Ignacio Wistuba (MD Anderson)*

I would like to know about potential targeted abnormalities (like EGRF which may be the most relevant based on the available clinical data).

**More Information about the patient's pathology provided by both Dr. Daniel Gwan-Nulla and the pathologist at Piedmont Columbus, Dr. Kathryn Rizzo.**

Foundation One was utilized.

On the original EBUS, PD-L1 showed high expression. Foundation One was tried on the smaller tissue specimen; there was not enough tissue. They did reflex to liquid biopsy portion of Foundation One. EGFR was not found to be mutated; however, the following were found TP-53 and MET were mutated. Microsatellite status was not detected, TMB was 3. This was the status in between EBUS and resected specimen. No further testing since then.

*Dr. Rodolfo Bordoni (Northside Cancer Institute)*

Few points and a question: Immunotherapy and PD-L1 is not a standard, but the data is promising (recent ASCO meeting and publication and in clinical trials). Clinical trials is a priority.

Question: Why did you request biomarker testing and PD-LI for this patient? Is it needed to do the full panel for this patient and others like them? Especially considering the cost.

Answer: We would need to discuss with the oncologist. At our institution, typically the oncologist orders the biomarker testing. This also happened pre-resection. This likely serves as part of the rationale for the full panel.

*Dr. Ignacio Wistuba (MD Anderson)*

One comment that I would share is that the interesting opportunity from the NGS panel is that with the same asset, it provides more information (than a single gene). It comes with the test (the full panel versus the single gene). You receive additional information and clinical opportunities. While I see your point (Dr. Bordoni), I think the full panel is a good thing as you may receive greater information to provide more options, even for better clinical trial options. One asset gives you so much more.

*Dr. Phil Lammers (Baptist)*

I agree with Dr. Wistuba. At our institution, the cost is about the same for testing a few genes versus the NGS and at our institution, our patients are not really paying anything either (thankfully). The field is moving so quickly with immunotherapy. Personally, I think the benefit, for a patient like this, is upfront treatment, e.g., chemo immune therapy based on recent presentation from checkpoint studies. There may be even more benefit from neoadjuvant treatment. Reference: IMpower010 Study Link

We know that immunotherapy is not as effective generally for EGFR mutant lung cancers or perhaps, even for ALK. Although we do not act on every component from the NGS, I think it good to have all of this information, if you can, at your fingertips, especially for clinical trials opportunity.

*Dr. Rodolfo Bordoni (Northside Cancer Institute)*

My comment had more to do with the financial confusion and perhaps, the clinical confusion sometimes. Too much information can create too much confusion sometimes. When we started this discussion, the first thing we focused on was the patient's high PD-L1 expression. This does not have any significance in the adjuvant setting at this point; however, this was first point of discussion. In our practice and in our network, I try to encourage to seek the data that we will use. My only point is that more data may be better, but not always.

*Dr. Phil Lammers (Baptist) and Dr. Pierre de Delva (UMMC)*

Expressed agreement with Dr. Bordoni.

*Dr. de Delva*:

Many times, we ask, can we do something about "insert whatever." However, this also fodders more questions about what is happening down the pipeline and keeps people interested. Some oncologists at our institution say they are interested in having the information for the future and I'm curious if the group finds this reliable? Let's say this patient had successful chemo-radiotherapy in the adjuvant setting, had a reasonable response, with no progression and then, a year later had metastatic disease. Is the NGS from one year ago good enough to drive decisions one year later or do they need another NGS, or they can they use both?

*Dr. Rodolfo Bordoni (Northside Cancer Institute)*

Too dynamic and we need new data. The old data can lead to mistakes. This is really part of my point of having too much data/too much information. We need to test the patient again.

*Dr. Ignacio Wistuba (MD Anderson)*

Agree with Dr. Bordoni. We need to test the tumor we are going to treat. But, if we cannot get enough tissue, then certainly explore testing resection of the former tissue, especially if you are running out of options. Yes, the preference is a new testing, but that may not always be possible (tissue or sample limitations).

*Dr. Pierre de Delva (UMMC)*

This highlights one of the challenges of reflex testing; yes, it is reliable, lowers the time, but it also creates confusion and may seem like a potential waste of resources. It does show the value of understanding your local environment and the value of your MDC team, knowing what is usable and what is not, competing interest in doing it right, etc.

**Question to Dr. Wistuba: Many programs are still trying to institute a biomarker protocol. If you were to advise a smaller community cancer program, what might you advise them to do from the pathology perspective?**

Yes, in favor of reflex testing. We have been doing this in breast cancer for years, even with the challenges. For lung (NSCLC NOS), at the minimum, reflex testing should at least include some of the basic genomic abnormalities like

EGFR, ALK, KRAS, BRAF, ROS1, MET, NTRK, etc. and then, PD-L1. Then, with that, you have a panel that qualifies for NGS, for so many other genes. If you have any good reliable technique that can give you the right information with the right specification, you should at least cover these genes at minimum. For squamous, then it depends on the clinical characteristics.

**In the future, do you see NGS as an in-house lab service that will be widely available (not just lung)?**

Yes, the costs are reducing significantly, and testing can be done with less tissue sample. The main issue is still turnaround time. 7 to 10 business days is most cases. Sometimes it takes longer, more like 15 days. There is always the case that takes even longer. Many of these delays are not because of the molecular technique; it may be part of the specimen. The role of pathology should also be available to provide assistance on the quality of the specimen and what is expected.

**Question from Dr. Stephen Bigler (Baptist) on perspectives from payers about NGS testing for future use and if that is covered. His experience has not been successful with payers covering this. Any actual cost analysis on the differences in the panels?**

Dr. Wistuba: Molecular testing has a high rate of denial especially in community centers, less in academic centers. I know some labs struggle with this and it is a major issue. Cost analysis should be done. We do know that sometimes is just as costly to do two genes versus a larger panel. Reimbursement is an issue. The NGS testing cannot only be done for future decisions (from a reimbursement perspective).

Dr. Bordoni recommended the ASCO presentation/publication: Economic Impact of Next-Generation Sequencing Versus Single-Gene Testing to Detect Genomic Alterations in Metastatic Non–Small-Cell Lung Cancer Using a Decision Analytic Model. This study showed that use of NGS testing for patients with NSCLC was associated with substantial cost savings and shorter time-to-test results for both CMS and commercial payers. Significant cost-savings.

*Dr. Zhonglin Hao (UK Markey) for Dr. Wistuba*

**At our institution, our lab tells us at times that we do not have enough tissue. Does your medical oncology team ask you to only test a few of the genes or limit to some of the genes versus the 500/600 in the NGS panel (due to the limited tissue at times)?**

One thing your lab needs to assess is the amount of DNA before putting in the acid. Then, you can decide. You need at least 10 ng-15 ng (preferable) to run a good NGS panel, along with assessing the quality of that material. From there, you can decide to continue with the large NGS panel OR maybe try a lower number of genes on the panel. It is not easy; it is challenging and requires resources to be flexible at the lab level. We use a limited panel in certain situations in which patients cannot wait or for other needs that emerge.

**Assigned Case Presentation Number:** 92021