

Liquid Biopsy Identifies Driver Mutations in Heterogeneous Tissue

Case Presentation:

- 70-year-old woman
- 1/4 ppd x 10 years
- Presented with shortness of breath and a cough

Diagnosis:

- Initial imaging workup identified an abnormal lung mass.
- Clinical staging indicated that the patient was stage IIB/IIIA NSCLC.
- Bronchoscopic biopsy and histological analysis identified tumor as squamous cell carcinoma (SSC).

Molecular Testing and Test Results:

- Standard follow-up included blood draw for the Biodesix Lung Reflex® testing strategy at the time of her procedure.
- GeneStrat® result: EGFR mutation positive
- Further analysis of the tumor tissue indicated that the patient actually had a mixed squamous adenocarcinoma.

Patient Treatment Plan:

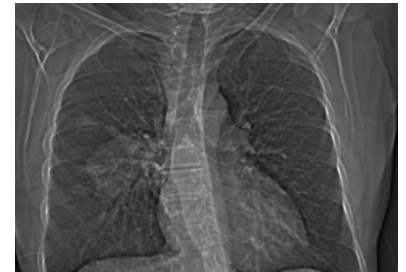
- Initial treatment plan was neoadjuvant therapy followed by surgery.
- Given GeneStrat results and tissue testing, treatment plan was revised to EGFR TKI therapy.

Patient Outcome:

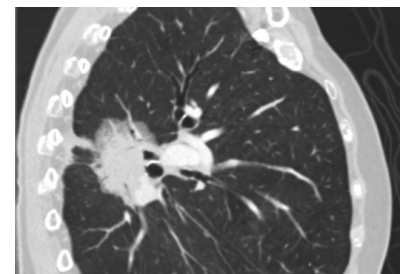
- At time of publication, patient was on EGFR TKI therapy.

Key Considerations

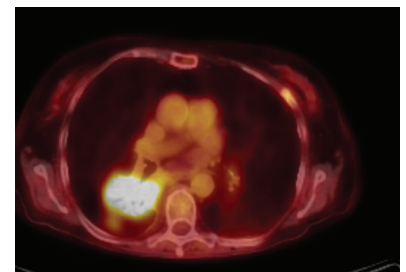
- Patient initially diagnosed with SCC lung cancer.
- GeneStrat result identified an actionable mutation, EGFR.
- Extensive tissue testing conducted and identified a mixed SCC and adenocarcinoma tumor type.
- Patient placed on appropriate TKI therapy.



Coronal X-ray



CT Scan



PET Scan



Coronal X-ray Post
Pneumonectomy



USING LIQUID BIOPSY WITHIN OUR MULTIDISCIPLINARY PRACTICE FOR NSCLC PATIENTS

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Can you tell me about your practice?

I am an interventional pulmonologist at Northwestern University. I am a part of a small practice with two interventional pulmonologists, a physician assistant, a nurse coordinator and a fellow. Due to the small size of the group, we are able to incorporate new technologies and diagnostic tests into our practice. Additionally, we are part of a multidisciplinary thoracic oncology clinic, composed of interventional pulmonology, thoracic surgery, medical oncology, radiation oncology as well as palliative care.

Who do you typically refer your patients to?

At Northwestern, interventional pulmonology is often the starting point for new patients. From within the hospital system, we receive referrals from primary care, emergency physicians, hospitalist and medical specialties, surgical services and oncology. From the community, various primary care or other community pulmonologists refer to us as they don't have the infrastructure to manage specific patient types.

Typically, patients are seen by as many specialties as possible on the first day. If we suspect cancer, we will see the patient initially and then refer them to either a radiation oncologist, thoracic surgeon or medical oncologist depending on their lung cancer stage. Alternatively, if we are not sure what the stage is going to be or if its cancer, we have them back for a follow-up where they can be seen by multiple subspecialties. We typically keep our referral network within the Northwestern group—unless there is a clinical trial that we do not offer, or the patient lives far away and wants to have a local provider.

When you look at your patient mix, do you typically have early-stage or late-stage patients?

We are starting to see more early-stage lung cancer patients, particularly with the adoption of lung cancer screening CT scans, but like most practices, we still see a lot of late-stage patients.

How do you incorporate liquid biopsies into your practice?

Any time lung cancer is a consideration, we have the Biodesix Lung Reflex® (BLR) testing drawn while they are getting their biopsy. Our patients provide consent in the clinic and I describe the BLR as a testing strategy that can identify targeted mutations should they have one with quick turnaround time. This approach helps us schedule an earlier oncology visit and begin treatment quicker.

Do you also use tissue-based genetic testing at the same time?

Yes, we order tissue testing for every patient. We use tissue for an initial 22 gene panel and PD-L1 and save the rest. We keep one full tissue block in-house in case additional studies are needed.

What percent of patients have been identified with targetable mutations?

5-7% of our GeneStrat® results have come back with identified targetable mutations.

If you get an EGFR positive result with the GeneStrat test, will you recommend treatment on that patient solely using liquid biopsy results?

Definitely. And we have done that a few times.

Has there been an occasion where you have rapidly identified a targetable mutation?

Yes, we ordered the GeneStrat test on a patient with squamous cell carcinoma (SCC) and she tested positive for an EGFR mutation. This was a surprise to us because we don't typically reflex for SCC patients at Northwestern. Upon further review, this patient had a mixed adenocarcinoma and squamous cell tumor that responded well

to TKIs. We've found a few other patients who were young and non-smokers where a mutation was found and the BLR results allowed them to start treatment much more expeditiously than if they had to wait for tissue molecular testing.

Do you find that the turnaround time of the test has helped your practice?

Our oncologists have appreciated the fast turnaround time of the BLR results as they typically review the data and discuss treatment and prognosis with the patients.

Can you share more on how you utilize VeriStrat results in your practice?

Our clinic is multidisciplinary, so I don't typically speak to patients about their prognosis as that is managed primarily by the oncologist. I do use the BLR results to help patients understand their expected response to treatment, what questions to ask their oncologist, and what treatment options they would want for their care.

How do your medical oncologists use VeriStrat results?

VeriStrat results are used in different ways within our group. Some only look at the GeneStrat results and others use both GeneStrat and VeriStrat.

Do you bring Biodesix Lung Reflex testing results into your multi-disciplinary clinic?

I always provide VeriStrat results within our multidisciplinary clinic.

When you diagnose a patient do they usually ask about their prognosis?

Every patient asks "how much time do I have" after they have been diagnosed with cancer. It's challenging to have a prognostic conversation with them because although we have their BLR results back

we still require tissue testing and any scans completed prior to sharing a full prognosis.

When you do have a prognostic conversation with the patient, how do you bring it up?

Patient prognosis conversations are primarily managed by our oncologists. When I do talk about results with patients, it's to guide patients who are unsure of whether they want to consult with the oncologist for treatment. If the patient isn't sure of treatment, then I'll share "you are VeriStrat Good" which means you will respond well to treatment, so you might want to consider a therapy option. If they are VeriStrat Poor, we provide them with their prognosis, so they can discuss it with their family. We explain that our testing suggests that they aren't going to do as well with standard chemotherapy and they may want to consider a clinical trial or may want to talk to their oncologist about alternative treatments.

How did you use a VeriStrat Good result to encourage a patient?

Every once in a while there is an older patient who says, "I know I have lung cancer, but I feel well, and I don't want to do chemo". They've had a family member who had a negative experience with chemotherapy and they don't want to go through it. I try to communicate that their tumor appears to be different and their VeriStrat results indicate that their response to treatment would likely be better than their family member. I've found that it has

been remarkably helpful to talk in that manner to my patients.

How do your palliative care specialists integrate into this process?

We bring our palliative care specialists in a bit earlier for patients who are VeriStrat Poor. Getting these patients scheduled with them a little sooner may help them with their progression of the disease, which tends to be accelerated compared to VeriStrat Good patients.

What were some of the obstacles you faced in implementing the BLR testing strategy into your practice?

Most reluctance for BLR adoption at our institution came from our medical oncologists as they were not familiar with the tests and did not understand the value of the quick turnaround time. After presenting BLR at our multidisciplinary tumor board, the team agreed to use it for 30 cases. If the team found value with the results, we would continue using the BLR testing strategy.

This was probably the easiest way to introduce the BLR testing strategy into our practice. When we began using the BLR test, we were very transparent with our multidisciplinary team on the process we used in identifying patients that were going to receive it. Our team has gotten used to BLR results being available and now the medical oncologists look for the results, so it has become part of our standard practice.