COSTS AND OUTCOMES COMPARISON OF TISSUE AND BLOOD BASED BIOPSIES FOR THE PURPOSE OF BIOMARKER TESTING FOR ADVANCED NON-SMALL CELL LUNG CANCER

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BACKGROUND AND OBJECTIVES

- Diagnosis, staging and histopathology of suspected advanced non-small cell lung cancer (NSCLC) patients is carried out through tissue biopsies.
- When feasible, remaining tissue is used for molecular profiling. In many cases however, molecular profiling requires repeat biopsies or is not performed.
- ASCO®, CAP/IASLC/AMP and NCCN Guidelines® recommend mutation testing in advanced non-small cell lung cancer at diagnosis to guide therapy.
- In 2015, studies showed that of the 72% of non-squamous NSCLC patients that undergo biomarker testing, only 21% were found to have results available at their first oncology visit (or 15.1% of all non-squamous patients). [1]
- Biomarker analysis in tissue biopsy have long turn-around-times delaying treatment. These delays can result in progression. [2]

This study aimed to quantify the value of a proposed pathway to treatment of advanced non-small cell lung cancer patients. Mainly, it compares tissue-based biopsy to advanced liquid biopsies (GeneStrat™ test) for the purpose of biomarker testing in NSCLC. Three outcomes were investigated: (1) clinical outcomes including availability of mutation results at treatment start and adverse events (2) clinical costs including biopsies, pathology, and treatment of adverse events and (3) time to treatment.

METHODS

In this study, we compared the clinical costs and outcomes of two pathways to obtaining mutation profiles for Non-small cell lung cancer patients at time of diagnosis. Tissue-based biopsy methods (CT-guided fine needle aspiration and electromagnetic navigational bronchoscopy), were compared to the blood-based GeneStrat test in collecting actionable mutation information (EGFR sensitizing and resistance, ALK, KRAS and BRAF) . In tissue based testing, left-over tissue blocks from diagnostic biopsies if sufficient in quantity can be used to carry out molecular analysis, otherwise, re-biopsy must be carried out. GeneStrat testing uses a blood draw and needs no biopsy procedure. Clinical outcomes, prices and turn around times were obtained from published clinical trials, comparative studies and test validation publications. [1,3-5]

CT guided fine needle aspirations

A common percutaneous procedure. A fine gauge needle is inserted to the lesion site where tissue is collected. Patients suffer high rates of complications which sometimes require hospitalization. Risks of complications increase with the number of investigated sites. Studies found tissue from CT biopsies were suitable for biomarker testing in 87.5% of cases.[6]

Navigational bronchoscopy

This procedure uses the normal passageways of the lungs. A catheter is guided through the bronchial pathways to the lesion using electromagnetic imaging. While more expensive, bronchoscopies result in significantly fewer complications. Studies showed bronchoscopies resulted in adequate tissue for biomarker testing for 93.3% of patients.[7]

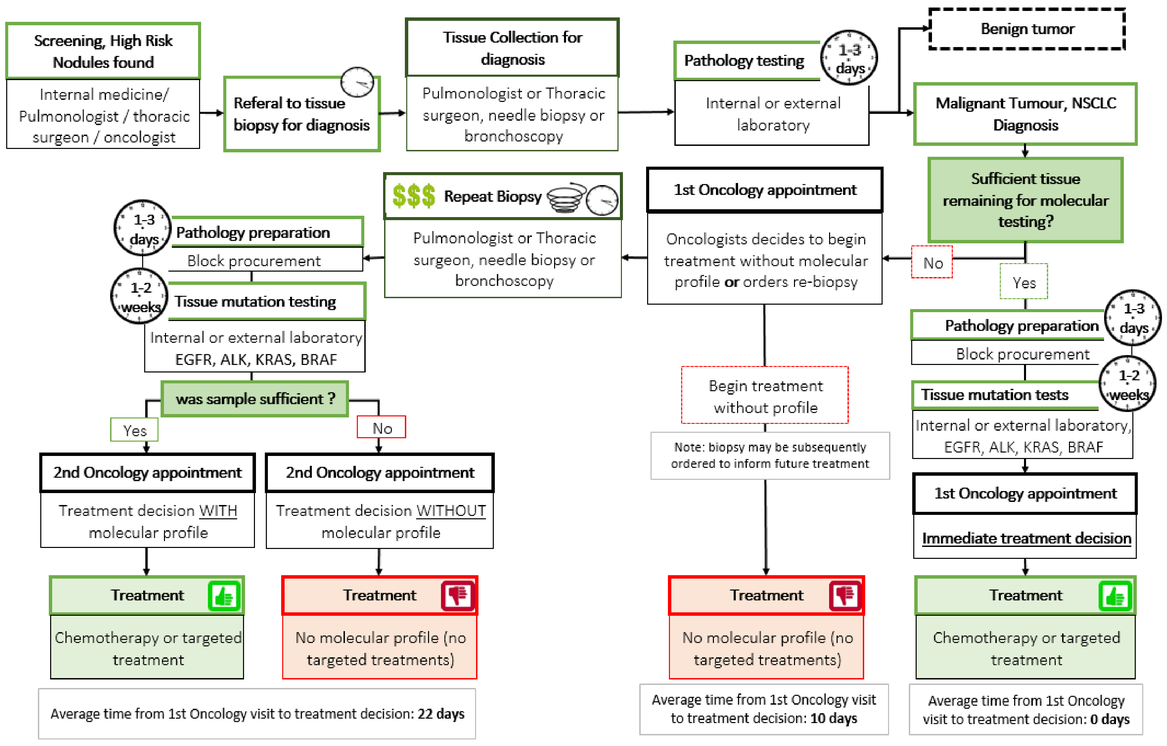
Assuming successful collection, the tissue is prepared and processed by a pathologist internally or sent out to an external laboratory. Guidelines recommend between 24 hrs and 3 days for block procurement and processing and a 1 to 2 week turnaround time for tissue biomarker results.[9]

GeneStrat

A blood based liquid biopsy, it uses ddPCR technology to analyze cell free DNA and RNA found in blood. The test focuses on actionable mutations for non-small cell lung cancer patients examining EGFR (sensitizing and resistance), EML4-ALK, KRAS and BRAF mutations. Concordance studies found a range of 92-99% concordance with tissue [8]. The test requires a simple blood draw.

The blood samples are sent and processed at the CLIA certified Biodesix® lab in Boulder, CO. Results are delivered within 72 hours.

Pathway 1: Tissue Biomarker process

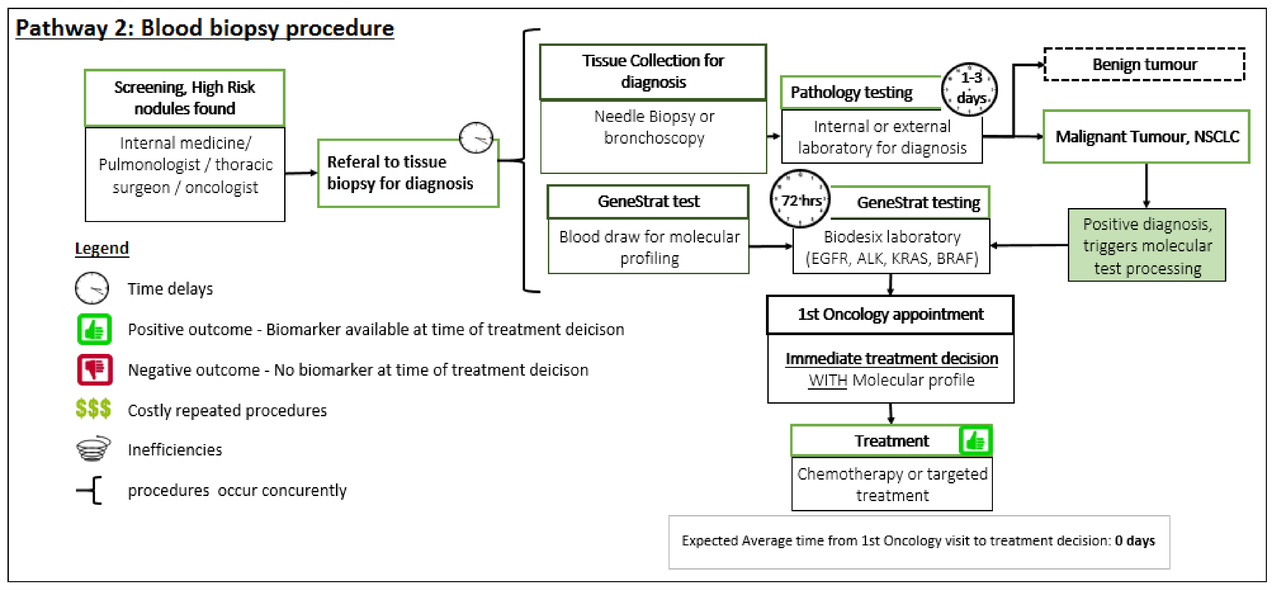


The following pathways represent:

(1) The tissue-based process as described by physicians and published evaluations of molecular testing processes. Molecular profiles may be performed on leftover tissue collected for diagnosis or may require a second biopsy to perform. Insufficient tissue or long turn around time can result in physicians making treatment decisions without mutation profile available.

(2) The proposed blood based biopsy process requires a blood draw taken at any medical consultation or through a home phlebotomist after diagnosis.

Pathway 2: Blood biopsy procedure



RESULTS

In the base case, assuming insufficient tissue from diagnostic procedure requiring a repeat biopsy, the costs (medicare perspective), adverse events and turn-around-times were compared. Blood-based mutation testing was the dominant procedure.

	CT Guided Fine Needle Aspiration	Electromagnetic Navigational Bronchoscopy	GeneStrat
Complication rates			
Pneumothorax requiring observation	8.40%	0.90%	-
Pneumothorax requiring hospitalization	6.60%	0.70%	-
Significant hemorrhage requiring hospitalization	1.00%	0.10%	-
respiratory failure	0.67%	0.10%	-
Costs			
Procedure Medicare costs	$ 3,253.52	$ 7,407.05	$ 3.00
Pathology cost	$ 876.57	$ 876.57	$ 833.45
Total cost of biopsy and biomarker testing	**$ 4,130.09**	**$ 8,283.62**	**$ 836.45**
Pathology turn-around-time	**1-2 weeks**	**1-2 weeks**	**72 hours**

Based on a 2016 estimate of 224,390 new cases of lung cancer and rates of referral to oncologists[10] as well as biomarker test statistics [1], an estimated 81,686 patients did not have had biomarker results at their first oncology visit.
Of these, 11,039 patients did not have sufficient tissue for analysis from the diagnostic biopsy, and 27,045 patients did not undergo biomarker testing. For patients without biomarker results at first oncology visit, median time from first oncology appointment to biomarker results availability was 21 days when testing was carried out. Assuming a GeneStrat test would have been ordered at the first oncology visit, liquid biopsy could have reduced delays in mutation results by a median of 18 days for 51 904 patients who received results after first oncology appointment and provided results for an additional 29,782 patients who would not have undergone biomarker testing.

Outcomes (adverse events)

- GeneStrat blood draw did not result in adverse events.
- CT guided needle biopsy had the highest rate of complications with 15% of patients presenting some form of pneumothorax or lung collapse. Additionally, a small minority of patients suffer from hemorrhage (1%) and respiratory distress (0.7%) following the biopsy procedure. Complications resulted in hospitalization for 8.27% percent of patients.
- Navigational bronchoscopies resulted in fewer complications with 1.6% pneumothorax and 0.1% respiratory failure leading to a 1% hospitalization rate.

Costs (including procedure, adverse events and pathology)

- GeneStrat costs were the lowest, the blood draw carried out in the same appointment as the diagnostic biopsy created minimal costs. With pathology, GeneStrat Medicare costs added up to $836.45
- Biomarker testing via CT-guided biopsy was the second most expensive procedure costing on average $4130.09 to perform including treatment of adverse events. For those who experience complications, the cost of biopsy, treatment and testing can rise up to and estimated $18,567.23 per patient.
- Navigational bronchoscopies, were highest in cost despite the fewer complications. Average costs were of $8,283.62 per procedure including treatment of complications. For those who experience complications, the cost of navigational bronchoscopy and testing can rise to $22,720.76.

Time to Treatment

- Time to treatment is the shortest when patients have biomarker results at the first oncology appointment.
- The use of blood based mutation testing as a reflex to diagnosis (pathway 2) decreases time from screening to treatment by making molecular profile status available earlier and reducing wait times due to re-biopsies and multiples appointments
- Tissue based molecular testing has been reported to take between 1 and 2 weeks between procedure and result delivery.

The dominance of blood testing was not sensitive to changes in price or complication rates.

CONCLUSION

- Blood-based biopsies can reduce time to treatment, decrease costs and morbidities as compared to tissue based biopsies.
- This study showed the blood based GeneStrat test is significantly less costly than tissue based biopsies with an average savings of $3,293.64 and $7,447.17 for CT guided and navigational bronchoscopies.
- While 15% of CT-guided needle aspirations result in adverse events sometimes requiring hospitalization, simple blood draws for liquid biopsies cause no significant adverse events.
- In confirm lung cancer patients, liquid biopsy results may greatly reduce time to treatment by making biomarker results available within 72 hours, additionally, GeneStrat can be drawn by any phlebotomist or in an office visit eliminating scheduling delays. Tissue based mutation results take between 1 and 2 weeks from time of biopsy.
- Blood-based tests eliminate the need to obtain large amounts of tissue for biomarker testing in turn reducing repeat biopsies and aggressive diagnostic biopsies (repeated sample collection within a single procedure)
- Blood-based biopsies should be considered instead of tissue-based biopsies in all patients with a confirmed NSCLC diagnosis to establish tumor biomarker status.

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