BACKGROUND AND OBJECTIVES

• Diagnosis, staging and histopathology of suspected advanced non-small cell lung cancer (NSCLC) patients is carried out through tissue biopsies.
• Blood draws are used for molecular profiling. In many cases however, molecular profiling requires repeat biopsies or is not performed.
• ASCO®, CAP/ASCl/CAMP 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). [4]
• Biomarker testing in many instances is expensive and time consuming.

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 obtain 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 actioning 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. [1–8]

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

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.

The following pathways represent:
(1) The tissue-based process as described by physicians and published evaluations of molecular testing processes.
(2) The proposed blood-based biopsy process requires a blood draw taken at any medical consultation or from a home phlebotomist after diagnosis.

Pathway 1: Tissue Biopsy process

Pathway 2: Blood biopsy process

CT guided fine needle aspirations

A common percutaneous procedure. A fine gauge needle is inserted to the lesion where tissue is collected. Patients suffer high rates of complications which sometimes require hospitalization and 10 to 15 days turn around time for the number of investigated sites. Studies found tissue from CT biopsies were suitable for biomarker testing in 87.5% of cases.[12]

GeneStrat blood draw did not result in adverse events.

Navigational bronchoscopy

This procedure involves the normal passageways of the lungs. A catheter is guided through the bronchial pathways to the lesion using electromagnetic imaging. With few expensive bronchoscopes result in significantly fewer complications. Studies showed bronchoscopies resulted in adequate tissue for biomarker testing for 93.5% of patients.[3]

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

Table 1: Tissue Biopsy process

<table>
<thead>
<tr>
<th>Complications</th>
<th>Costs (including procedure, adverse events and pathology)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax requiring observation</td>
<td>$7,407.05</td>
</tr>
<tr>
<td>Pneumothorax requiring hospitalization</td>
<td>$7,407.05</td>
</tr>
<tr>
<td>Significant hemorrhage requiring hospitalization</td>
<td>$876.57</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>$876.57</td>
</tr>
<tr>
<td>Total cost of biopsy and biomarker testing</td>
<td>$13,100.39</td>
</tr>
<tr>
<td>Pathology turn-around time</td>
<td>0-2 weeks</td>
</tr>
<tr>
<td>Pathology cost</td>
<td>$876.57</td>
</tr>
</tbody>
</table>

Based on a 2016 estimate of 224,390 new cases of lung cancer and rates of referral to oncology, as well as biopsy tissue test statistics,[12] an estimated 81,686 patients did not have 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 treatment 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 57,104 patients who received results after first oncology appointment and provided results for an additional 29,782 patients who would not have undergone biomarker testing.

• 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 $3,203.64 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 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 a patient with confirmed NSCLC diagnosis to establish tumor biomarker status.

CONCLUSION

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 2.72% percent of patients.
• Navigational bronchoscopies resulted in fewer complications with 0.1% 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
• Biopsies testing via CT guided biopsy was the second most expensive with an average cost of $415.90 per procedure including treatment of adverse events. For those who experience complications, the cost of biopsy, treatment and testing can rise up to and estimated $15,587.23 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 treatment 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 reflect 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 to changes in price or cost rates.

References


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

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