[redacted]

LUNG CANCER MUTATION PANEL

SPECIMEN SOURCE: LEFT LOWER LOBE LUNG
SPECIMEN/BLOCK NUMBER

EGFR Mutation: NOT DETECTED
This result was reviewed and interpreted by

The following polymorphism was detected: 2361g>A.

Sequencing of the entire coding region and splice junction sites of exons 18-21 of the EGFR gene revealed no previously published mutations or any sequence changes that could result in amino acid changes. However, one or more polymorphic sequence changes were discovered in the EGFR gene. These
polymorphisms are interpreted as non-pathogenic because they do not lead to amino acid changes. These polymorphisms are not expected to have any clinical significance. As 7% of patients who respond to EGFR inhibitors do not show mutations in exons 18-21 of EGFR gene, a negative result does not preclude the possibility of a clinical response to EGFR inhibitors.

KRAS Mutation Analysis

KRAS Mutation: NOT DETECTED
Based on sequence analysis, no mutations were detected in K-Ras exon 1 (codon 12 & 13) and exon 2 (codon 61)
This result was reviewed and interpreted by

FISH, ALK, 2p23

FISH, ALK, 2P23: SEE BELOW

Specimen Type: Paraffin Embedded Tumor Tissue

Clinical Indication: FISH study for oncology

Method : FISH
Total Cells : 100
Images Captured : 2

RESULT :

[redacted]

INTERPRETATION :

FISH RESULT NEGATIVE FOR REARRANGEMENT OF ALK GENE, SUGGESTIVE OF GAIN OF ALK REGION.

Fluorescence in-situ hybridization (FISH) analysis, using break-apart probes specific for ALK gene (2p23; Abbott Molecular), did not exhibit a break-apart pattern. Thus, this result is not indicative of a translocation involving the ALK gene.

As an incidental finding, additional 1-6 copies of the ALK region were observed in 79% of cells. This suggests gain of the ALK region. The clinical significance of this incidental finding is unknown.

A small proportion of tumors (approximately 5%) with ALK rearrangement demonstrated by other methods may be missed by this study.

This result does not rule out a malignancy or other genetic changes. This result should be considered in combination with other clinical and/or laboratory data. The cutoff values for ALK rearrangement are 12% for paraffin-embedded specimens, 3% for bone marrow, 5% for peripheral blood. Please expect the result of any other concurrent test in a separate report.

This test was developed and its performance characteristics were determined by
not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

[redacted]

Performance characteristics refer to the analytical performance of the test.

Laboratory results reviewed and Clinical Interpretation provided by

Mutational analysis of the EGFR and KRAS genes and ALK locus rearrangement by FISH were performed to survey the most common tumor-associated genetic changes that have been shown to have prognostic and therapeutic consequences in non-small cell lung cancer (NSCLC).

EGFR kinase domain mutations are found in 10-15% of lung adenocarcinomas, particularly those occurring in younger patients without a smoking history, and identify tumors that may have significant clinical response to EGFR-targeted kinase inhibitors. Secondary somatic mutations in EGFR, particularly T790M in exon 20, may accompany acquired resistance to these inhibitors.

KRAS point mutations occur in 20-30% of lung adenocarcinomas and are largely mutually exclusive with EGFR mutations. KRAS mutations are associated with a poor prognosis and resistance to anti-EGFR-directed immunotherapy.

ALK locus rearrangement resulting in the EML4-ALK gene fusion is present in 3-5% of NSCLC, is most commonly seen in adenocarcinomas from younger patients, and produces overexpression of the ALK tyrosine kinase. Patients who harbor ALK rearrangement do not benefit from EGFR tyrosine kinase inhibitors and are recommended to be directed to trials of ALK-targeted agents.

The exons tested cumulatively comprise greater than 95% of the known activating mutations in the selected genes; rare mutations occurring at other sites or in other genes that may influence outcome cannot be excluded.

Genomic DNA was extracted from microdissected paraffin-embedded tissue sections isolated from the submitted block. PCR-based DNA sequencing was used to assess for mutations in exon 1 (including codon 12 & 13) and exon 2 (including codon 61) of KRAS and exons 18-21 of the EGFR tyrosine kinase (TK) domain. The sensitivity for mutation detection for these assays is approximately 10% mutant allele in the background of normal allele in the microdissected area.

The KRAS and EGFR test was developed and its performance characteristics have been determined by Capistrano. Performance characteristics refer to the analytical performance of the test.

The FISH test was developed and its performance characteristics have been determined by It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. Performance characteristics refer to the analytical performance of the test.

Test performed at

Addendum Report Issued By:

DIAGNOSIS

DIAGNOSIS:

A. Left lower lobe lung, lobectomy:

Tumor Characteristics:

1. Histologic type: Adenocarcinoma.
2. Histologic grade: Well differentiated with focal mucin production.
3. Tumor site: Left lower lobe lung.
4. Tumor focality: Unifocal.
5. Tumor size: 2.8 x 2.7 x 2.4 cm.
6. Visceral pleural invasion: No.
7. Lymphovascular space invasion: No.
8. Tumor extension: Confined to the left lower lobe.

Surgical Margin Status:

1. Tumor distance from bronchial margin: 0.7 cm.
2. Tumor distance from parenchymal (stapled) margin: 0.5 cm.
3. Tumor distance from pleural surface: Adjacent to though does not involve the pleura.

TNM: pT1b

B. Level 5 lymph node, biopsies:
Single node negative for malignancy (0/1).

C. Level 15 lymph node, biopsy:
Single lymph node negative for malignancy (0/1).

[redacted]

COMMENTS:
TTF1 by immunoperoxidase is positive consistent with a lung primary.

Ancillary studies (lung carcinoma cascade) will be performed and an addenum report will follow.

CLINICAL INFORMATION

CLINICAL HISTORY:
Preoperative Diagnosis: [redacted]
Postoperative Diagnosis
Symptoms/Radiologic Findings:

SPECIMENS:
A. Left lower lobe lung
B. Level 9 lymph node
C. Level 5 lymph node

SPECIMEN DATA

GROSS DESCRIPTION:
A. Container A is labeled left lower lobe. Received in formalin is a 182 gm, 16.5 x 7.8 x 7.0 cm lobe of lung. The pleura is markedly violaceous, with a palpable, indurated, puckered area. This area is inked black. The surgical resection margin is inked blue. Sectioning of the parenchyma deep to the aforementioned indurated pleura reveals a 2.7 x 2.8 x 2.4 cm ill-defined, slightly mucoid, tan-white tumor which extends to within 0.7 cm of the bronchial resection margin, 0.5 cm from the surgical resection margin. The remaining parenchyma is spongy, red-tan. Representative sections are submitted for genomics studies in two cassettes labeled [redacted] Representative sections of the remaining tissue are submitted in cassettes labeled as follows: A1) Bronchial resection margin; A2-A3) Representative tumor to inked surgical resection margin and pleura; A4-A6) Representative remaining tumor to pleura; A7-A8) Representative remaining pleural parenchyma.

B. Container B is labeled , level 9 lymph node. Received in formalin is a 1.7 x 1.0 x 0.5 cm anthracotic lymph node. The entire specimen is sectioned and submitted in cassette B1 labeled

C. Container C is labeled , level 5 lymph node. Received in formalin is a 1.2 x 0.8 x 0.6 cm red-tan lymph node. The lymph node is trisected and submitted in cassette C1 labeled [redacted]

A. Additional sections of tumor to pleura are submitted in cassettes A9 - A12 labeled

[redacted]