[redacted]

COLLECTION DATE: [redacted]

SPECIMENS:
1. F/S LUL WEDGE RESECTION (CHEST)
2. STATION 9 LYMPH NODE
3. STATION 11 LYMPH NODE
4. LEFT UPPER LOBE COMPLETION LOBECTOMY
SEE ADDENDUM

Reason For Addendum #1: Molecular Studies
Reason For Addendum #2: Molecular Studies
Reason For Addendum #3: Molecular Studies
Reason For Addendum #4: Biomarker Report

DIAGNOSIS:

1,4. LUNG, LEFT UPPER LOBE: WEDGE RESECTION AND COMPLETION LOBECTOMY
- ADENOCARCINOMA, MICROPAPILLARY PREDOMINANT (3.5 CM), SEE NOTE.
- THE MARGINS OF RESECTION ARE FREE OF TUMOR.
- THREE BENIGN LYMPH NODES (0/3).

Note: The tumor consists of micropapillary (70%), acinar (10%), lepidic (10%) and giant cell (10%) components. Material will be sent to an outside laboratory for mutational studies and the results will be reported in addendum.
Specimens: 1: F/S LUL WEDGE RESECTION (CHEST)
4: LEFT UPPER LOBE COMPLETION LOBECTOMY

LUNG: Resection
SPECIMEN
Specimen: Lobe(s) of lung (specify)
Left Upper
Procedure: Lobectomy
Specimen Integrity: Intact
Specimen Laterality: Left
Tumor Site: Upper lobe
Tumor Focality: Unifocal
TUMOR
Histologic Type: Adenocarcinoma
Histologic Grade: G3: Poorly differentiated
EXTENT
Tumor Size: Greatest dimension (cm)

3.5cm
Additional Dimension (cm): 3.4cm x 1.8cm
Visceral Pleura Invasion: Not identified
Tumor Extension: Not identified
MARGINS
Bronchial Margin
Bronchial Margin Involvement by Invasive Carcinoma: Uninvolved by invasive carcinoma
Vascular Margin: Uninvolved by invasive carcinoma
Parenchymal Margin: Not applicable
Parietal Pleural Margin: Not applicable
Chest Wall Margin: Not applicable
ACCESSORY FINDINGS
Treatment Effect: Not applicable
Lymph-Vascular Invasion: Present
LYMPH NODES
Extranodal Extension: Not identified
STAGE (pTNM)
Primary Tumor (pT):
pT2a: Tumor greater than 3 cm, but 5 cm or less in greatest dimension surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus); or Tumor 5 cm or less in greatest dimension with any of the following features of extent: involves main bronchus, 2 cm or more distal to the carina; invades the visceral pleura; associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not inolve the entire lung
Regional Lymph Nodes (pN)
pN0: No regional lymph node metastasis
Distant Metastases (pM): Not applicable
ADDITIONAL NON-TUMOR
Additional Pathologic Finding(s): Emphysema

2. LYMPH NODE, LEVEL 9: BIOPSY
- ONE BENIGN LYMPH NODE (0/1).

3. LYMPH NODE, LEVEL 11: BIOPSY
- ONE BENIGN LYMPH NODE (0/1).

[redacted]
Pathologist

CLINICAL HISTORY AND PRE - OPERATIVE DIAGNOSIS:
Lung mass.

MACROSCOPIC DESCRIPTION:
The specimen is received in four parts, each labeled with the

patient's name.

1. Part one is received fresh, labeled 'left upper lobe wedge resection, r/o carcinoma'. It consists of a wedge shaped portion of lung, measuring 9 x 4 x 4 cm. The specimen weighs 36 grams. There is a staple line identified on the specimen measuring 9 cm and 3 cm in length. The staple line is inked black and the pleural surface is inked blue. The pleural surface shows dimpling at one area. Serial sectioning of the specimen reveals a gray white firm irregular mass, measuring 3.5 x 3.4 x 1.8 cm. The mass is 1 cm away from the staple line. The mass has a gray white cut surface. The remainder of the lung has tan pink spongy parenchyma. One piece cut from the mass is submitted for intraoperative microscopic examination. Representative sections are submitted.

2. Part two is received in formalin, labeled 'station #9 lymph node'. It consists of a single piece of tan maroon irregular soft tissue, measuring 0.6 x 0.5 x 0.2 cm. The specimen is bisected and entirely submitted.

3. Part three is received in formalin, labeled 'station #11 lymph node'. It consists of a single piece of tan maroon irregular soft tissue consistent with lymph node, measuring 1.5 x 0.9 x 0.2 cm. The specimen is bisected and entirely submitted for microscopic examination.

4. Part four is labeled 'upper lobe completion lobectomy'. It consists of a lobe of lung measuring 15 x 8 x 4 cm. The specimen weighs 169 grams. There are two staple lines identified on the specimen, measuring 15 cm and 8 cm in length. The staple line is inked black. The bronchus measures 2.5 cm in diameter and the bronchial vessels measures 2.0 cm in diameter. The bronchial vascular margin is shaved. Serial sectioning of the specimen shows tan maroon spongy parenchyma. No definite mass lesion or fibrosis is identified. Representative sections are submitted for microscopic examination.

[redacted]

SUMMARY OF SECTIONS:
1A mass, frozen section control
1B-1C mass (entire measurement)
1D-1E mass
1F stapled margin, entirely submitted
1G tumor, with adjacent to lung parenchyma close to the staple line
1H normal lung parenchyma
2A single bisected lymph node
3A single bisected lymph node

4A bronchial margin of resection
4B vascular margin of resection
4C three peribronchial lymph nodes
4D stapled margins
4E-4H random sections from the unremarkable lung parenchyma

SPECIAL PROCEDURES:

INTRA - OPERATIVE CONSULTATION:

1. Lung left upper lobe: wedge resection (Frozen Section)
- Adenocarcinoma, probably invasive.

Result reported by [redacted]

Intra-Operative Consultation #1 performed by [redacted]

ADDENDUM #1 FOR MOLECULAR TESTS:

KRAS and EGFR were sent on [redacted] for patient [redacted]. The test is to be performed on tissue from case [redacted] The case report, slides, and blocks for the cited accession number were retrieved from archives. The pathologist whose signature appears below reviewed the original pathology report, examined candidate H&E slides, and selected block 1D appropriate to the specifications of the ordered molecular analysis. x9 unstained slides were prepared and forwarded to [redacted] where the subject molecular test will be performed. An addendum report will be issued when the results of this molecular test are available.

Addendum #1 performed by
[redacted]

ADDENDUM #2:

MOLECULAR ONCOLOGY

KRAS MUTATION ANALYSIS

[redacted] Specimen # [redacted]
Body Site: Left upper lobe of lung
Specimen Type: Slides
Clinical Data: Adenocarcinoma

RESULTS: Wild-type gene.

INTERPRETATION:
No mutations were identified at codons 12 and 13 of the KRAS gene.

COMMENT:
Mutations in the KRAS gene are reported to be associated with poor prognosis, and resistance to targeted tyrosine kinase inhibitor therapies in patients with non-small-cell lung cancer (NSCLC). KRAS mutations occur in 15-30% of NSCLC patients and are strongly associated with adenocarcinoma and smoking history.

This assay analyzes codons 12 and 13 in exon 2 of the KRAS gene; based on the current literature, approximately 98% of mutations are expected to occur in these codons. The analytical sensitivity of the assay is approximately 10%; thus mutations present in a low percentage of cells may not be detected. This test is validated for use in identifying KRAS codon 12 and codon 13 mutations in fresh, frozen, or formalin-fixed paraffin embedded tissue. In particular the test performance has been established in samples of colorectal cancer and non-small cell lung carcinoma which harbor these mutations, although several other tissues are also known to harbor KRAS mutations (e.g. tumors of pancreas, bile duct, ovary, appendix, etc.).

Analysis of EGFR mutation or gene amplification status may provide additional information regarding this patient's probability of

response to targeted tyrosine kinase inhibitor therapies, if clinically indicated. See references.

METHOD/LIMITATIONS:
Tissue sections are reviewed by a pathologist and relevant tumor is selected for analysis. DNA is isolated from the sample, quantified and amplified by polymerase chain reaction (PCR) using primers to exon 2 of the KRAS gene. PCR products are subjected to single nucleotide primer extension to detect mutations at codons 12 and 13; primer extension products are analyzed using capillary gel electrophoresis and fluorescence detection. False positive or negative results may occur for reasons that include genetic variants or somatic heterogeneity of the tissue sample.

REFERENCES:

[redacted]

This test was developed and its performance characteristics determined by [redacted]. The laboratory is regulated under the [redacted] as qualified to perform high complexity clinical testing. This particular test is not considered a stand along test and should be used only in the context of other diagnostic tests or clinical work-up related to treatment decisions.

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Electronically signed by: [redacted]

[redacted]

Addendum #2 performed by
[redacted]

ADDENDUM #3:

EGFR Mutation Analysis

[redacted]

Body Site: Left upper lobe of lung

Clinical Data: Adenocarcinoma

RESULTS: No mutation detected

INTERPRETATION: No mutations were identified; however 18-20% of patients with non-small-cell lung cancer and without identifiable mutations are reported to be responsive to EGFR tyrosine kinase inhibitor therapies.

COMMENT: This assay analyzes exons 18-21 of the EGFR tyrosine kinase domain; based on the current literature, the vast majority of mutations are expected to occur in these exons. The analytical sensitivity of the assay is 10-20%, thus mutations present in a low percentage of cells may not be detected.

Most data published to date pertain to gefitinib (Iressa(r)).
Similar data have been seen in studies using erlotinib (Tarceva(r)).

Homozygosity for the frequently occurring sequence change 2361 G>A was identified. The polymorphism is not likely to have clinical significance.

This test is validated for non-small cell lung carcinoma. The clinical significance and utility of this test in other tumor types is unknown.

METHOD/LIMITATION:
Tissue sections are reviewed by a pathologist and relevant tumor is selected for analysis. DNA is isolated from the samples, quantified

and amplified by polymerase chain reaction (PCR) using primers to exons 18-21 of the EGFR gene. PCR products are analyzed by bi-directional direct DNA sequencing using capillary electrophoresis and fluorescence detection. False positive or negative results may occur for reasons that include genetic variants or somatic heterogeneity of the tissue sample.

REFERENCES:

[redacted]

DISCLAIMER:
This test was developed and its performance characteristics determined by [redacted]. The laboratory is regulated under the [redacted] as qualified to perform high complexity clinical testing. This particular test is not considered a stand alone test and should be used only in the context of other diagnostic tests or clinical work-up related to treatment decisions.

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Electronically signed by: [redacted]

[redacted]
Telephone [redacted]

Addendum #3 performed by
[redacted]

ADDENDUM 4:

[redacted]

Fluorescence In-Situ Hybridization (FISH)

[redacted]
Body Site: Left upper lobe of lung
Clinical Data: Adenocarcinoma

INTERPRETATION:
Negative for a rearrangement involving the ALK gene. Three to four copies of ALK were observed in 64.0% of cells, and five to six copies of ALK were observed in 16.5% of cells, suggesting the presence of a neoplasm with gains of chromosome 2 or 2p.

Probe #Nuclei Examined % Positive Nuclei %
Control values
2p23(ALK)V 200 0 0-2.2
A total of 200 cells were scored.

FINDINGS: FISH was performed on paraffin embedded tissue sections using dual color break-apart probe[redacted]) to the[redacted] gene at 2p23. this probe flanks the entire gene. If a rearrangement involving ALK is present, inversion or translocation, one of the two probe signals separates as one red (orange) and one green signal. In this specimen, separated signals were present in 0% of the nuclei scored. Based on laboratory validation data, these results are within the normal limits.

COMMENTS: N/A

ISCN RESULTS: nuc ish(ALKx3 4)[128/200]/(ALKx5 6)[33/200]

This test was developed and its performance characteristics determined by[redacted]. It has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is regulated under the[redacted]CLIA) as qualified to perform high complexity clinical testing.

Electronically signed by: [redacted]
[redacted]

[redacted]

Addendum #4 performed by
[redacted]
The electronic signature attests that the named Attending Pathologist has evaluated the specimen referred to in the signed section of the report and formulated the diagnosis therein.

This report may include one or more immunohistochemical stain results that use analyte specific reagents.
The tests were developed and their performance characteristics determined by [redacted] Department of Pathology.

They have not been cleared or approved by the US Food and Drug Administration.
The FDA has determined that such clearance or approval is not necessary.