[redacted]

COLLECTION DATE: [redacted]

SPECIMENS:
1. LEVEL 9 LYMPH NODES
2. LUNG, RIGHT UPPER LOBE
3. LEVEL 7 LYMPH NODES
4. LEVEL 4 LYMPH NODES
5. ADDITIONAL RIGHT UPPER LOBE MARGIN
6. RIB
SEE ADDENDUM

Reason For Addendum #1: Molecular Studies
DIAGNOSIS:
1. LYMPH NODES, LEVEL 9: BIOPSY
- FRAGMENTS OF BENIGN ANTHRACOTIC LYMPH NODE, NEGATIVE FOR CARCINOMA.

2. LUNG, RIGHT, UPPER LOBE: RESECTION
- ADENOCARCINOMA (1.5 CM), PREDOMINANTLY BRONCHIOLOALVEOLAR (LEPIDIC), WITH A 0.9 CM FOCUS OF INVASIVE ADENOCARCINOMA OF ACINAR AND MICROPAPILLARY PATTERNS.
- BRONCHOVASCULAR MARGIN, NEGATIVE FOR CARCINOMA.
- FIBRONECROTIZING GRANULOMAS, SPECIAL STAINS NEGATIVE FOR FUNGI AND
ACID FAST ORGANISMS (SEE COMMENT).
- PLEURAL FIBROSIS.
- BENIGN ANTHRACOTIC LYMPH NODES (0/2)

3. LYMPH NODES, LEVEL 7: BIOPSY
- FRAGMENTS OF BENIGN ANTHRACOTIC LYMPH NODE, NEGATIVE FOR CARCINOMA.

4. LYMPH NODES, LEVEL 4: EXCISION
- BENIGN ANTHRACOTIC LYMPH NODE, NEGATIVE FOR CARCINOMA.

5. LUNG, RIGHT, UPPER LOBE, ADDITIONAL MARGIN: RESECTION
- NO CARCINOMA IDENTIFIED.
- CARCINOID TUMORLET IN THREE FOCI (SPANNING 3 MM, 3 MM AND 2 MM).

6. RIB: RESECTION
- SEGMENT OF RIB WITH NO DIAGNOSTIC ABNORMALITY, NEGATIVE FOR CARCINOMA.

Specimens: 1: LEVEL 9 LYMPH NODES
2: LUNG, RIGHT UPPER LOBE
3: LEVEL 7 LYMPH NODES
4: LEVEL 4 LYMPH NODES
5: ADDITIONAL RIGHT UPPER LOBE MARGIN
6: RIB

LUNG: Resection
SPECIMEN
Procedure: Lobectomy
Specimen Integrity: Intact
Specimen Laterality: Right
Tumor Site: Upper lobe
Tumor Focality: Unifocal
TUMOR
Histologic Type: Adenocarcinoma
EXTENT
Tumor Size: Greatest dimension (cm)
1.5cm
Additional Dimension (cm): 1.5cm x 1cm
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: Uninvolved by invasive carcinoma
ACCESSORY FINDINGS
Treatment Effect: Not applicable
Lymph-Vascular Invasion: Not identified
SPECIAL STUDIES
Epidermal Growth Factor Receptor (EGFR) Analysis Results (specify method): To follow
KRAS Mutational Analysis (specify results):
Positive for a p.G12C (c.34G>T) mutation in codon 12 of the KRAS gene (see below)
STAGE (pTNM)
Primary Tumor (pT):
pT1a: Tumor 2 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 Superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus
Regional Lymph Nodes (pN)
pN0: No regional lymph node metastasis
Distant Metastases (pM): Not applicable
ADDITIONAL NON-TUMOR

Additional Pathologic Finding(s): Inflammation (specify type)
Necrotizing granuloma
interstitial fibrosis
Comment(s):
The adenocarcinoma is positive for TTF-1. The carcinoid tumorlets stain positively with [redacted] Correlation with microbiology results suggested. Case reviewed in department consensus conference.

[redacted]
Pathologist

CLINICAL HISTORY AND PRE - OPERATIVE DIAGNOSIS:
Lung cancer

MACROSCOPIC DESCRIPTION:
The specimen is received in six parts, each labeled with the patient's name.

1. Part one is received in saline, labeled 'level 9 lymph node'. It consists of two irregular fragments of tan soft tissue measuring 0.8 x 0.5 x 0.2 cm and 0.6 x 0.4 x 0.2 cm. Entirely submitted in one cassette.

2. Part two is received fresh, labeled 'right upper lobectomy'. It consists of a portion of right upper lobe of lung, measuring 15.6 x 3.8 cm. The staple line measures 15.5 cm. The staple line is shaved and the pleura around the staple line is inked in green. The pleural surface is pink tan glistening and reveals a thickened, bossellated area with fibrous thickening. The bronchial margin measures 1.5 cm and the vascular margin 1.2 cm. Beneath the thickened pleura there is a firm gray area, measuring 1.5 x 1.5 x 1.0 cm, located 4.5 cm from the staple line margin. Also noted a second separate firm gray white area, measuring 1.5 cm in greatest dimension which upon pressure exudes cheesy material. This mass is located 1 cm from the staple line margin, also multiple anthracotic lymph nodes, ranging from 0.2 cm to 0.5 cm identified from the hilar area. Representative sections are submitted.

3. Part three is received in saline, labeled 'level 7 lymph node'. It consists of three irregular fragments of tan soft tissue measuring 1.5 x 0.7 x 0.3 cm, 1.5 x 1 x 0.2 cm and 0.5 x 0.5 x 0.2 cm. Entirely submitted in two cassettes.

4. Part four is received in saline, labeled 'level 4 lymph node'. It consists of a 0.7 x 0.4 x 0.1 cm irregular portion of tan soft tissue. Entirely submitted in one cassette.

5. Part five is received in saline, labeled 'additional right upper lobe margin'. It consists of a 6.5 x 4.5 x 2.5 cm triangular-shaped wedge of lung tissue, with a 6.5 cm long stapled line along one edge, and two stapled lines along an adjacent edge measuring 3 cm and 4 cm respectively. The specimen is photographed. The 6.5 cm long stapled edge is inked black; the 3 cm long stapled edge (adjacent to the 6.5cm long one) is inked blue; and the 4 cm long stapled edge is inked green. The black and blue inked stapled lines are at acute angles. The staples are trimmed off and the specimen is serially sectioned, revealing no focal lesions or masses. Representative sections are submitted.

6. Part six is received in formalin, labeled 'rib'. It consists of a 1.4 x 1.4 x 0.6 cm segment of rib with red marrow. Entire specimen is submitted in one cassette, after decalcification.

[redacted]

SUMMARY OF SECTIONS:
1A entirely submitted
2A vascular margin
2B bronchial margin
2C-2J firm area
2K staple line margin
2L-2M second mass close to the staple line margin
2N anthracotic lymph nodes
3A-3B entirely submitted
4A entirely submitted
5A-5E representative sections
6A rib, after decalcification

SPECIAL PROCEDURES:
Decalcification, AFB, GMS, Chromogranin, TTF1

[redacted]

RESULTS: Positive for a p.G12C (c.34G>T) mutation in codon 12 of the KRAS gene.

INTERPRETATION: Mutations in the KRAS gene are reported to correlate with poor prognosis and resistance to tyrosine kinase inhibitor therapies in patients with non-small lung cancer.

COMMENT:
KRAS mutations occur in 15-30% of non-small-cell lung cancer (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.).

METHOD/LIMITATION:

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] 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] as qualified to perform high complexity clinical testing. This particular test is not considered a stand alone test and should be only used in the context of other diagnostic tests or clinical work-up related to

treatment decisions.

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Electronically signed by: [redacted]
[redacted]

Final Diagnosis performed by
[redacted]

ADDENDUM #1:

EGFR Mutation Analysis

Genzyme Specimen # [redacted]
Referring Physician: [redacted]
Body Site: 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 ([redacted]
Similar data have been seen in studies using erlotinib (Tarceva(r)).

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]

Addendum 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.