[redacted]

SURGICAL PATHOLOGY REPORT

COLLECTION DATE: [redacted]

SPECIMENS:
1. RT. LOWER LOBE (PRECISION)
2. RT. LEVEL 11 LYMPH NODE
3. LUNG, RIGHT LOWER LOBE
4. RIGHT LEVEL 11 LYMPH NODE NEAR RIGHT UPPER LOBE
5. RIGHT LEVEL 7 LYMPH NODE
6. RT. LEVEL 4 LYMPH NODE
7. RIB
SEE ADDENDUM

Reason For Addendum #1: Molecular Studies
Reason For Addendum #2: Molecular Studies
DIAGNOSIS:
1. LUNG, RIGHT, LOWER LOBE: BIOPSY
- SENT TO PRECISION THERAPEUTICS (GROSS ONLY).

2. LYMPH NODE, RIGHT LEVEL 11: BIOPSY
- METASTATIC CARCINOMA IN FRAGMENTS OF ANTHRACOTIC LYMPH NODE AND

SOFT TISSUE.

3. LUNG, RIGHT, LOWER LOBE: LOBECTOMY
- MODERATELY DIFFERENTIATED ADENOCARCINOMA (4 cm) WITH MICROPAPILLARY (60%), ACINAR (30%) AND LEPIDIC (10%) patterns (SEE SUMMARY).

4. LYMPH NODE, LEVEL 11, RIGHT: BIOPSY
- METASTATIC CARCINOMA IN LYMPH NODE.

5. LYMPH NODE, LEVEL 7, RIGHT: BIOPSY
- METASTATIC CARCINOMA IN FRAGMENTS OF LYMPH NODE.

6. LYMPH NODE, LEVEL 4, RIGHT: BIOPSY
- FRAGMENTS OF LYMPH NODE, NEGATIVE FOR CARCINOMA.

7. RIB: EXCISION
- SEGMENT OF RIB WITH NO DIAGNOSTIC ABNORMALITY.

SUMMARY
Specimens: 2: RT. LEVEL 11 LYMPH NODE
3: LUNG, RIGHT LOWER LOBE
4: RIGHT LEVEL 11 LYMPH NODE NEAR RIGHT UPPER LOBE
5: RIGHT LEVEL 7 LYMPH NODE
6: RT. LEVEL 4 LYMPH NODE

LUNG: Resection
SPECIMEN
Procedure: Lobectomy
Specimen Integrity: Intact
Specimen Laterality: Right
Tumor Site: Lower lobe
Tumor Focality: Unifocal
TUMOR
Histologic Type: Adenocarcinoma, mixed subtype
EXTENT
Tumor Size: Greatest dimension (cm)
4cm
Additional Dimension (cm): 3.5cm x 2.5cm
Visceral Pleura Invasion: Present
MARGINS
Bronchial Margin
Bronchial Margin Involvement by Invasive Carcinoma: Uninvolved by invasive carcinoma
Bronchial Margin Involvement by Squamous Cell Carcinoma in situ (CIS):
Squamous cell carcinoma in situ (CIS) not identified at bronchial margin
Vascular Margin: Uninvolved by invasive carcinoma
ACCESSORY FINDINGS
Treatment Effect: Not applicable
Lymph-Vascular Invasion: Present
LYMPH NODES
Extranodal Extension: Present
STAGE (pTNM)
TNM Descriptors: Not applicable
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)
pN2: Metastasis in ipsilateral mediastinal and / or subcarinal lymph node(s)
Comment(s):
The tumor is positive for TTF1 and negative for PAX-8, compatible with a primary pulmonary neoplasm. Lymphovascular invasion is seen on an ERG immunostain. Foci of visceral pleural invasion are demonstrated on an elastic stain. Tumor is present in soft tissue adjacent to vascular margin. Rounded foci of tissue necrosis in the superior portion of the lobe are negative for acid fast and fungal organisms on special stains. Case reviewed in department consensus conference.

[redacted]
Pathologist

CLINICAL HISTORY AND PRE - OPERATIVE DIAGNOSIS:
Lung cancer

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

1. Part one is received fresh, labeled 'right lower lobe'. It consists of two irregular portions of grey and tan-yellow rubbery to firm tissue measuring 1 x 0.8 x 0.5 cm and 1.1 x 0.9 x 0.6 cm. Entirely submitted to [redacted]

2. Part two is received in saline, labeled 'right level 11 lymph node'. It consists of a 1.8 x 1.5 x 0.8 cm aggregate of black soft rubbery anthracotic lymphoid tissue. Entirely submitted in one cassette.

3. Part three is received fresh, labeled 'right lower lobe'. It consists of a 174 gram, 14.5 x 10 x 3 cm right lower lobe of the lung. At the hilum, a 2.5 cm diameter, 0.3 cm long portion of bronchus and large vessels are noted. The lung is previously incised through its visceral pleural surface revealing a 4 x 3.5 x 2.5 cm poorly-circumscribed, firm, tan tumor with central tan-white necrosis deep to the overlying puckered pleura. The overlying pleura is inked black and the specimen is serially sectioned along the long axis of the lobe. The tumor abuts the pleural surface and

is approximately 0.2 cm from the vascular margin and 0.6 cm from the bronchial margin. There is also an ill-defined, patchy tan-yellow area that extends from the tumor to the superior portion of the lobe and terminates in two firm tan-yellow nodules measuring 1.0 cm and 0.8 cm in greatest dimension. The uninvolved pleural surface is smooth, glistening and tan-red. The uninvolved pulmonary parenchyma is homogeneous, tan-pink and aerated. Representative sections of the specimen are submitted.

4. Part four is received in saline, labeled 'level 11 lymph node near right upper lobe'. It consists of a 2.4 x 1.2 x 0.3 cm irregular portion of black soft rubbery anthracotic lymph node. Entirely submitted in one cassette.

5. Part five is received in saline, labeled 'level 7 lymph node'. It consists of a 3.8 x 3.5 x 1 cm aggregate of black soft rubbery anthracotic lymphoid tissue. Entirely submitted in three cassettes.

6. Part six is received in saline, labeled 'right level 4 lymph node'. It consists of a 2 x 1.5 x 0.8 cm aggregate of black soft rubbery anthracotic lymphoid tissue admixed with pink soft tissue. Entirely submitted in one cassette.

7. Part seven is received in formalin, labeled 'rib'. It consists of a 1.5 cm in length x 1.3 cm in width and 0.7 cm in thickness portion of rib. The surface is tan-brown and smooth. The marrow cavity is red and porous. There are no abnormalities identified. Representative sections are submitted in one cassette following decalcification.

[redacted]

SUMMARY OF SECTIONS:
2A entirely submitted
3A bronchial margin, en face
3B vascular margin, en face
3C tumor, adjacent bronchus
3D tumor, adjacent vasculature
3E-3G tumor, pleura
3H-3J tumor, uninvolved parenchyma
3K firm nodules, superior portion of lobe
3L uninvolved parenchyma
3M possible hilar lymph nodes
4A entirely submitted

5A-5C entirely submitted
6A entirely submitted
7A representative

SPECIAL PROCEDURES:
TTF1, PAX-8, ERG. AFB, GMS, ELASTIC

[redacted]

ADDENDUM #1:

INTEGRATED ONCOLOGY

MOLECULAR ONCOLOGY
KRAS MUTATION ANALYSIS

[redacted]
Body Site: 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 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.).

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]

Addendum #1 performed by
[redacted]

ADDENDUM #2:

INTEGRATED ONCOLOGY

EGFR Mutation Analysis
[redacted]
Body Site: Lung

Clinical Data: Adenocarcinoma

RESULTS: Positive for the E746_A750del5 mutation in Exon 19.

INTERPRETATION: Deletion mutations in exon 19, mostly involving the LREA motif, are reported to correlate with responsiveness to EGFR tyrosine kinase inhibitor therapies in patients with non-small-cell lung carcinoma.

COMMENT: Forty percent (40%) or more tumor cellularity is optimal for this mutation analysis. The sample submitted showed 30% tumor cellularity upon pathologist review.

E746_A750del15 corresponds to 2235_2249del15.

A frequently occurring sequence change 2361G>A (Q787Q) was identified. This polymorphism is known not to have clinical significance.

Mutations in the tyrosine domain of the epidermal growth factor receptor (EGFR) gene are reported to be associated with differential responsiveness or resistance to EGFR tyrosine kinase inhibitor (TKI) therapies. The objective response rate among patients with a sensitizing mutation ranges from 55 to 82%.

This assay analyzes exons 18-21 of the EGFR tyrosine kinase domain; based on the current literature, most mutations in non-small-cell lung carcinoma (NSCLC) are expected to occur in these exons. Mutations present in less than 10-20% of extracted DNA may not be detected by this method. Mutation status in a sample may change during tumor progression or the course of therapy; therefore, this result cannot be used to infer the presence or absence of a mutation in another sample or sub-sample obtained from this tumor.

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 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]

[redacted]

Addendum #2 performed by

[redacted]

[redacted]

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.