ICD-O-3
Carcinoma, Infiltrating Duct, NOS 8500/3
Site Code: breast, NOS C50.9 12/9/10 lw

TSS Pt ID: [redacted]

UUID:5DAC95DD-5DA6-475B-AC14-5C79FC2F30A6
TCGA-E2-A10B-01A-PR Redacted

SPECIMENS:

A. BREAST CA INFERIOR LEFT BREAST
B. SENTINEL LYMPH NODE #1
C. SENTINEL LYMPH NODE #2
D. COMPLETE AXILLARY CONTENTS-LEFT

SPECIMEN(S):

A. BREAST CA INFERIOR LEFT BREAST
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INTRAOPERATIVE CONSULTATION DIAGNOSIS:

FSA: Breast cancer, inferior, left breast: One mass measures 3.8 x 3.4 x 2.6 cm. The mass is 0.3 cm from medial margin and 0.3 cm from lateral margin.
By called to at
TPB. Sentinel lymph node #1: Metastatic carcinoma.
By Dr, called to Dr. at

GROSS DESCRIPTION:

A. BREAST CA INFERIOR LEFT BREAST
Received fresh labeled with patient name designated "a. breast ca inferior left breast" is a portion of resected breast tissue weighing 50 gm and measuring 6.0 x 4.0 x 3.5 cm. The overlying beige-tan ellipse of skin measures 5.0 x 3.0 cm. The surface of the skin has a thickened rough appearance. The specimen is received with orientation, the single suture designating anterior, double-lateral and triple-superior. Specimen is inked as follows: superior-red, inferior-orange, posterior-black, medial-green, lateral-yellow. The specimen is serially sectioned from superior to inferior. Cut section shows a firm ill defined beige-tan mass measuring 3.8 x 3.4 x 2.6 cm approaching the closest medial margin at distance of 0.3 cm and lateral margin at distance of 0.3 cm. The skin appears grossly involved by the lesion. The remainder of the specimen shows dark yellow lobulated adipose tissue with focal areas of firm white fibrous parenchyma. A portion of the specimen is submitted for tissue procurement.
Representative sections are submitted as follows:
A1-A2: slice 1, bisected serial section of the mass and skin with lateral and medial margins
A3-A4: sections of inferior margin with skin, slice 1
A5-A6: slice 2 additional lesion and skin with medial and lateral margins
A7-A8: slice 2 additional sections of lesion with lateral and posterior margins
A9-A14: slice 3 totally submitted
A15-A18: slice 4 entirely submitted
A19-A20: perpendicular sections superior margin
B. SENTINEL LYMPH NODE #1
Received fresh labeled with the patient name designated "b. sentinel lymph node #1" are 2 firm lymph nodes measuring 0.9 x 0.6 x 0.5 cm and 0.8 x 0.5 x 0.5 cm. Both lymph nodes are bisected to show white cut surface. Touch preps are performed. Both lymph nodes are entirely submitted in cassettes B1-B2.
C. SENTINEL LYMPH NODE #2
Received fresh labeled with the patient name designated "c. sentinel lymph node #2" is a fragment of firm yellow-tan fibroadipose tissue measuring 5.0 x 1.5 x 0.5 cm. The entire specimen is submitted in cassettes C1-C2.
D. COMPLETE AXILLARY CONTENTS-LEFT
Received in formalin in a container labeled with patient name designated "d. complete axillary contents-left" is a portion of yellow-tan fibroadipose tissue measuring 9.4 x 6.2 x 3.1 cm. Multiple possible lymph nodes are identified ranging in size from 2.2 x 0.5 x 0.5 to 0.2 x 0.1 x 0.1 cm. Cassettes are submitted as follows:
D1: 2 possible lymph nodes
D2: 3 possible lymph nodes
D3: 3 possible lymph nodes
D4: 3 possible lymph nodes
D5-D15: multiple additional possible lymph nodes

DIAGNOSIS:

A. BREAST, LEFT, INFERIOR, EXCISIONAL BIOPSY:
- INVASIVE, DUCTAL CARCINOMA, SBR GRADE 3, MEASURING 2.6-CM,

INVOLVING FIBROADENOMA AND EXTENDING INTO SUPERFICIAL DERMIS
- INTERMEDIATE, NUCLEAR GRADE, DUCTAL CARCINOMA IN SITU, WITH CENTRAL NECROSIS, CRIBRIFORM AND SOLID TYPES
- TUMOR PRESENT WITHIN 1 MM FROM MEDIAL, LATERAL, AND SUPERIOR SURGICAL RESECTION MARGINS
- PERINEURAL INVASION AND FOCAL LYMPHOVASCULAR INVASION IDENTIFIED
- FIBROCYSTIC CHANGES WITH FIBROSIS AND SCLEROSING ADENOSIS
- SEE SYNOPTIC REPORT.

B. LYMPH NODE, SENTINEL #1, LEFT, BIOPSY:
- METASTATIC CARCINOMA TO TWO OF TWO LYMPH NODES (2/2), LARGEST MEASURING 0.8 CM, WITH FOCAL EXTRANODAL EXTENSION.

C. LYMPH NODE, SENTINEL #2, LEFT, BIOPSY:
- ONE LYMPH NODE, NEGATIVE FOR METASTASES (0/1).

D. LYMPH NODES, LEFT AXILLARY CONTENTS, EXCISIONAL BIOPSY:
- TWENTY FIVE LYMPH NODES, NEGATIVE FOR METASTASES (0/25).

SYNOPTIC REPORT - BREAST
Specimen Type: Excision
Needle Localization: No
Laterality: Left
Invasive tumor: Present
Multifocality: No
WHO CLASSIFICATION
Invasive ductal carcinoma, NOS 8500/3
Tumor size: 2.6cm
Tumor site: Not specified
Margins: Negative
Distance from closest margin: 0.1cm
medial lateral and superior
Tubular score: 3
Nuclear grade: 2
Mitotic score: 3
Modified Scarff Bloom Richardson Grade: 3
Necrosis: Absent
Vascular/Lymphatic Invasion: Present
Extent: focal
Lobular neoplasia: None
Lymph nodes: Sentinel lymph node and axillary dissection
Lymph node status: Positive 2 / 28

DCIS present
Margins uninvolved by DCIS:
DCIS Quantity: Estimate 5%
DCIS type: Solid
Cribriform
DCIS location: Associated with invasive tumor
Nuclear grade: Intermediate
Necrosis: Present

ER/PR/HER2 Results
ER: Pending
PR: Pending
HER2: Pending

Pathological staging (pTN): pT 2 N 1a

CLINICAL HISTORY:
Left breast cancer invading skin

PRE-OPERATIVE DIAGNOSIS:
Left breast ca

ADDENDUM:
SYNOPTIC REPORT - BREAST, ER/PR RESULTS
Specimen: Surgical Excision
Block Number: A1

ER: Positive Allred Score: 8 = Proportion score: 5 + Intensity Score 3
PR: Positive Allred Score: 8 = Proportion Score 5 + Intensity Score 3

COMMENT:
The Allred score for estrogen and progesterone receptors is calculated by adding the sum of the proportion score (0 = no staining, 1 = <1% of cells staining, 2 = 1 - 10% of cells staining, 3 = 11-30% of cells staining, 4 = 31-60% of cells staining, 5 = >60% of cells staining) to the intensity score (1 = weak intensity of staining, 2 = intermediate intensity of staining, 3 = strong intensity of staining), with a scoring range from 0 to 8.
ER/PR positive is defined as an Allred score of >2 and ER/PR negative is defined as an Allred score of less than or equal to 2.
Methodology: Fixation Type and Length: Tissue was fixed in 10% neutral buffered formalin ( ) for no less than 8 and no longer than 24 hours. Antibody and Assay Methodology: Mouse anti-human ER and PR,
Comment: This assay can be used to select invasive breast cancer patients for hormone therapy (1). ER and PR analysis was performed on this case by immunohistochemistry utilizing the ER (ER 1D5, 1:100) and PR (PGR 136, 1:100) antibody provided by , following the manufacturer's instructions listed in the package insert. This assay was not modified, and adherence to all instruction and guidelines were strictly followed. Interpretation of the ER/PR immunohistochemical staining characteristics is guided by published results in the medical literature (1), information provided by the reagent manufacturer and by internal review of staining performance within the Pathology Department.
1. Harvey JM, et al. Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer. J Clin Oncol. 17:1474-1481, 1999

SYNOPTIC REPORT - BREAST HER-2 RESULTS
HER2 Status Results, Immunohistochemistry Evaluation
Specimen: Surgical Excision
Block Number: A1

Interpretation: EQUIVOCAL
Intensity: 2+
% Tumor Staining: 10%
Fish Ordered: Yes , on Date

METHODOLOGY
Methodology: Fixation Type and Length: Tissue was fixed in 10% neutral buffered formalin ( ) for no less than 8 and no longer than 24 hours. Antibody and Assay Methodology: Rabbit anti-human HER2, HerceptestTM (FDA-approved test kit), Control Slides Examined: External kit-slides provided by manufacturer (cell lines with high, low and negative HER2 protein expression), and in-house known HER2 amplified control tissue were evaluated along with the test tissue. These control slides run along side of this patient's sample showed appropriate staining. Adequacy of Specimen: Adequate, well preserved, clear-cut invasive carcinoma identified for HER2 evaluation.
Scoring Criterion and Scoring System:
IHC Level of Expression(Score) /Tumor Cell Membrane Staining Pattern
Negative (0)/Absence of Staining
Negative (1+)/Faint Incomplete membrane Staining, >10% of Cells
Equivocal (2+)/Weak complete membrane Staining, >10% of Cells
Positive (3+)/Strong complete membrane Staining, >10% of Cells
Equivocal Category for HER2 IHC results: A HER2, 2+ staining result that is interpreted as equivocal may not indicate gene amplification. A FISH test for HER2 gene amplification will be ordered for all HER2 IHC 2+ results.
COMMENT
This assay can be used to select invasive breast cancer patients for Trastuzumab (Hereptin) therapy (1,2). Clinical Trials have shown that Trastuzumab substantially increases the likelihood for an objective

response and overall survival for patients with metastatic HER2-positive breast cancer, regardless of whether HER2 tumor status was determined as IHC 3+ or FISH positive. Trastuzumab added to adjuvant chemotherapy substantially increase disease-free survival and decreases the risk of disease recurrence by about 50% for patients with early-stage HER2 protein over-expressed or gene amplified invasive breast cancer (3).

HER2 analysis was performed on this case by immunohistochemistry utilizing the FDA approved HercepTest (TM) test kit following the manufacturer's instructions listed in the package insert. This assay was not modified, and adherence to all instruction and guidelines were strictly followed. Interpretation of the HER2 immunohistochemical staining characteristics is guided by published results in the medical literature (4), information provided by the reagent manufacturer and by internal review of staining performance within the Pathology Department.

HER2 TEST VALIDATION

This HER2 immunohistochemical assay has been validated according to the recently revised recommendations and guidelines from the NCCN HER2 testing in Breast Cancer Task Force, and the jointly issued recommendations and guidelines from ASCO and the CAP (5). 80 randomly selected breast cancer samples were tested for HER2 by IHC as outline above and interpreted as, negative (score 0/1+) equivocal (score 2+) and positive (score 3+) without knowledge of the previous reported results.

These cases were also blindly read using two different FISH assay as amplified or non-amplified and the HER2/CEP17 ratios were recorded. After analyzing these results, there was 100% concordance between the IHC and FISH results for cases that were interpreted as either positive or negative by IHC. 9 of the 80 cases were interpreted as equivocal by IHC and of these 3/9 (33%) were non-amplified by FISH and 6/9 (66%) were found to be amplified.

The Pathology Department Immunohistochemistry laboratory takes full responsibility for this tests performance and has programs in place to regularly monitor the proficiency and the interpretation of HER2 assays. The laboratory also participates in external quality assurance HER2 programs including the CAP proficiency testing program.

REFERENCE

1. Carlson RW, Anderson BO, Burstein HJ, et al., NCCN breast cancer clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2005;3:238-289.
2. Carlson RW, Brown E, Burstein HJ, et al., NCCN Task Force Report: adjuvant therapy for breast cancer. J Natl Compr Canc Netw. 2006;4:S1-S26.
3. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Eng J Med 2005;353(16):1673-84
4. Leong ASY, Formby M, Haffajee Z, et al. Refinement of immunohistologic parameters for Her2/neu scoring validation by FISH and CISH. Appl Immunohistochem Mol Morphol. 2006;14:384-389.
5. Wolff AC, Hammond EH, Schwartz JN, et al., American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Recepto 2 Testing in Breast Cancer. Arch of Path and Lab Med 2007; 131:18-43.

PathVysion HER-2 DNA Probe Kit

Case No

Analytical Interpretation of Results: HER-2 NOT AMPLIFIED

Clinical Interpretation of results

Amplification of the HER-2 gene was evaluated with interphase fluorescence in-situ hybridization (FISH) on formalin-fixed paraffin embedded tissue sections using a chromosome 17 centromeric probe and a HER-2 probe that spans the entire HER-2 gene in the . A majority of tumors cells displayed 2 chromosome 17 signals and 2 HER-2 signals, with a HER-2/CEP 17 Ratio </=2.0, consistent with no amplification of the HER2/neu gene.

Block used A1 Source of case: RPCI

Tissue fixation formalin-fixed tissue Outside Case No: NA

Tissue source breast Results interpreted: yes

HER2/CEP17 ratio: 1.11

This ratio is derived by dividing the total number of LSI HER-2/neu signals by the total number of CEP17 signals in at least 20 interphase nuclei with nonoverlapping nuclei in the neoplastic mammary epithelial cells. Cells with no signals or with signals of only one color are disregarded.

Method of ratio enumeration: manual count

Limitations

The Vysis PathVysion Kit is not intended for use to screen for or diagnose breast cancer. It is intended to be used as an adjunct to other prognostic factors currently used to predict disease-free and overall survival in stage II, node-positive breast cancer patients. In making decisions regarding adjuvant CAF treatment, all other available clinical information should also be taken into consideration, such as tumor size, number of involved lymph nodes, and steroid receptor status.

No

treatment decision for stage II, node-positive breast cancer patients should be based on HER-2/neu gene amplification status alone.

Overview of this test

FDA APPROVED REAGENT

PathVysion HER-2 DNA Probe Kit is FDA approved for selection of patients for whom Herceptin® therapy is being considered. These tests were performed in the . under the direction of Dr.. The results of these studies should always be interpreted in the context of the clinical, morphological, and immunophenotypic diagnosis.

Gross Dictation: Pathologist,
Microscopic/Diagnostic Dictation:., Pathologist,
Final Review: Pathologist
Final: Pathologis
Addendum: Pathologist,
Addendum Final:., Pathologist,
Addendum: Pathologist,
Addendum Final:., Pathologist,

Criteria	Yes	No
Diagnosis Discrepancy		
Primary Tumor Site Discrepancy		
HIPAA Discrepancy		
Prior Malignancy History		
Dual/Synchronous Primary Noted		
Case is (circle): QUALIFIED / DISQUALIFIED		
Reviewer Initials (Date Reviewed: / /		