CEDARS-SINAI MEDICAL CENTER®

[redacted]

Patient: ABRAMS, ROXANN LYNN

Accession Number: [redacted]

Hospital No: [redacted]
Date of Birth: [redacted]
Age/Sex: [redacted] F

Location: [redacted]
AKA:
Outreach Location:
Outreach CPN:

Pathologist: [redacted]
Assistant:
Date of Procedure: 11/21/2023
Date Received: 11/21/2023

Ordering M.D.: [redacted]

SURGICAL PATHOLOGY REPORT

********** **AMENDED REPORT** **********

Reason for Addendum #1: Breast profile results
Reason for Amendment/Correction #1: Additional breast profile results

DIAGNOSIS:

A. LEFT BREAST, 3:00 7 CM FN, CORE BIOPSY:
- **Invasive lobular carcinoma, with low to intermediate nuclear grade**
- **Breast Biomarker Profile: Block A3 - to be reported in an addendum**

B. RIGHT BREAST, 3:00 5 CM FN, CORE BIOPSY:
- **Atypical ductal hyperplasia (ADH) approaching ductal carcinoma in-situ (DCIS)**
- **Atypical lobular hyperplasia (ALH) and lobular carcinoma in-situ (LCIS)**

[redacted] **were informed via campus email on 11/22/2023.**

HISTORY:
Part A - mass of left breast, unspecified quadrant.
Part B - mass of right breast, unspecified quadrant.

MICROSCOPIC FINDINGS:
See diagnosis.

SPECIAL STUDIES:
Step section x2 (A1-B4)

IMMUNOHISTOCHEMISTRY:

Antibody (Clone) / Probe	Block	Result
E-cadherin (36B5)	A2	Negative in invasive carcinoma
E-cadherin (36B5)	B3	Negative in ALH and LCIS

These IHC studies were interpreted in conjunction with appropriate positive and negative controls which demonstrated the expected positive and negative reactivity.
*IHC stain was performed at an approved outside reference laboratory with appropriate positive and negative controls. Interpretation of the stain is performed by Cedars-Sinai Pathologists.

[redacted]

If this report includes immunohistochemical (IHC) test results, please note the following: IHC studies were interpreted in conjunction with appropriate positive and negative controls which demonstrate the expected positive and negative reactivity. Multiple IHC tests were developed and their performance characteristics determined by Cedars-Sinai Medical Center Department of Pathology and Laboratory Medicine. These IHC tests have not been cleared or approved by the U.S. Food and Drug Administration (FDA) and FDA approval is not required. This laboratory is regulated under CLIA as qualified to perform high-complexity testing. IHC tests are used for clinical purposes. They should not be regarded as investigational or research.

Copy For : [redacted]

[redacted]

DS=Multiplex IHC stain

GROSS:

A. BREAST TISSUE LEFT 3:00 7 CM FN 8 CORES
Labeled: "Abrams, Roxann Lynn", designated "breast tissue left 3:00 7 cm FN 8 cores"
Received: In formalin
Cold ischemic time: 1 minute
Duration of formalin fixation: 6-8 hours
Specimen type: Core biopsy
Number of cores: 13
Size of individual cores:
Length: 0.6 to 1.2 cm
Diameter: 0.2 cm
Entirely submitted.

Slide key:
A1. 3
A2. 3
A3. 3
A4. 2
A5. 2
A6. Additional fragments - multiple

B. BREAST TISSUE RIGHT 3:00 5 CM FN 5 CORES
Labeled: "Abrams, Roxann Lynn", designated "breast tissue right 3:00 5 cm FN 5 cores"
Received: In formalin
Cold ischemic time: 1 minute
Duration of formalin fixation: 6-8 hours
Specimen type: Core biopsy
Number of cores: 9
Size of individual cores:
Length: 0.6 to 1.4 cm
Diameter: 0.2 cm
Entirely submitted.

Slide key:
B1. 3
B2. 3
B3. 3
B4. Additional fragments - multiple

Gross dictated by [redacted]
11/21/2023
[redacted]11/22/2023/270029

***** ADDENDUM *****
(11/24/2023)

BREAST BIOMARKER PROFILE FOR INVASIVE CARCINOMA

BLOCK: A3

Prognostic/Predictive Marker	Antibody	Results of IHC (invasive tumor cells)		Test Result
		% Positive	Staining intensity	
Estrogen Receptor	Ventana Clone SPI	93%	3+	Positive
Progesterone Receptor	Ventana Clone 1E2	67%	2+	Positive

HER2 Overexpression		Score	Test Result
Her2 IHC Test (Pathway)	Ventana Clone 4B5	1+	Negative

HER2 (FISH)	Average Her2 copies/tumor cell	Average Chr17 copies/tumor cell	Her2/Chr17 ratio	Test Result
No. of tumor cells analyzed: 20	2.6	2.2	1.2	Negative

Prognostic/Predictive Marker	Antibody	% Positive
Ki-67 Antigen	Ventana Clone 30-9	7%

DETAILS (IHC and FISH):

Human breast cancer tissues processed at CSMC are fixed in 10% neutral buffered formalin and paraffin-embedded. They are handled according to ASCO/CAP recommendations unless otherwise specified. For Outside Consult Cases, see original outside report for specimen fixation specifics.

ImmunoHistoChemical (IHC) Stains:

- are digitalized by the Hamamatsu Nano Zoomer S360 scanner and analyzed using the computer assisted Visiopharm Imaging System. Positive and negative controls are performed showing appropriate reactivity.
- use Polymer and/or SA-HRP Detection System. These assays have not been validated on decalcified tissues. Results on decalcified specimens should be interpreted with caution given the possibility of false negative results on decalcified specimens.

IHC Interpretation:

- Estrogen and progesterone: <1% tumor nuclei staining is negative, ≥ 1% tumor nuclei staining is positive. The intensity of nuclear immunohistochemical staining for hormone receptors is graded: *0 for negative; 1+ weak; 2+ moderate; 3+ strong.*
- Low level (1-10%) ER expression in invasive carcinoma may benefit from endocrine treatment based on limited data although there are data that suggest invasive cancers with these results are heterogenous both in behaviour and biology and often have gene expression profiles more similar to ER-negative cancers.
- If internal controls are not present but external controls are appropriately positive, testing another specimen that contains internal controls may be warranted for confirmation of ER status.

HER2 PATHWAY TEST INTERPRETATION (2018 ASCO/CAP criteria)

TEST RESULTS

Staining Pattern	Score	HER2 Overexpression
No staining observed or membrane staining that is incomplete and is faint/barely perceptible in ≤ 10% of tumor cells	0	Negative

Incomplete membrane staining that is faint/barely perceptible in >10% of tumor cells	1+	Negative
Weak to moderate complete membrane staining in >10% of tumor cells or intense circumferential membrane staining in ≤ 10% of tumor cells	2+	Equivocal
Complete, intense, circumferential membrane staining in >10% of tumor cells	3+	Positive

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All Fluorescence in situ Hybridization (FISH) tests:

- ☒ are analyzed with Abbott probes specific for the centromere of chromosome 17 (control probe) and HER2 (17q12). It was performed and scored by a technologist, and results interpreted by a pathologist.
- ☒ use Abbott PathVysion HER-2 DNA Probe kit for amplification
- ☒ are analyzed with adequate number of tumor cells.
- ☒ the nuclei counted were within the region selected by a pathologist.
- ☒ are run with positive controls that gave expected results.

HER2 FISH Interpretation:

HER2 FISH is considered:

a. Positive if:

- ☒ HER2/CEP 17 ratio ≥ 2.0 with an average HER2 copy number ≥ 4.0 signals/cell
- ☒ HER2/CEP 17 ratio <2.0 with an average HER2 copy number ≥ 6.0 signals/cell and IHC 3+ or 2+
- ☒ HER2/CEP 17 ratio ≥ 2.0 with an average HER2 copy number <4.0 signals/cell and IHC 3+
- ☒ HER2/CEP 17 ratio < 2.0 with an average HER2 copy number ≥ 4.0 and <6.0 signals/cell and IHC 3+

b. Negative if:

- ☒ HER2/CEP 17 ratio <2.0 with an average HER2 copy number < 4.0 signals
- ☒ HER2/CEP 17 ratio ≥ 2.0 with an average HER2 copy number <4.0 signals/cell and IHC 2+,1+, or 0 (SEE COMMENT)
  - ☒ COMMENT: Evidence is limited on the efficacy of HER2-targeted therapy in the small subset of cases with HER2/CEP17 ratio ≥ 2.0 and an average HER2 copy number < 4.0/cell. In the first generation of adjuvant trastuzumab trials, patients in this subgroup were randomized to the trastuzumab arm did not appear to derive an improvement in disease free or overall survival, but there were too few such cases to draw definitive conclusions. IHC expression for HER2 should be used to complement ISH and define HER status. IF IHC is not 3+ positive, it is recommended that the specimen be considered HER2 negative because of the low HER2 copy number by ISH and lack of protein overexpression.
- ☒ HER2/CEP17 ratio < 2.0 with an average HER2 copy number ≥ 4.0 and <6.0 signals/cell and IHC 2+, 1+ or 0 (SEE COMMENT)
  - ☒ COMMENT: It is uncertain whether patients with ≥ 4.0 and < 6.0 average HER2 signals/cell and HER2/CEP17 ratio < 2.0 benefit from HER2 targeted therapy in the absence of protein overexpression (IHC 3+). If the specimen test result is close to the ISH ratio threshold for positive, there is a high likelihood that repeat testing will result in different results by chance alone. Therefore, when IHC results are not 3+ positive, it is recommended that the sample be considered HER2 negative without additional testing on the same specimen.
- ☒ HER2/CEP17 ratio < 2.0 with an average HER2 copy number ≥ 6.0 signals/cell and IHC 1+ or 0 (SEE COMMENT)
  - ☒ COMMENT: There are insufficient data on the efficacy of Her2-targeted therapy in cases with HER2 ratio <2.0 in the absence of protein overexpression because such patients were not eligible for the first generation of adjuvant trastuzumab clinical trials. When concurrent IHC results are negative (0 or 1+), it is recommended that the specimen be considered HER2 negative

References:

- ☒ Allison K. et al. Estrogen and Progesterone Receptor Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Guideline Update. Arch Pathol Lab Med:do1:10.5858/arpa.2019-0904-SA
- ☒ Wolff A, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. Arch Pathol Lab Med 2018; 142: 1364-1382

I, the pathologist of record on the above addendum, personally examined the material described in the addendum, interpreted the results, reviewed this addended report and signed it electronically.

[redacted]
11/24/2023

I have personally examined the specimen, interpreted the results, reviewed the report and signed it electronically.

[redacted]