ARUP LABORATORIES
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Jonathan R. Genzen, MD, PhD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	8/22/1957
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

ERBB2 (HER2/neu) Gene Amplification by FISH with Reflex, Tissue

ARUP test code 2008603

ERBB2 (HER2) by FISH

See Note

IHC GUIDED:
HER2 (ERBB2) Amplified

HER2/CEP17 Ratio: 2.5
Average HER2 Signal Number per Cell: 6.2
Average CEP17 Signal Number per Cell: 2.5
Number of Cells Scored: 40
Number of Observers: 2
Scoring Method: Manual

HERCEP IHC Result (performed at ARUP): 2+

Hercep IHC for this case was reviewed and approved by [redacted] See separate report for detailed interpretation.

Controls were run and performed as expected. This result has been reviewed and approved by [redacted]

(pathologist signature)

ERBB2 FISH METHODOLOGY AND INTERPRETIVE DATA:
Fluorescence in situ hybridization (FISH) analysis for ERBB2 (HER2) gene amplification was performed on a section from a paraffin embedded tissue block using the Dako HER2 IQFISH PharmDx DNA Probe kit. Cells were evaluated from regions of tumor identified on histopathologic review of a matching hematoxylin and eosin stained section. Controls performed appropriately.

The Dako HER2 IQFISH test result was interpreted according to the American Society of Clinical Oncology / College of American Pathologists (ASCO/CAP) 2018 Guideline Recommendations for breast cancer fixed in formalin for 6-72 hours. Accordingly, an amplified result indicates an ERBB2/CEP17 ratio of 2.0 or greater with an average copy number of 4.0 or greater (group 1). A non-amplified result indicates an ERBB2/CEP17 ratio less than 2.0 with an average ERBB2 copy number less than 4.0 (group 5). Groups 2-4 encompass findings previously designated as either positive or equivocal. Specifically, group 2 indicates an ERBB2/CEP17 ratio of 2.0 or greater with an average ERBB2 copy number of less than 4.0. Group 3 indicates an ERBB2/CEP17 ratio of less than 2.0 with an average ERBB2 copy number of 6.0 or greater. Group 4 indicates an ERBB2/CEP17 ratio of less than 2.0 with an average ERBB2 copy number of at least 4.0 but less than 6.0.

H=High, L=Low, *=Abnormal, C=Critical

For groups 2-4, concomitant review of HER2 IHC is performed according to the 2018 Guidelines, when such slides are available. If the IHC score is 3+, then the final result is considered positive for amplification. If 0 or 1+, then the final result is negative for amplification. If the IHC score is 2+, then additional tumor nuclei are enumerated with FISH from the area of highest IHC intensity by an individual blinded to the original results. If the results remain consistent with groups 2 or 4, then the final interpretation is considered negative. An amplified result is reserved for cases in which the recounted population remains consistent with the original results of group 3 (ERBB2/CEP17 ratio of less than 2.0 with an average ERBB2 copy number of 6.0 or greater).

Genetic heterogeneity is reported when there is an aggregate population of amplified cells comprising >10 percent of the tumor cell population on a slide. Cases with amplification of 50 percent or more of the tumor population are considered non-heterogeneous.

Based on the assay performance during test validation, the test is expected to detect HER2 amplification status correctly in 100% of patients. Assay range and limit of detection were generated using normal and known positive cases respectively.

The Dako HER2 IQFISH PharmDx test kit is validated and FDA-approved for the evaluation of ERBB2 (HER2) gene amplification in formalin fixed, paraffin embedded breast and gastroesophageal adenocarcinomas. In the absence of guidelines for interpretation of ERBB2 (HER2) amplification in all other specimen types the test results are interpreted according to 2017 ASCO/CAP guidelines for HER2 in gastroesophageal adenocarcinoma. The results should be interpreted within the appropriate clinical context.

Fixative Used	Formalin
Time from Bx to Fixative	<10 Mins
Duration of Fixation	12-24 Hrs
Sample Adequacy	Adequate
ERBB2 Reference Number	DSP25-48840 A1
ERBB2 Tissue Source	R Breast

ERBB2 (HER2/neu) (HercepTest) by Immunohistochemistry, Tissue with Reflex to FISH if 2+

ARUP test code 0049178

H=High, L=Low, *=Abnormal, C=Critical

ERBB2(HercepTest)Rflx to FISH if 2+	2+ Equivocal Clinical Interpretation: This result has been reviewed and approved by [redacted] INTERPRETIVE INFORMATION: HercepTest Breast Tumors: DESTINY-Breast04 trial showed patients with IHC 2+/ISH not-amplified ("HER2-low") metastatic breast cancer had significantly longer progression-free and overall survival with trastuzumab deruxtecan (T-DXd). The result of the HercepTest by Dako (Agilent) is interpreted in a semiquantitative manner. Test is FDA approved for breast and gastric cancer only, and performed on formalin-fixed, paraffin-embedded tissue. Antibody clone is polyclonal and uses a proprietary detection system. ARUP Laboratories uses the 2018 ASCO/CAP guidelines for interpretation of ERBB2 (HER2) protein expression in breast cancers fixed in formalin for 6-72 hours with a cold ischemic time of less than 1 hour. Tissue not meeting these requirements or tissue placed in decalcification solution should be interpreted with caution due to the likelihood of false-negative results. Controls stained appropriately. For more information refer to the ASCO/CAP guidelines found at CAP.org, or www.jco.org.
Percent of Cells/Circumferential	80
Intensity of Staining	Moderate
Homogenous Pattern	Linear
Fixative Used	Formalin
Time from Bx to Fixative	<10 Mins
Duration of Fixation	12-24 Hrs
Sample Adequacy	Adequate
HER2 Reference Number	DSP25-48840 A1

H=High, L=Low, *=Abnormal, C=Critical

HER2 Tissue Source R Breast

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
ERBB2 (HER2) by FISH	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
ERBB2(HercepTest)Rflx to FISH if 2+	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Percent of Cells/Circumferential	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Intensity of Staining	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Homogenous Pattern	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Fixative Used	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Time from Bx to Fixative	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duration of Fixation	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Sample Adequacy	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
HER2 Reference Number	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
HER2 Tissue Source	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Fixative Used	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Time from Bx to Fixative	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Duration of Fixation	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Sample Adequacy	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
ERBB2 Reference Number	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
ERBB2 Tissue Source	25-323-164990	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical