

# ERBB2 (HER-2/neu) Gene Amplification by FISH

## DETECTION OF ERBB2 GENE AMPLIFICATION BY FISH FOR IDENTIFICATION OF BREAST CARCINOMAS RESPONSIVE TO TRASTUZUMAB (HERCEPTIN<sup>®</sup>)

### Test Highlights

- *ERBB2* fluorescent in situ hybridization (FISH) is an FDA-approved assay for detection of *ERBB2* gene amplification in formalin-fixed, paraffin-embedded (FFPE) breast carcinoma tissue.
- *ERBB2* amplification is associated with more aggressive disease and increased patient mortality.
- *ERBB2* FISH aids in the selection of patients for treatment with trastuzumab (Herceptin).

### Disease Overview

- Breast cancer is the most common malignancy and second leading cause of cancer death in women. Amplification of the human epidermal growth factor receptor-2 gene (*ERBB2*) occurs in approximately 18–20 percent of breast cancers and is the primary mechanism of *ERBB2* protein overexpression. Overexpression of *ERBB2* increases signal transduction, which stimulates cell division and growth. Consequently, *ERBB2* positivity is associated with poor prognosis (higher rate of recurrence and mortality) and resistance to endocrine therapies.
- Determination of *ERBB2* status is essential for therapeutic decisions. Antibodies directed against the extracellular portion of *ERBB2* (i.e., trastuzumab) inhibit *ERBB2*-overexpressing breast cancers. Trastuzumab (Herceptin) has been shown to prolong the overall survival of patients with metastatic breast cancer whose tumors overexpress *ERBB2*.
- Assessment of *ERBB2* protein status by immunohistochemistry (IHC) or gene amplification by FISH is the standard for evaluation of newly diagnosed carcinomas of the breast.

### Indications for Ordering

*ERBB2* testing by should be routinely performed on all newly diagnosed cases of invasive breast carcinoma.

### Additional Ordering Notes

- The biopsy site, fixative used, time to fixation, and fixation time should be provided. The submitted sample should contain sufficient viable tumor. Only formalin-fixed (10 percent neutral buffered formalin), paraffin-embedded tissue samples should be submitted.
- Fixation less than six hours or more than 48 hours is not recommended.
- Area of tumor must be invasive; ductal carcinoma in situ will not be scored.

### Interpretation

Presence of *ERBB2* gene amplification predicts a favorable response to trastuzumab (Herceptin).

### Limitations

Results may be compromised if correct fixation procedures have not been followed.

### Methodology

The determination of amplification for the *ERBB2* oncogene is based on enumeration of probe signals for LSI *ERBB2* and CEP17 contained within the interphase nuclei of invasive carcinoma cells.

### Related Tests

- *ERBB2* (HercepTest<sup>®</sup>) Tissue Assay, Paraffin (0049174)
- *HER-2* Gene Amplification by Monoplex PCR, Paraffin (0049390)
- *HER-2/neu* by CISH (Spot-Light<sup>®</sup>) (2002443)

### References

1. Wolff AC, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol* 2007; 25(1):118–45.
2. Vogel CL, et al. Efficacy and safety of trastuzumab as a single agent in first-line treatment of HER2-overexpressing metastatic breast cancer. *J Clin Oncol* 2002; 20:719–26.
3. Vysis, Inc. Pathvysion<sup>®</sup> HER-2 DNA Probe Kit. Package Insert. 2010. Des Plaines, IL: Abbott Molecular.

## Test Information

0049218

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For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).

### **AUTHOR**

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