

ERBB2 (HER2/neu) (HercepTest) by Immunohistochemistry

Indications for Ordering

- Aid in prediction of response to HER2-directed therapy [eg, trastuzumab (Herceptin)] in patients with breast or gastric cancer
- Alternate test to confirm equivocal dual in situ hybridization (ISH) or fluorescence in situ hybridization (FISH) result

Test Description

Dako HercepTest test kit in combination with a proprietary polymer detection kit

- Uses a visualization reagent based on dextran technology to locate the human ERBB2 (HER2) protein
- Graded negative (0 or 1+), equivocal (2+), positive (3+)

Tests to Consider

Typical Testing Strategy

Standard practice for evaluating primary, recurrent, and metastatic breast carcinoma, and gastric or gastroesophageal carcinoma

- Assess ERBB2 status by immunohistochemistry (IHC) or ISH/FISH
 - Concordance between the methods can vary due to subjective interpretation
- Use alternate test if equivocal results are reported on initial test
 - If IHC equivocal (2+), confirm by ISH/FISH
 - If ISH/FISH equivocal, confirm by IHC
- Use gene amplification by FISH to resolve discrepancies between IHC and ISH/FISH

Primary Tests

[ERBB2 \(HER2/neu\) \(HercepTest\) by Immunohistochemistry, Tissue with Reflex to FISH if 2+ 0049178](#)

- Measure protein expression
- Reflex to FISH if IHC is 2+

[ERBB2 \(HER2/neu\) \(HercepTest\) with Interpretation by Immunohistochemistry, Tissue 0049174](#)

- Measure protein expression

Related Tests

[ERBB2 \(HER2\) \(HercepTest\) by Immunohistochemistry 2007332](#)

- Measure protein expression

[ERBB2 \(HER2/neu\) Gene Amplification by FISH with Reflex, Tissue 2008603](#)

- Aid in prediction of response to HER2-directed therapy [eg, trastuzumab (Herceptin)] in patients with breast or gastric cancer
- Use to confirm equivocal HercepTest of 4B5 IHC result (2+)

Disease Overview

Incidence – ~232,000 new invasive breast and ~21,000 new gastric cancers are diagnosed in the U.S. per year; common causes of cancer-related deaths

Treatment issues

Amplification of the *ERBB2* gene occurs in ~15-20% of breast cancers and ~20% of gastric cancers

- Predicts poor prognosis in invasive breast cancer
- Trastuzumab prolongs the overall survival rate in individuals with breast or gastric cancer when tumors overexpress ERBB2
 - Trastuzumab antibodies are directed against the extracellular portion of ERBB2 protein
 - Inhibits ERBB2-overexpressing cancers
 - Due to high drug costs and cardiac toxicity, use of trastuzumab requires identification of tumors that demonstrate *ERBB2* gene amplification or protein overexpression (3+ IHC result)

Test interpretation

See tables

Limitations

- Testing using tissue fixed in alcohol-based or nonformalin fixatives has not been validated using this method
- Specimens placed in decal may have a false-negative result
- Repeat testing is recommended for discordant results

ASCO/CAP 2013 HER2 IHC scoring criteria used in the interpretation of the HercepTest for breast cancer		
Score	Interpretation	Microscopic finding
0	Negative	No staining or membrane staining that is incomplete, faint/barely perceptible and within ≤10% of the invasive tumor cells
1+	Negative	Incomplete membrane staining that is faint/barely perceptible and within >10% of the invasive tumor cells
2+	Equivocal	Circumferential membrane staining that is incomplete, weak, or moderate within >10% of the invasive tumor cells; or complete and circumferential intense membrane staining within ≤10% of invasive tumor cells
3+	Positive	Circumferential membrane staining that is complete, intense and in >10% of invasive tumor cells
Positive results (3+) indicate possible response to trastuzumab Equivocal results (2+) should be confirmed by ISH testing		

Biopsies of gastric and gastroesophageal adenocarcinoma using ERBB2 IHC scoring		
Score	Interpretation	Staining pattern
0	Negative	No reactivity or no membranous reactivity in any tumor cell
1+	Negative	Tumor cell clusters (5 cells) with faint/barely perceptible membranous reactivity irrespective of percentage of tumor cells stained
2+	Equivocal	Tumor cell cluster with a weak to moderate complete, basolateral or lateral membranous reactivity irrespective of percentage of tumor cells stained
3+	Positive	Tumor cell cluster with a strong complete, basolateral or lateral membranous reactivity irrespective of percentage of tumor cells stained
Hofmann M, et al. Histopath. 2008;52:797-805		

Resections of gastric and gastroesophageal adenocarcinoma using ERBB2 IHC scoring		
Score	Interpretation	Staining pattern
0	Negative	No reactivity or membranous reactivity in <10% of tumor cells
1+	Negative	Faint/barely perceptible membranous reactivity in ≥ 10% of tumor cells. Cells are reactive only in part of their membrane
2+	Equivocal	Weak to moderate complete, basolateral or lateral membranous reactivity in ≥ 10% of tumor cells
3+	Positive	Strong complete, basolateral or lateral membranous in ≥ 10% of tumor cells
Hofmann M, et al. Histopath. 2008;52:797-805		