Test Definition: H2GE

HER2, Gastroesophageal FISH, Tissue

Overview

Useful For

Guiding therapy for patients with primary or metastatic gastroesophageal tumors, as patients with *HER2* amplification may be candidates for therapies that target the human epidermal growth factor receptor 2 (HER2) protein (eg, trastuzumab [Herceptin], pertuzumab)

Confirming the presence or absence of *HER2* amplification in cases with 2+ (equivocal) *HER2* overexpression by immunohistochemistry

Testing Algorithm

This test does not include a pathology consult. If a pathology consult is requested, PATHC / Pathology Consultation should be ordered and the appropriate FISH test will be ordered and performed at an additional charge.

A charge and CPT code is applied for each probe set hybridized, analyzed, and reported.

Note: In accordance to criteria set forth in the 2013 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guideline for breast cancer, reflex testing will not be performed using an alternative chromosome 17 probe when the FISH result is equivocal.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test is only for primary or metastatic gastroesophageal tumors.

-For breast tumors, order H2BR / *HER2* Amplification Associated with Breast Cancer, FISH, Tissue.

-For urothelial tumors, order H2UR / *HER2* Amplification Associated with Urothelial Carcinoma, FISH, Tissue.

-For all other tumor types (other than primary or metastatic gastroesophageal tumors), order H2MT / *HER2* Amplification, Miscellaneous Tumor, FISH, Tissue.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required in order for testing to be performed. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.

2. A reason for testing must be provided. If this information is not provided, an appropriate indication for testing

may be entered by Mayo Clinic Laboratories.

3. The pathology report must include type of fixation used as well as the time of fixation (recommended: >6 hours and <72 hours).

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue

Preferred: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block. Blocks prepared with alternative fixation methods may be acceptable; provide fixation method used.

Acceptable: Slides

Collection Instructions: Four consecutive, unstained, 5 micron-thick sections placed on positively charged slides, and 1 hematoxylin and eosin-stained slide.

Specimen Minimum Volume

Two consecutive, unstained, 5-micron-thick sections placed on positively charged slides and 1 hematoxylin and eosin-stained slide.

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Ambient (preferred)		
	Refrigerated		

Clinical and Interpretive

Clinical Information

Gastroesophageal cancer is one of the most commonly diagnosed cancers. To date, chemotherapy for gastroesophageal cancer is often ineffective and its prognosis remains poor. Recent studies suggest that the *HER2* oncogene can be used as a marker to identify aggressive disease.

In much the same way as was demonstrated for *HER2*-positive breast cancer, the *HER2* gene status in gastroesophageal cancers can be used to determine treatment approaches. Amplification of the *HER2* gene and overexpression of the human epidermal growth factor receptor 2 (HER2) protein have been associated with a shorter disease-free survival and shorter overall survival in gastric and gastroesophageal junction cancers. Patients whose tumors demonstrate *HER2* amplification or overexpression may be candidates for treatment with the drugs that target the HER2 protein or its downstream pathways (eg, trastuzumab [Herceptin], pertuzumab).

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided. Results are interpreted utilizing the 2016 College of American Pathologists (CAP)/American Society for Clinical Pathology (ASCP)/American Society of Clinical Oncology (ASCO) guidelines for gastric tumors, and the guidelines used by the Traztuzumab for Gastric Cancer (ToGA) trial.

Specimens with equivocal results as defined by 2016 CAP/ASCP/ASCO guidelines will not have reflex testing performed using an alternative FISH probe set. The report will include a complete interpretation including the *HER2*:D17Z1 results.

The degree of *HER2* amplification varies in tumors. Some exhibit high levels of amplification (*HER2*:D17Z1 ratio >4.0), whereas others exhibit low-level amplification (*HER2*:D17Z1 ratio of 2.0-4.0). It is not currently known if patients with different levels of amplification have the same prognosis or response to therapy.

Reports also interpret the *HER2* copy number changes relative to chromosome 17 copy number (aneusomy) or potential structural genomic abnormalities that increase *HER2* copy number.

Rare cases may not show *HER2* amplification but still have human epidermal growth factor receptor 2 (HER2) protein overexpression demonstrated by immunohistochemistry. The clinical significance of HER2 protein overexpression in the absence of *HER2* gene amplification is unclear. However, these patients may have a worse prognosis and be candidates for treatments that target the HER2 protein or its downstream pathways.

Cautions

The *HER2* FISH test is not approved by the FDA for this indication and should be used as an adjunct to existing clinical and pathologic information.

The assay has been optimized for formalin-fixed, paraffin-embedded tissue specimens. Optimal fixation should be between 6 and 72 hours in 10% neutral buffered formalin.

The prognostic information provided by the *HER2* status of a patient's tumor should not be interpreted in isolation because other prognostic features (eg, lymph node status, tumor size) may be of equal or greater importance in determining the patient's prognosis.

Supportive Data

Retrospective data was reviewed on 85 gastroesophageal tumors using the PathVysion HER2 probe set. The FISH results were compared to immunohistochemistry (IHC) testing. Of 36 specimens with *HER2* amplification, 20 were 3+ by IHC, 8 were 2+, 1 was 1+, and 7 had unknown IHC results. Twenty-five normal gastric tissue control specimens were also tested. The correlation of FISH and IHC results are similar to those observed in validation studies for breast tumor specimens, so the interpretative guidelines will be the same.

Clinical Reference

1. Bartley AN, Washington MK, Ventura CB, et al: HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma: Guideline From the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Am J Clin Pathol 2016;146(6):647-669

2. Bang YJ, Van Cutsem E, Feyereislova A, et al: Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): a phase 3, open-label, randomized controlled trial. Lancet 2010;376(9742):687-697

3. Hofmann M, Stoss O, Shi D, et al: Assessment of a HER2 scoring system for gastric cancer: results from a validation study. Histopathology 2008;52:797-805

4. Reichelt U, Duesedau P, Tsourlakis MCh, et al: Frequent homogeneous HER-2 amplification in primary and metastatic adenocarcinoma of the esophagus. Mod Pathol 2007;20:120-129

5. Wolff AC, Hammond ME, Hicks DG, et al: Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society for Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol 2013 Nov 1;31(31):3997-4013

Performance

Method Description

The test is performed using the PathVysion HER2 DNA probe set (Abbott Molecular) with a *HER2* probe and a chromosome 17 centromere probe (D17Z1). Paraffin-embedded tissues are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped etcher on the back of the unstained slide to be assayed. The probe set is hybridized to the appropriate target areas and 2 technologists each analyze 30 interphase nuclei (60 total) with the results expressed as a ratio of *HER2:*D17Z1 signals. The results are interpreted based on the 2016 College of American Pathologists (CAP)/American Society for Clinical Pathology (ASCP)/American Society of Clinical Oncology (ASCO) guidelines.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

6 to 8 days

Specimen Retention Time

Slides and H&E used for analysis are retained by the laboratory in accordance to CAP and NYS requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

88377

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
H2GE	HER2, Gastroesophageal FISH, Tissue	96893-3

Result ID	Test Result Name	Result LOINC Value
603085	Result Summary	50397-9
603086	Interpretation	69965-2
603087	Result	62356-1
GC030	Reason for Referral	42349-1
603088	Specimen	31208-2
603089	Source	85298-8
603090	Tissue ID	80398-1
603091	Fixative	8100-0
603092	Method	85069-3
603093	Additional Information	48767-8
603094	Disclaimer	62364-5
603095	Released By	18771-6