MAYO CLINIC LABORATORIES

Test Definition: H2UR

HER2, Urothelial Tumor, FISH,Tissue

Overview

Useful For

Guiding therapy for patients with primary or metastatic urothelial 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 of *HER2* amplification in cases with 2+ (low level) or 3+ (high level) HER2 protein overexpression by immunohistochemistry, and for certain histologic subtypes with aberrant patterns of HER2 expression seen by immunohistochemistry (eg, micropapillary carcinoma).

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.

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.

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

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 urothelial tumors.

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

-For gastroesophageal tumors, order H2GE / *HER2* Amplification Associated with Gastroesophageal Cancer, FISH, Tissue.

-For all other tumor types, 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.

Forms

If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Reject Due To

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

Specimen Minimum Volume

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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Human epidermal growth factor receptor 2 (HER2) plays a fundamental role in cell growth, survival, and migration. The assessment of *HER2* gene status is crucial for the management of breast cancer. Studies have shown that *HER2* is also expressed in a proportion of urothelial carcinoma of the urinary bladder (UCB), making it a potential target for UCB therapy.

HER2-positive gene status is associated with aggressive UCB and provides independent prognostic information. Assessment of *HER2* status may be used to identify patients at high risk of disease progression.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided. Results are interpreted utilizing the 2013 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines for breast tumors.

Specimens with equivocal (Group 4) results as defined by 2013 ASCO/CAP guidelines will no longer 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 and 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.

Optimum fixation should be between 6 and 72 hours in 10% neutral buffered formalin. Other types of fixatives should not be used.

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

Urothelial carcinoma samples (170) were analyzed using the PathVysion *HER2* probe set and 18 (10.6%) showed *HER2* amplification. These results are consistent with a published report describing 93/1005 (9.2%) samples from bladder cancer patients with *HER2* amplification.

Clinical Reference

1. Bolenz C, Shariat SF, Karakiewicz PI, et al: Human epidermal growth factor receptor 2 expression status provides independent prognostic information in patients with urothelial carcinoma of the urinary bladder. BJU Int 2010 Oct;106(8):1216-1222

2. Lae M, Couturier J, Oudard S, et al: Assessing HER2 gene amplification as a potential target for therapy in invasive urothelial bladder cancer with a standardized methodology: results in 1005 patients. Ann Oncol 2010 Apr;21(4):815-819

3. 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 Onc 2013 Nov 1;31(31):3997-4013

Performance

Method Description

The test is performed using the dual-color PathVysion HER2 DNA probe set (Abbott Molecular) with a *HER2* probe and a chromosome 17 centromere probe (CEP17; 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 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 2013 guidelines established by the American Society of Clinical Oncology (ASCO) and College of American Pathologists (CAP), available at www.cap.org/apps/docs/committees/immunohistochemistry/validated_dual_probe_ish_assay.pdf.

(Unpublished Mayo method).

PDF Report

No

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 & Codes

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

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LOINC® Information

Test ID	Test Order Name	Order LOINC Value
H2UR	HER2, Urothelial Tumor, FISH,Tissue	96893-3

Result ID	Reporting Name	LOINC®
603107	Result Summary	50397-9
603108	Interpretation	69965-2
603109	Result	62356-1
GC034	Reason for Referral	42349-1
603110	Specimen	31208-2
603111	Source	85298-8
603112	Tissue ID	80398-1
603113	Fixative	8100-0
603114	Method	85069-3
603115	Additional Information	48767-8
603116	Disclaimer	62364-5
603117	Released By	18771-6