

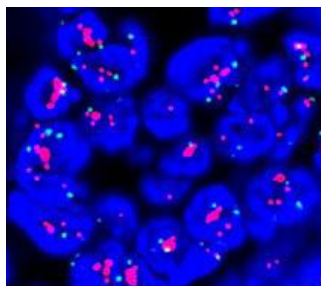


What's New in Pathology:

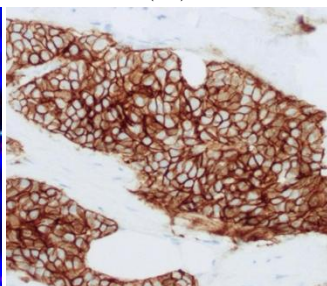
Revised ASCO-CAP HER2 Test Guideline Recommendations

The ASCO-CAP HER2 test guideline recommendations have been revised in 2013. This is a summary of changes to the 2007 guidelines.

Positive FISH



Positive IHC (3+)



HER2 Positive Breast Cancer

Human epidermal growth factor receptor 2 (HER2) is a receptor protein on the surface of all breast cells. The HER2 gene may be upregulated in breast cancer cells (15-20% of cases). HER2 positivity portends a worse prognosis, however indicates susceptibility to targeted therapies such as trastuzumab, lapatinib and pertuzumab.

When the test is performed

All newly diagnosed primary breast cancer specimens should have at least one HER2 test performed. Patients who develop metastatic disease must have a HER2 test performed in a metastatic site. HER2 may be tested with either immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH). If either test is equivocal, reflex testing using a different method or a new specimen must be performed.

HER2 testing by IHC

In an IHC test, an antibody binds to the cell surface Her2 antigen. The antibody is linked to an enzyme, causing a color-producing reaction.

Changes to testing by IHC

Positive (3+): complete, intense, circumferential membrane staining in >10% tumor cells (*modified from >30% of tumor cells*)

Equivocal (2+): complete, intense, circumferential membrane staining in <10% tumor cells OR incomplete, weak/moderate circumferential staining in >10% tumor cells

Negative (1+): faint, barely visible staining in >10% tumor cells

Negative (0): no staining OR faint barely visible staining in <10% tumor cells

HER2 testing by FISH

Fluorescence-tagged probes bind to and detect DNA sequences (genes) in the cell. There are typically 2 copies of HER2 in a cell. Increased copy number indicates HER2 amplification (see criteria below). CEP17 is a centromere probe, a stable gene sequence that typically has 2 copies in every cell and is used as a control, reported as the HER2/CEP17 ratio.

Changes to testing by FISH

Positive:

- $HER2/CEP17 \geq 2.0$ (*modified from >2.2*)
- Her2 copy number ≥ 6.0 signals/cell

Equivocal:

- $HER2/CEP17 < 2.0$ AND average HER2 copy number ≥ 4.0 and < 6.0 signals/cell (*modified from 1.8-2.2*)

Negative:

- $HER2/CEP17 < 2.0$ AND average HER2 copy number of < 4.0 signals/cell (*modified from <1.8*)

Tissue requirements

The duration of formalin fixation requirements has been modified from 6 to 48 hours to 6 to 72 hours allowing for a longer duration of fixation time. The specimen must still be placed into 10% neutral buffered formalin as soon as possible to minimize cold ischemic time (which must be ≤ 1 hour).

HER2 testing at TOPA

TOPA performs both IHC and FISH HER2 testing on all newly diagnosed breast cancer cases and metastatic breast cancers. TOPA currently performs in house FDA-approved HER2 testing by IHC. HER2 FISH interpretation is also performed by TOPA pathologists. The average turn around time for HER2 reporting is 4 days after diagnosis. HER2 testing is repeated in cases of discordant findings between IHC and FISH and at the request of the clinician.

Reference:

J Clin Oncology. 2013;31(31):3997-4013.

For more information on HER2 testing, please contact Danielle Westfall, M.D. at TOPA Diagnostics (805-373-8582).