HER2-neu Testing for Breast Specimens with Invasive Carcinoma

Effective Date: January 1, 2014

Clinical Significance: The American Society of Clinical Oncology and the College of American Pathologists recently released a joint Clinical Practice Guideline Update that impacts how HER2-neu tests for breast cancer are processed and reported. The Medical Foundation performs two types of validated HER2-neu assay, an immunohistochemistry (IHC) test, and HER2-neu detection by Fluorescence in situ Hybridization (FISH). Beginning in 2014, the primary HER2 assay performed on all invasive breast cancer cases will be IHC, based on a testing algorithm in the new ASCO/CAP guideline. If the IHC HER2 result is EQUIVOCAL, this will automatically reflex to performance of a HER2 FISH test. This ensures that a pathologist will have the opportunity to assess the IHC pattern of HER2 expression, in addition to standard morphology. This information will be used to target appropriate areas for cell counting on the FISH preparation.

Other issues that may prompt a reflex order for a HER2 FISH test:
- The HER2 IHC Result is INDETERMINATE (technical issues prevent valid IHC result and FISH is felt to be a reasonable alternative test)
- Histopathologic discordance is identified, based on ASCP/CAP guideline criteria, between the HER2 result and other pathologist observations after review of case material.

The new guidelines also update reporting criteria for both IHC and FISH HER2-neu tests as follows:

**HER2 by IHC:**
- **NEGATIVE:** 0 or 1+ (No or incomplete membrane staining that is barely perceptible in ≤ 10% or >10% of invasive tumor cells, respectively).
- **POSITIVE:** 3+ (Strong circumferential membrane staining in >10% of invasive tumor cells).
- **EQUIVOCAL:** 2+ (Circumferential membrane staining that is incomplete, weak, or moderate within >10% of invasive tumor cells, or complete and circumferential intense staining in ≤10% of invasive tumor cells).

**HER2 by FISH:**
- **NEGATIVE:** HER2/CEP17 Signal ratio <2.0 and HER2 signal copies/nucleus <4, regardless of ratio.
- **POSITIVE:** HER2/CEP17 signal ratio ≥ 2.0 OR average HER2 signals/nucleus of ≥ 6.0, regardless of ratio, in >10% of invasive tumor cells.
- **EQUIVOCAL:** HER2/CEP17 signal ratio < 2.0 with an average HER2 signal copies/nucleus ≥ 4.0 but < 6.0 signals per cells
- **INDETERMINATE:** A valid result is not possible due to technical issues (fixation, crush artifact, etc). May occur with either assay.

Specimen Requirements: Paraffin embedded tissue block demonstrating invasive breast carcinoma fixed in neutral buffered formalin for a least 6 to no more than 72 hours. Aspiration cytology cell block material may be acceptable if fixed in formalin as above.

Test availability: The IHC HER2-neu test will be run weekly on Monday, Wednesday and Friday along with other IHC breast markers such as Estrogen and Progesterone receptor studies, and typically will be resulted the on the same day.
HER2 FISH turnaround time is 4 to 7 days.

**Test Order Numbers:**
- HER2 by IHC with reflex to FISH, if indicated: 38521  **CPT:** 88360
- HER2 by FISH: 38553  **CPT:** 88367x2

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**References**