HER2 testing (invasive component) by validated single-probe ISH assay

Batch controls and on-slide controls show appropriate hybridization

Average HER2 copy number $\geq 6.0$ signals/cell
- ISH positive

Average HER2 copy number $\geq 4.0$ and $< 6.0$ signals/cell
- ISH equivocal

Average HER2 copy number $< 4.0$ signals/cell
- ISH negative

Must order a reflex test (same specimen using dual-probe ISH or using IHC) or order a new test (new specimen if available, using ISH or IHC)

HER2 testing (invasive component) by validated IHC assay

Batch controls and on-slide controls show appropriate staining

Circumferential membrane staining that is complete, intense, and within > 10% of tumor cells*

IHC 3+ positive

Circumferential membrane staining that is incomplete and/or weak/moderate and within > 10% of tumor cells*

or

Complete and circumferential membrane staining that is intense and within ≤ 10% of tumor cells*

IHC 2+ equivocal

Incomplete membrane staining that is faint/barely perceptible and within > 10% of tumor cells*

IHC 1+ negative

No staining is observed* or Membrane staining that is incomplete and is faint/barely perceptible and within ≤ 10% of tumor cells

IHC 0 negative

Must order reflex test (same specimen using ISH) or order a new test (new specimen if available, using IHC or ISH)

HER2 testing (invasive component) by validated dual-probe ISH assay

Batch controls and on-slide controls show appropriate hybridization

**HER2/CEP17 ratio ≥ 2.0***

- Average HER2 copy number ≥ 4.0 signals/cell*
  - ISH positive

- Average HER2 copy number < 4.0 signals/cell*
  - ISH positive†

**HER2/CEP17 ratio < 2.0**

- Average HER2 copy number ≥ 6.0 signals/cell*
  - ISH positive

- Average HER2 copy number ≥ 4.0 and < 6.0 signals/cell*
  - ISH positive

- Average HER2 copy number < 4.0 signals/cell
  - ISH equivocal

- ISH negative

Must order a reflex test (same specimen using IHC), test with alternative ISH chromosome 17 probe, or order a new test (new specimen if available, ISH or IHC)

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