HER2 Testing in Gastroesophageal Adenocarcinoma

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The CAP/ASCP/ASCO guidelines strongly recommend HER2 testing in patients with GEA

- The HER2 oncogene is amplified and/or overexpressed in 7% to 38% of GEA cases

GEA=gastroesophageal adenocarcinoma.
Guideline-recommended sample preparation helps to improve test accuracy

Sample sources¹:

- **Test primary or metastatic tumor tissue** in the biopsy or resection specimens
  - A minimum of 5 biopsy specimens are needed, but optimally 6-8 specimens should be obtained
  - FNA specimens (cell blocks) are an acceptable alternative

- **Select tissue block with the areas of lowest grade** tumor morphology in biopsy and resection specimens

- **More than 1 tissue block** may be selected if different morphologic patterns are present

Fixation guidelines¹:

- Limit cold ischemic time by fixing specimens **within 1 hour** after resection or pathological inspection

- Fix specimens in **10% NBF** (10:1 NBF-to-tissue ratio) for 6 to 72 hours
The guidelines for scoring IHC in GEA differ from those used for breast cancer.

<table>
<thead>
<tr>
<th>HER2 status</th>
<th>Breast cancer</th>
<th>GEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (negative)</td>
<td>No staining OR incomplete, faint membrane staining in ≤10% of cells</td>
<td>No reactivity or membranous reactivity in &lt;10% of tumor cells</td>
</tr>
<tr>
<td>1+ (negative)</td>
<td>Incomplete, faint membrane staining in &gt;10% of cells</td>
<td>Faint/barely perceptible membranous reactivity in ≥10% of tumor cells, cells are reactive only in part of their membranes</td>
</tr>
<tr>
<td>2+ (equivocal)</td>
<td>Incomplete, weak-to-moderate circumferential staining in &gt;10% of cells OR complete, intense circumferential membrane staining in ≤10% of cells</td>
<td>Weak to moderate, complete, basolateral or lateral membranous reactivity in ≥10% of tumor cells</td>
</tr>
<tr>
<td>3+ (positive)</td>
<td>Complete, intense circumferential membrane staining in &gt;10% of cells</td>
<td>Strong, complete, basolateral or lateral membranous reactivity in ≥10% of tumor cells</td>
</tr>
</tbody>
</table>

*Images representative of a biopsy.*
Dual-probe ISH should be used to retest IHC 2+ samples

- The CAP/ASCP/ASCO guidelines recommend IHC testing first, followed by dual-probe ISH in IHC 2+ (equivocal) samples
  - Use 4-μm-thick paraffin sections for ISH analysis
  - Identify areas of invasive adenocarcinoma and mark areas with the strongest intensity of HER2 expression by IHC for subsequent ISH scoring
  - Evaluate ≥20 nonoverlapping nuclei of tumor cells for HER2 and CEP17 probe signal enumeration

The guidelines for scoring ISH differ from those used for breast cancer to compensate for the greater heterogeneity of GEA

<table>
<thead>
<tr>
<th>HER2/CEP17 ratio</th>
<th>HER2 signals/cell</th>
<th>CEP17 signals/cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2/CEP17 ≥2.0</td>
<td>3.0</td>
<td>1.7</td>
</tr>
<tr>
<td>HER2/CEP17 &lt;2.0</td>
<td>1.3</td>
<td>3.0</td>
</tr>
<tr>
<td>HER2/CEP17 &lt;2.0</td>
<td>1.0</td>
<td>1.8</td>
</tr>
</tbody>
</table>
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References


3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.1.2017. © National Comprehensive Cancer Network, Inc 2017. All rights reserved. Accessed April 24, 2017. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.