COLLEGE of AMERICAN PATHOLOGISTS

HER2 Testing and Clinical Decision Making in Gastroesophageal Adenocarcinoma Update

Statements and Strengths of Recommendations

SUMMARY OF RECOMMENDATIONS

Guideline Statement	Strength of Recommendation
1. At initial diagnosis of advanced GEA, treating clinicians or pathologists should request HER2 testing on the highest quality tumor specimen (primary or metastasis). Pathologists should select the tissue block with the areas of lowest grade tumor morphology in biopsy, resection, or FNA specimens. More than one tissue block may be selected if different morphologic patterns are present. *Note*: Highest quality tumor for HER2 testing in GEA: highest neoplastic cellularity, minimal necrosis, artifact or treatment effect.	Strong Recommendation
2. In specimens from patients with advanced GEA, pathologists should use IHC/ISH as the primary assessment for HER2 status. Genomic testing (liquid and/or solid) may be used concurrently or subsequently for clinical decision making.	Strong Recommendation
3. In patients with advanced HER2-positive GEA being considered for subsequent therapy after disease progression, HER2 assessment may be performed on relapsed/recurrent tumor sample. Tissue is preferred but if not available/feasible, liquid testing may be performed.	Strong Recommendation
4. Clinicians should check PD-L1 results in patients with advanced HER2-positive GEA to inform treatment decisions.	Strong Recommendation
5. In patients with advanced GEA who are potential candidates for HER2-targeted therapy, the treating clinician should request HER2 testing on tumor tissue.	Good Practice Statement
6. Treating clinicians should offer combination chemotherapy and HER2-targeted therapy as the initial treatment for appropriate patients with HER2-positive tumors who have metastatic or recurrent GEA.	Good Practice Statement
7. Laboratories/pathologists must specify the antibodies and probes used for the test and ensure that assays are appropriately validated for HER2 immunohistochemistry (IHC) and in-situ hybridization (ISH) on GEA specimens.	Good Practice Statement
8. When GEA HER2 status is being evaluated, laboratories/pathologists should perform/order IHC testing first, followed by ISH confirmation when IHC result is 2+ (equivocal). Positive (3+) or negative (0 or 1+) HER2 IHC results do not require further ISH testing.	Good Practice Statement

9. Pathologists should use the Rüschoff-Hoffmann method for HER2 IHC scoring in GEA and apply standard ISH interpretation criteria when indicated.	Good Practice Statement
10. Laboratories should incorporate GEA HER2 testing methods into their overall laboratory quality improvement program, following the requirements of applicable local regulatory bodies and accreditation organizations.	Good Practice Statement