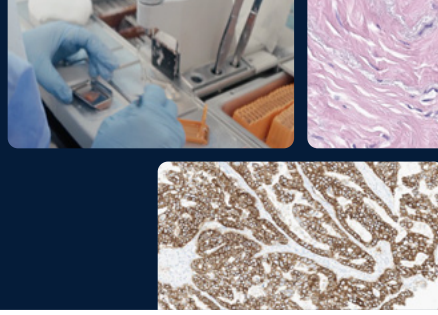
HER2 IHC Testing in Breast Cancer



The 2023 ASCO-CAP guideline update affirms the 2018 ASCO-CAP guideline recommendations on HER2 testing in breast cancer and offers additional guidance around reporting HER2 IHC 1+, IHC 2+/ISH- results, and best practices for differentiating HER2 IHC 1+ and 0 tumors.[1]

Key best practice recommendations for HER2 IHC testing

Test ordering

- All newly diagnosed patients with breast cancer must have a HER2 test performed[1]
- Patients who then develop metastatic disease must have a HER2 test performed in a metastatic site, if tissue sample is available[1]

Pre-analytic considerations

- Pay careful attention to pre-analytic conditions and follow guidelines for optimal tissue handling requirements[1]

Interpretation

- Use controls with a range of HER2 expression, including with HER2 IHC 1+ staining[1]
- Examine HER2 IHC at 40X magnification when distinguishing between HER2 IHC 0 from 1+ staining[1]

Second opinion

- Consider second pathologist review when results are close to the 0 versus 1+ interpretive threshold[1]

Reporting

- Always report semiquantitative (discrete) HER2 IHC scores[1]
- Include a footnote in the pathology report on the therapeutic implications of the results (see next page)[1a]

To practice scoring HER2 IHC 0 and IHC 1+ breast cancer cases, visit **HER2Know.com**

[a]Please refer to 'The Bottom Line' in the 2023 ASCO-CAP guideline update for HER2 testing report footnote comment recommendation.[1]

Reporting HER2 IHC Results

The updated CAP Reporting Template for Reporting Results of Biomarker Testing of Specimens from Patients with Carcinoma of the Breast (v1.6.0.0, March 2025) includes recommendations on reporting HER2 IHC results.[2]

Score	Staining description[1,2]	Result category[2]	Reflex ISH	Recommended result reporting[2]
IHC 0	No membrane staining detected	Negative (Score 0)		**0/absent membrane staining[a]**
	Membrane staining that is incomplete and is faint/barely perceptible and in ≤10% of tumor cells	Negative (Score 0)		**0+/with membrane staining[a]**
IHC 1+	Incomplete membrane staining that is faint/barely perceptible and in >10% of tumor cells	Negative (Score 1+)		**1+[a]**
IHC 2+	Weak to moderate complete membrane staining observed in >10% of tumor cells#	Equivocal (Score 2+)	Non-amplified	**2+/ISH-[a]**
			Amplified	**2+/ISH+**
IHC 3+	Circumferential membrane staining that is complete, intense, and in >10% of tumor cells	Positive (Score 3+)		**3+**
Cannot be determined (explain)[2]	*Please see the 2023 ASCO-CAP guideline update for conditions for reporting results as indeterminate[1]*			
CAP comment recommendation[2]	[a]*Consider using the optional standardized HER2 IHC report comment to explain the clinical relevance of lower levels of HER2 IHC staining, included on page 8 of the CAP Breast Biomarker Reporting Template (v1.6.0.0)[2] which can be found here: https://www.cap.org/protocols-and-guidelines/cancer-reporting-tools/cancer-protocol-templates*			

#Most often equivocal staining has the staining pattern defined here, but other less common staining patterns are also included as reporting options, including moderate to intense but incomplete membrane staining (basolateral), less than or equal to 10% of the cancer that has circumferential staining that is complete and intense (3+) (heterogeneous, but very limited in extent; consider results of additional samples - there should be a clearly clustered pattern of heterogeneity) and abundant cytoplasmic staining obscuring evaluation of membrane stain intensity. If other artifacts preclude evaluation of membrane stain intensity (crush, etc.), it can be described in the "Other (specify)" category.[2]

ASCO, American Society of Clinical Oncology; CAP, College of American Pathologists; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, *in situ* hybridization.

1. Wolff AC, et al. Arch Pathol Lab Med 2023;147(9):993-1000. 2. CAP. Reporting Template for Reporting Results of Biomarker Testing of Specimens from Patients with Carcinoma of the Breast. Version: 1.6.0.0.

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