HER2Know | By pathologists, for pathologists

Scoring definition guidance for HER2 in breast cancer

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Guidance on evaluating staining pattern and intensity[1-5]

Membrane staining	Visual estimate	Staining pattern and intensity	Magnification rule	Score
None		Membrane staining not present	No staining visible at any magnification, **4X(5X)*** to **40X**	**IHC 0**
Incomplete	Weak/faint ≤10%	Faint/barely perceptible membrane staining observed in ≤10% of tumor cells	Staining hardly perceptible at **4X(5X)*** and **10X**, visible at **20X** and confirmed at **40X**	**IHC 0**
	Weak/faint >10%	Faint/barely perceptible incomplete membrane staining observed in >10% of tumor cells	Staining hardly perceptible at **4X(5X)*** and **10X**, visible at **20X** and confirmed at **40X**	**IHC 1+**
	Moderate/strong >10%	Moderate to strong incomplete membrane staining observed in >10% of tumor cells	Staining visible at **4X(5X)***, confirmed at **10-20X**	**IHC 2+**
Complete	Weak/moderate >10%	Weak to moderate complete membrane staining observed in >10% of tumor cells	Staining visible at **4X(5X)***, confirmed at **10-20X**	**IHC 2+**
	Strong ≤10%	Strong complete membrane staining observed in ≤10% of tumor cells	Staining visible at **4X(5X)***, confirmed at **10-20X**	**IHC 2+**
	Strong >10%	Strong/intense, complete membrane staining observed in >10% of tumor cells and uniform 'chicken wire' pattern	Readily visible 'chicken wire' pattern at **4X(5X)***	**IHC 3+**

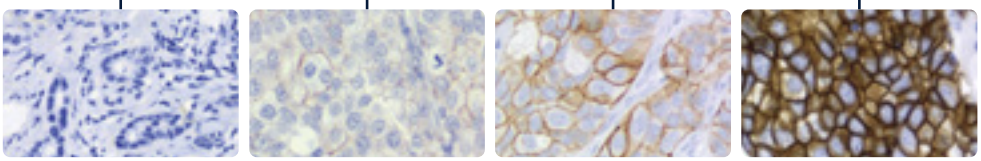
When close to the cut-off point, it may be necessary to perform actual cell counts.
Three representative fields at 40X or greater magnification should be chosen, and 100 cancer cells per field counted.[6]

*Depending on the type of objectives available, pathologists will use 4X or 5X.

Exclusion criteria for interpretation of HER2 IHC[7]

- Cold ischemic time of >1 hour
- Tissue samples
  - fixed for less than a minimum of 6-8 hours or for >72 hours in NBF
  - fixed in an alternative fixative other than formalin, unless that process has been specifically validated by the laboratory
  - with no invasive carcinoma present
  - unstained slides stored for >6 weeks prior to testing
  - with significant crush artifact and/or edge artifact (particularly core needle biopsies) and extensive staining artifacts

Definition of staining patterns[1,8]



No staining is observed **or** Membrane staining that is incomplete and is faint/barely perceptible and in ≤10% of tumor cells	Incomplete membrane staining that is faint/barely perceptible and in >10% of tumor cells	Weak to moderate complete membrane staining in >10% of tumor cells	Circumferential membrane staining that is complete, intense, and in >10% of tumor cells
IHC 0	**IHC 1+**	**IHC 2+**	**IHC 3+**

Breast cancers with IHC 1+ or IHC 2+ with a negative ISH result may be reported as HER2-low[3]

*This definition does not cover unusual staining patterns that are considered HER2 IHC 2+, such as moderate to intense but incomplete membrane staining and circumferential membrane staining that is intense but in ≤10% of tumor cells.[1]

Figure adapted from Wolff et al. 2023. Images from Marchiò et al. 2020.

Method for consensus scoring
Select breast cancer cases within the HER2Know **IHC image gallery** were independently reviewed and scored by expert breast pathologists to establish consensus. HER2 IHC interpretation was based on recommendations from the 2023 ASCO-CAP guideline updates,[1] and expert alignment on analyzing staining patterns and intensity.

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

1. Wolff AC, et al. Arch Pathol Lab Med 2023. 2. CAP. Template for reporting results of biomarker testing of specimens from patients with carcinoma of the breast. Version 1.5.0.1. Available at: https://documents.cap.org/documents/Breast.Bmk_1.5.0.1.REL_CAPCP.pdf. Accessed: November 2023. 3. Zhang H et al. Am J Clin Pathol. 2021; ajab117: 1-9. 4. Tarantino P et al. J Clin Oncol. 2020; 38(17): 1951-1962. 5. Franchet C et al. Annales de Pathologie 2021;41(6):507-520 6. Interpretation Guide PATHWAY anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody Staining of Breast Carcinoma, 1499100 Rev K, 2019-07-15. 7. Hicks DG & Schieffhauer L. Lab Medicine 2011; 42(8): 459–467. 8. Marchiò C et al. Semin Cancer Biol 2021;72:123-135.

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