HER2Know
A HER2-FOCUSED, PEER-LED EDUCATIONAL PLATFORM

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Identifying low levels of HER2 expression in breast cancer

A significant proportion (about 50%) of breast cancers express low levels of HER2 in the absence of gene amplification, and are described as IHC 1+ or IHC 2+ with negative ISH.[1] This proposed algorithm[2] represents a pragmatic approach to HER2 IHC interpretation, as we evolve towards distinguishing tumors that are HER2 negative from those with low levels of HER2 expression.

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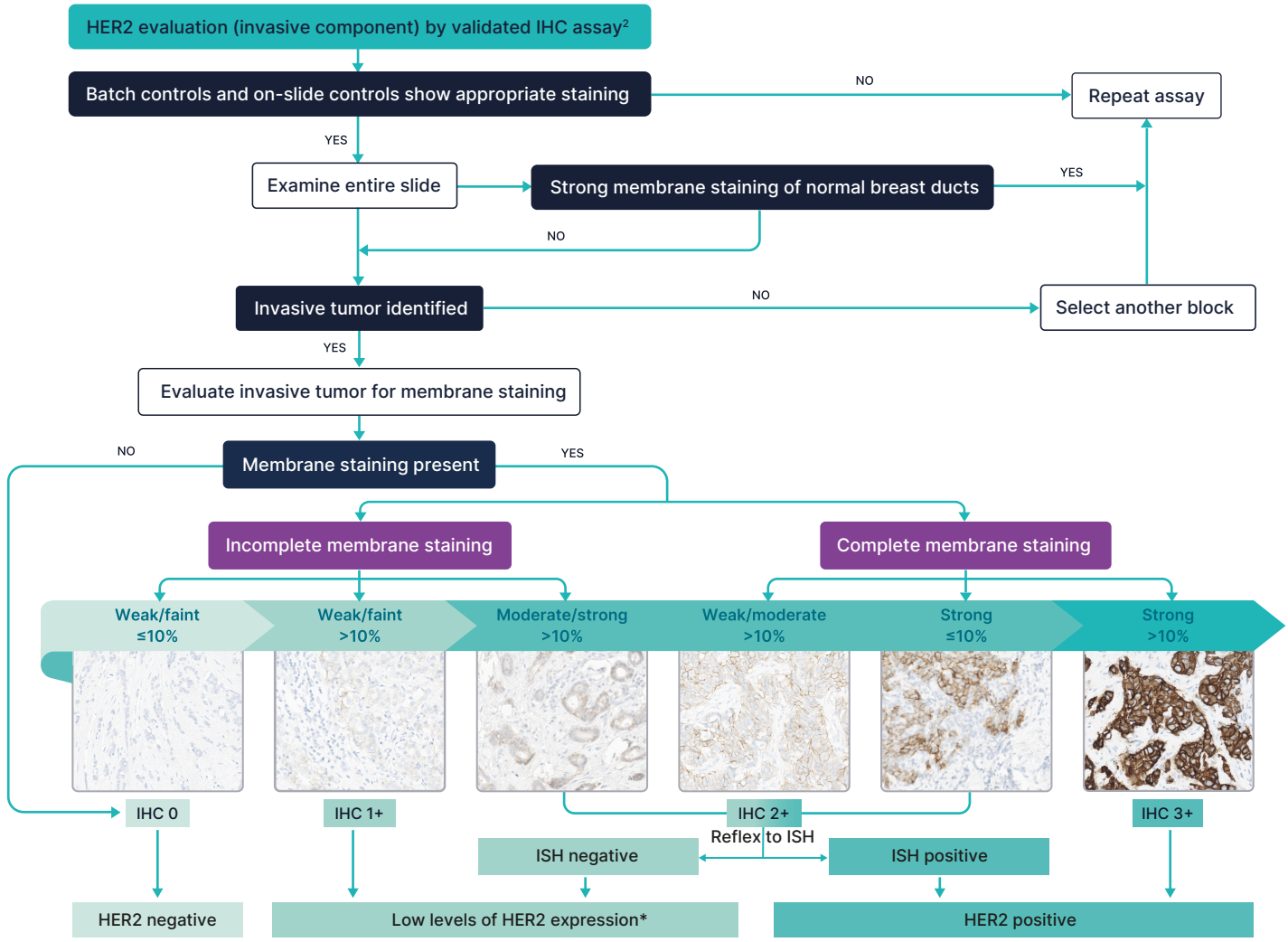

*Low levels of HER2 expression are not currently classified within the 2018 ASCO/CAP guidelines, but are recognized as HER2 negative.[3]

Guidance on evaluating staining pattern and intensity

	Staining intensity[1,2,4]	Magnification rule[5,6]	Score
	Membrane staining not present		IHC 0
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+
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	Staining visible at **4X(5X)***	IHC 3+

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

When close to the cut-off point, it may be necessary to perform actual cell counts.

Three representative fields at 40X or greater magification should be chosen, and 100 cancer cells per field counted.[7]

This resource is intended for use by US healthcare professionals only.

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization.
1. Tarantino P et al. J Clin Oncol. 2020; 38(17): 1951-1962. 2. AstraZeneca and Daiichi Sankyo. Data on file. REF-18013. 2021. 3. Wolff AC, et al. J Clin Oncol 2018; 36(20): 2105–2121. 4. Zhang H et al. Am J Clin Pathol. 2021; ajab117: 1-9. 5. AstraZeneca and Daiichi Sankyo. Data on file. REF-18100. 2022. 6. Franchet C et al. Annales de Pathologie 2021; 41(6): 507-520. 7. Interpretation Guide PATHWAY anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody Staining of Breast Carcinoma, 1499100 Rev K, 2019-07-15.

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