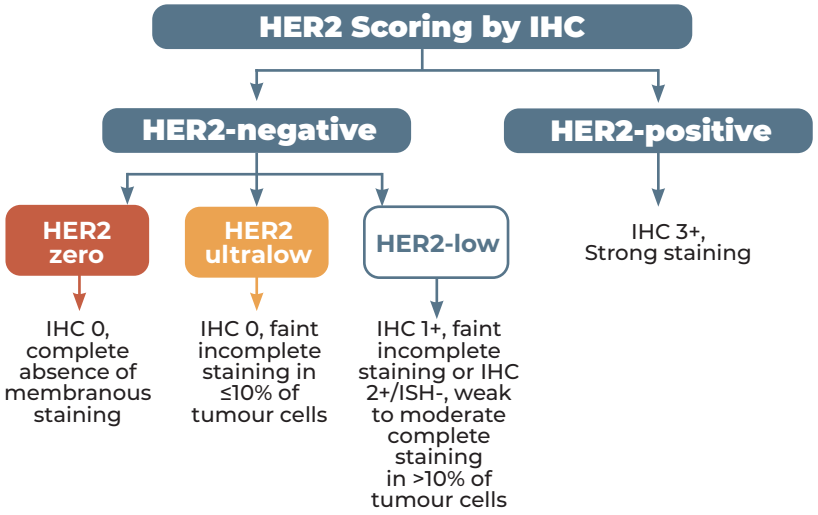
# Pre-analytical phase challenges and biomarker testing in HER2 metastatic breast cancer

## HER2 SCORING HAS EVOLVED[1,2]

HER2 expression now exists on a **continuum**, expanding eligibility for targeted therapies such as **ADCs**




**HER2-low and–ultralow** expression now exists on a **continuum**, expanding eligibility for HER2-targeted **ADCs**, such as trastuzumab deruxtecan

## PRE-ANALYTICAL QUALITY MATTERS[3]

High-quality pre-analytical handling and nuanced interpretation are essential for accurate HER2 classification, particularly for HER2-low and–ultralow disease

Small errors in testing or interpretation can lead to missed treatment opportunities particularly in HER2-low or ultra-low disease

Accurate HER2 assessment begins **before the test**

**Best practice includes:**

- Cold ischaemic time <1 hour
- 10% neutral buffered formalin fixation (6–72 hours)
- Freshly cut slides for staining
- EDTA-based decalcification for bone specimens

## TESTING FOR HER2[2,3]

**Immunohistochemistry (IHC):** Primary method for HER2 protein expression

**In-situ hybridisation (ISH):** Confirms HER2 gene amplification in equivocal cases

## MULTIDISCIPLINARY COLLABORATION MATTERS[4]

Optimal testing and interpretation require close communication between: **Pathologists, Medical Oncologists, Radiologists, Surgeons, Laboratory Teams, Patients**

Accurate biomarker assessment supports **appropriate treatment selection and improved patient outcomes.**

ADCs, antibody-drug conjugates; IHC, immunohistochemistry; ISH, in-situ hybridisation

1. Niu D, et al. Pathology & Oncology Research 2020; 26: 2577-2585;
2. Allison K, et al. College of American Pathologists. Breast Cancer Protocol. March 2025. Available at: https://documents.cap.org/documents/New-Cancer-Protocols-March-2025/Breast.Bmk_1.6.0.0.REL.CAPCP.pdf;
3. Marabi M; Tse GM. Human Pathology 2025; 162: 105818;
4. Mirham L, et al. Am J Clin Pathol 2021; 156 (4): 521-528

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This educational programme is supported by an Independent Educational Grant from Daiichi Sankyo. This content is intended for healthcare professionals only.