

UNDERSTANDING HER2-LOW & ULTRALOW CLASSIFICATION:

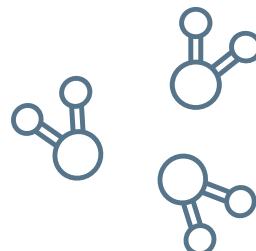
A Modern Therapeutic Framework



HER2: FROM BINARY TO CONTINUUM

T-DXd showed efficacy in HER2-low & ultralow mBC

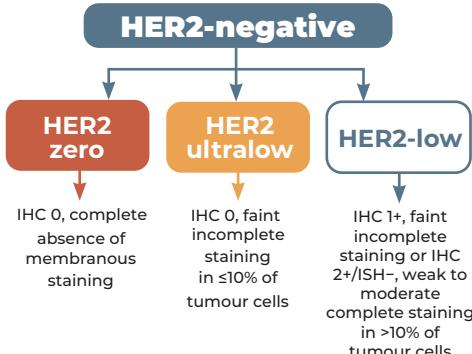
DESTINY-Breast04/06^{1,2} showed improved PFS and OS even at minimal HER2 expression, reinforcing the shift from a binary to a continuum-based HER2 classification that informs treatment decisions.



WHY HER2 CATEGORISATION MATTERS

CAP reporting template³ defines treatment-relevant strata

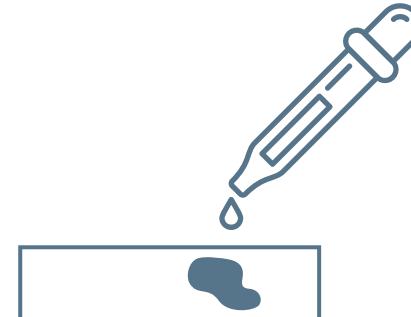
HER2-low & ultralow vs true HER2-0 determine eligibility for HER2-targeted ADCs.



HER2 EXPRESSION IS DYNAMIC

Re-biopsy can impact treatment options

Repeat biopsy at progression⁴, especially after previously scored HER2-0, may reveal eligibility for T-DXd.



IHC testing



SAFETY FIRST WITH T-DXD

Proactive AE management ensures safe treatment^{1,2,5}

- **Nausea:** 3 or 4 drug antiemetic prophylaxis.



- **Fatigue:** Monitor; encourage light exercise; reduce dose if persistent.



- **ILD/pneumonitis:** Monitor early; interrupt and give steroids; rechallenge only if G1 resolves <28 days (dose-reduce if longer); permanently discontinue for ≥G2.



ADC, antibody-drug conjugate; AE, adverse event; CAP, College of American Pathologists; IHC, immunohistochemistry; ILD, interstitial lung disease; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan.

1. Modi S, et al. N Engl J Med. 2022;387(1):9–20; 2. Bardia A, et al. N Engl J Med. 2024;391(22):2110–2122.; 3. 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;

4. Shami R, et al. ESMO Open. 2025;10(6):105310; 5. Based on the expert opinion and clinical experience of Dr Komal Jhaveri.