

HER2 Low Breast Cancer and ADCs - TDXd

Posttest Rationale

1. What treatment would you select for a patient with TNBC whose disease is found to be HER2-low following relapse after 1L chemotherapy?

- a) Margetuximab
- b) Trastuzumab
- c) T-DM1
- d) T-DXd

Rationale: T-DXd is the best choice for this patient and recently received FDA approval for adults with unresectable or metastatic HER2-low breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within six months of completing adjuvant chemotherapy. In the phase 3 DESTINY-Breast-04 trial, T-DXd compared with chemotherapy prolonged mPFS (9.9 vs 5.1 months) and mOS (23.4 vs 16.8 months) in patients with unresectable or metastatic breast cancer. Margetuximab was evaluated in a phase 1 trial that included patients that were negative for HER2 expression (IHC 0 or IHC, FISH non-amplified); partial response occurred only in HER2-positive patients (IHC 3+ or IHC 2+ and FISH amplified). Adjuvant trastuzumab ± chemotherapy was evaluated in a phase 3 trial that enrolled patients with high-risk, HER2-negative (FISH negative and IHC 1+ or 2+), invasive breast cancer, but the combination did not improve IDFS (5-year IDFS: 89.8% v 89.2%; HR) regardless of HER2 expression. In retrospective analyses, T-DM1 resulted in significantly inferior PFS and ORR in patients with HER2-low vs HER2-positive disease who had received prior HER2-directed therapy and chemotherapy.

References: FDA. FDA approves fam-trastuzumab deruxtecan-nxki for HER2-low breast cancer. Accessed August 8, 2022. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-fam-trastuzumab-deruxtecan-nxki-her2-low-breast-cancer>

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