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BREAST CANCER WITH LOW HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 EXPRESSION STATUS: A NEW THERAPEUTIC ENTITY

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Targeted human epidermal growth factor receptor 2 (HER2) therapies used in the treatment of HER2-positive early and metastatic breast cancer (mBC) include monoclonal antibodies such as trastuzumab, pertuzumab and margetuximab, as well as antibody-drug conjugates (ADC) trastuzumab emtansine (T-DM1) and trastuzumab deruxtecan (T-DXd), and tyrosine kinase inhibitors such as tucatinib, lapatinib, and neratinib. The introduction of these drugs into clinical practice has dramatically improved the course of treatment for HER2-positive breast cancer. However, the clinical evaluation of trastuzumab, pertuzumab, and T-DM1 in the HER2-low group of patients did not show significant benefits. Consequently, these patients were classified as HER2-negative cancers and treated in accordance with the expression of hormone receptors (HR) or other biomarkers. Trastuzumab deruxtecan, an ADC, which initially demonstrated its efficacy in the treatment of metastatic HER2-positive breast cancer, and subsequently in breast cancer with low HER2 expression, classified as immunohistochemistry IHC 1+ and IHC 2+ with a negative fluorescence *in situ* hybridization (FISH) introduced into clinical practice a new entity of HER2 breast cancers called HER2-low tumors. Following the publication of the DESTINY-Breast04 study results, it is clear that low HER2 positivity can be considered a rational target for the treatment of breast cancer. The results have changed clinical practice in both HR-positive and HR-negative HER2-low metastatic breast cancer. Further research is necessary in order to standardize HER2 testing, prevent T-DXd-related side effects and resistance to therapy, and identify the optimal sequence of available therapeutic options. Future research should also explore the role of these drugs in the treatment of early HER2-low breast cancer.

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