

Enhertu for HER2-Ultralow Breast Cancer

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Enhertu (fam-trastuzumab deruxtecan), previously approved for the treatment of metastatic breast cancer with high or low HER2 expression, also works for women with ultralow HER2 levels.

Around 15% of breast cancer has a high level of HER2, a receptor for a protein that promotes cell growth. But some 60% of people traditionally classified as HER2-negative actually have some HER2 receptors—a group now considered HER2-low—and around 25% have HER2-ultralow tumors.

Enhertu is an antibody-drug conjugate that uses a monoclonal antibody (purple in image) to deliver toxic chemotherapy (orange) directly to tumors. The DESTINY-Breast06 trial enrolled previously treated patients with hormone receptor-positive metastatic breast cancer who once would have been classified as HER2-negative. The study included 713 people with HER2-low tumors (a score of +1 or +2) and 153 with HER2-ultralow tumors (0 but detectable).

Enhertu extended progression-free survival by five months compared with standard chemotherapy (about 13 versus 8 months), reducing the risk of disease progression or death by 37% overall and by 22% in the HER2-ultralow group. Nine people with HER2-low tumors and four with HER2-ultralow tumors experienced complete remission.

These results “represent a potential shift in how we classify and treat metastatic breast cancer,” says lead investigator Giuseppe Curigliano, MD, PhD, of the University of Milan. “Enhertu could become a new standard of care” for patients with HER2-low and HER2-ultralow tumors.
