

# HER2-Low Breast Cancer

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The antibody-drug conjugate Enhertu (fam-trastuzumab deruxtecan), approved in 2019 for the treatment of metastatic breast cancer with high HER2 expression, has now been approved for people with low HER2 levels as well.

Breast cancer is classified by the type of receptors on tumors. Around 15% of patients have a high level of HER2, a receptor for a protein that promotes cell growth. But some 60% of people who were traditionally classified as HER2-negative actually have some HER2 receptors, a group now defined as HER2-low.

The Phase III DESTINY-Breast04 trial included 557 previously treated women with HER2-low metastatic breast cancer. They were randomly assigned to receive Enhertu or their physician's choice of chemotherapy. Antibody-drug conjugates like Enhertu use monoclonal antibodies to deliver toxic chemotherapy drugs directly to tumors.

Among women with hormone-receptor-positive, HER2-low tumors, the median overall survival time was 23.9 months in the Enhertu group versus 17.5 months in the chemotherapy group. Enhertu reduced the risk of disease progression by 49% and the risk of death by 36%. The presentation earned a standing ovation, and some experts say the results are "practice changing."

"Our study shows that trastuzumab deruxtecan may be a new and highly effective targeted therapy option available for this newly defined patient population," says investigator Shantu Modi, MD, of Memorial Sloan Kettering Cancer Center. The results could also be relevant for people with other types of HER2-low cancer.