# FDA Approves Enhertu for HER2-Positive Advanced Breast Cancer

60% of women treated with the antibody-drug conjugate experienced complete or partial tumor shrinkage.

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On December 20, the Food and Drug Administration (FDA) granted accelerated approval of Enhertu (fam-trastuzumab deruxtecan-nxki, or T-DXd) for the treatment of people with inoperable or metastatic HER2-positive breast cancer who have tried at least two prior anti-HER2 targeted therapies.

Researchers at the recent San Antonio Breast Cancer Symposium (SABCS) suggested that Enhertu could become a new standard of care for advanced HER2-positive breast cancer.

Around 20% of breast tumors overexpress the human epidermal growth factor receptor 2 (HER2)—a protein that promotes cancer cell growth—and can therefore be treated with HER2 inhibitors like Herceptin (trastuzumab). But treatment options are limited for people with nonresponsive or relapsed disease that has metastasized, or spread elsewhere in the body.

Enhertu, from Daiichi Sankyo and AstraZeneca, is an antibody-drug conjugate. The antibody targets HER2 and carries a topoisomerase inhibitor chemotherapy drug that kills cancer cells. It differs from Kadcyla (ado-trastuzumab emtansine, or T-DM1), another antibody-drug conjugate that carries a microtubule inhibitor payload.

Approval of Enhertu was based on the findings from the DESTINY-Breast01 trial (ClinialTrials.gov number NCT03248492), which were presented at SABCS and published in The New England Journal of Medicine.

This Phase II study enrolled more than 200 women with HER2-positive breast cancer that could not be surgically removed or that had metastasized. About half also had hormone receptor-positive tumors. The median age was 55. Most (92%) had visceral metastasis affecting the internal organs, 29% had bone metastases and 13% had brain metastases.

Participants had extensive treatment experience, including two or more prior anti-HER2 therapies. Everyone had used Herceptin and Kadcyla, and two thirds had also tried Perjeta (pertuzumab).

Participants in this open-label study received Enhertu as monotherapy, administered by IV infusion every three weeks until they experienced disease progression or unacceptable side effects.

Among the 184 participants treated with the best dose, the overall response rate—meaning complete or partial tumor shrinkage—was 60.9%, including 6.0% with complete remission. The median duration of response was 14.8 months. An additional 36.4% had stable disease.

Based on this interim analysis, the estimated median progression-free survival, or the time to disease progression or death, was 16.4 months. It is too soon to determine the median overall survival.

“Both of these measures of efficacy are substantially higher than that seen in any other study of patients with pretreated HER2-positive metastatic breast cancer,” senior study author Ian Krop, MD, PhD, of Dana-Farber Cancer Institute, said in a conference press release.

Enhertu is generally safe but side effects are common. The most frequently reported adverse events in the DESTINY trial were nausea, vomiting, fatigue, hair loss, diarrhea constipation, decreased appetite and cough. Enhertu can cause depletion of red blood cells (anemia), white blood cells (neutropenia) and platelets (thrombocytopenia), which can lead to fatigue, infections and easy bleeding.

Potential serious adverse events include lung disease (affecting 13.6% of DESTINY-Breast01 participants) and left ventricular dysfunction, a decrease in the heart’s ability to pump blood. People taking Enhertu should be monitored for potential signs of interstitial lung disease or pneumonitis and managed with dose modification and steroid treatment. Enhertu can cause fetal harm if used during pregnancy.

Speaking at a SABCS press briefing, Krop said these findings lend support for Enhertu as a new standard of care for people with advanced HER2-positive breast cancer. Carlos Arteaga, MD, of the Harold C. Simmons Comprehensive Cancer Center at the University of Texas Southwestern Medical Center, suggested that Enhertu might work even better if started at earlier stages of disease.

Enhertu received an FDA breakthrough therapy designation and fast track status; it was approved three months ahead of its goal date, according to an FDA news release. The FDA may grant accelerated approval based on overall response rates for drugs that address an unmet medical need. However, trials are expected to continue to confirm clinical benefits such as improved survival, and approval may be withdrawn if they fail to do so.

Phase III clinical trials of Enhertu for people with inoperable or metastatic breast cancer are currently underway (ClincialTrials.gov numbers NCT03523585, NCT03529110 and NCT03734029). Other studies are evaluating Enhertu for additional cancers including stomach, colon and non-small-cell lung cancer. It is also being studied in combination with checkpoint inhibitor immunotherapy.

Click here for full prescribing information for Enhertu.

Click here to read the DESTINY-Breast01 study abstract.

Click here to learn more about breast cancer.

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