Enhertu Effective Against Breast Cancer Brain Metastasis

Antibody-drug conjugate trastuzumab deruxtecan was found effective against brain metastases in patients with HER2-positive breast cancer.

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A drug that delivers chemotherapy directly to tumors has shown impressive activity against some of the hardest-to-reach cancer cells: those that have spread to the brain in patients with advanced HER2-positive breast cancer. The findings, from an international clinical trial led by Dana-Farber Cancer Institute researchers, reinforce earlier findings of the benefits of the drug – trastuzumab deruxtecan (T-DXd), an antibody-drug conjugate – in these patients, trial leaders say.

The results of the trial, dubbed the DESTINY-Breast12 study, were presented today at the European Society of Medical Oncology (ESMO) Congress 2024 in Barcelona, Spain, and published simultaneously in a paper in the journal Nature Medicine.

The findings point to T-DXd as a valuable new treatment option for patients with a particularly challenging form of cancer, researchers say.

“As many as half of patients with HER2-positive breast cancer develop brain metastases, which often has a poorer prognosis than breast cancer that hasn’t spread to the brain,” says Nancy Lin, MD, leader of the trial and senior author of the study in Nature Medicine. Lin is the associate chief of the Division of Breast Oncology, Dana-Farber, Susan F. Smith Center for Women’s Cancers, and the director of the Metastatic Breast Cancer Program.

Localized therapies such as surgery, radiosurgery, and radiation therapy to the brain, are used to treat brain metastases, but the disease usually progresses in the central nervous system – the brain and spinal cord – within six to 12 months of treatment.

Trastuzumab deruxtecan consists of the drug deruxtecan – a chemotherapy agent – linked to an antibody that targets the HER2 protein on breast cancer cells. Trastuzumab itself is a mainstay treatment of HER2-positive breast cancer that has spread to other parts of the body, including the brain. But as with treatments directed specifically at the brain, patients receiving trastuzumab usually have their disease progress, often in the central nervous system.

“Additional systemic therapies for patients with brain metastases are urgently needed,” Lin

remarks.

The DESTINY-Breast12 trial involved 504 patients with HER-2 positive breast cancer treated at 78 cancer centers in Western Europe, Japan, Australia, and the U.S. Two hundred sixty-three participants had active or stable brain metastases and 241 had no brain metastases. All had received at least one therapy before enrolling in the trial.

After a median follow-up of 15.4 months, progression-free survival of participants with brain metastases – the length of time patients lived with the cancer before it worsened – was a median of 17.3 months, investigators found. 12- month progression-free survival was 61.6%. 71% of participants had an intracranial objective response – a measurable decrease of their cancer in the central nervous system. As expected, there was also a high rate of response in tumors outside of the central nervous system in patients with or without brain metastases. Ninety percent of patients in both groups were alive a year after beginning T-DXd treatment.

The side effects associated with T-DXd were consistent with those reported in previous studies and included nausea, constipation, neutropenia (low levels of a type of white blood cells), fatigue, and anemia. Interstitial lung disease, a known risk of T-DXd, was observed at similar rates to prior studies, and vigilance to this potentially fatal side effect remains critical.

“Our data show that T-DXd has substantial and durable activity within the brain in patients with HER2-positive breast cancer that has metastasized there,” Lin says. “These results support the use of the drug going forward in this patient population.”

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