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T-DM1 improved overall survival for heavily pretreated patients with HER2-pos breast cancer

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Among patients with HER2-positive, metastatic breast cancer that had progressed despite treatment with two or more forms of HER2-targeted therapy (trastuzumab [Herceptin] and lapatinib [Tykerb]), median overall survival was increased for those treated with trastuzumab emtansine (T-DM1 [Kadcyla]) compared with those who received treatment of physician's choice, according to results from the phase III TH3RESA clinical trial presented at the 2015 San Antonio Breast Cancer Symposium, held Dec. 8-12.

The HER2-targeted antibody-drug conjugate T-DM1 was approved by the U.S. Food and Drug Administration in February 2013 for treating patients with HER2-positive, metastatic breast cancer that had progressed after treatment with trastuzumab and a taxane.

"The National Comprehensive Cancer Network guidelines, which are widely used as the standard for cancer care, were recently changed to recommend using T-DM1 as a preferred treatment for patients with trastuzumab-exposed HER2-positive, metastatic breast cancer, meaning that it is generally used after a patient's metastatic disease has progressed following treatment with a combination of a taxane-based chemotherapy and trastuzumab, with or without pertuzumab (Perjeta)," said Hans Wildiers, MD, PhD, a professor of medical oncology at KU Leuven in Belgium. "However, there are a lot of patients who received second- or later-line treatment before this recommendation was put in place and

TH3RESA was designed to establish whether T-DM1 could benefit patients in later lines as well.

"Previously published results from TH3RESA showed that T-DM1 almost doubled progression-free survival," continued Wildiers. "Here we show that T-DM1 actually increased overall survival for heavily pretreated patients with HER2-positive, metastatic breast cancer. This is very important because several breast cancer therapies that increase progression-free survival do not in fact increase overall survival, and these patients urgently need new treatment options."

All 602 patients with HER2-positive, metastatic breast cancer enrolled in TH3RESA had been previously treated with a chemotherapy regimen that included a taxane and, after a diagnosis of metastatic disease, two or more regimens that included HER2-targeted therapeutics, including trastuzumab and lapatinib. Patients were randomly assigned 3.6 milligrams of T-DM1 per kilogram of body weight every three weeks or treatment of physician's choice.

After a median follow-up of 30.5 months, the median overall survival was significantly longer among the 404 patients assigned T-DM1 compared with the 198 patients assigned treatment of physician's choice: 22.7 months compared with 15.8 months. The overall survival benefit was seen regardless of patient age, hormone-receptor status, visceral involvement, and number of prior treatment regimens.

The incidence of grade 3 or higher adverse events was higher among patients assigned treatment of physician's choice compared with those assigned T-DM1: 47.3 percent compared with 40.0 percent.

"Not only did the population of patients assigned T-DM1 have increased median overall survival, they also had reduced incidence of grade 3 and higher adverse events," said Wildiers. "The fact that these patients lived

longer with less toxicity suggests that T-DM1 is a good treatment option even for patients who have received two or more HER2-targeted treatment regimens."

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