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Nursing Perspectives on Trastuzumab Emtansine for the Treatment of Metastatic Breast Cancer

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Increased understanding of the molecular composition of breast cancer tumors has led to the development of targeted anticancer agents. Novel therapies directed against human epidermal growth factor receptor 2 (HER2) in breast cancer have been developed. One such agent, trastuzumab emtansine (T-DM1), is an antibody drug conjugate that has been shown to be effective in the treatment of women with HER2-positive breast cancer. Phase I and II studies have determined a maximum tolerated dose, and several phase Ib/II, II, and III studies have shown improved tolerability and efficacy compared with the combination of trastuzumab and chemotherapy. The most concerning grade 3 or higher adverse events associated with T-DM1 include thrombocytopenia and transaminitis. To ensure that these adverse events do not delay or interrupt treatment, oncology nurses need to familiarize themselves with these risks and their management. This article reviews the clinical development of T-DM1 and its usage, with a focus on the nurse's role in preventing and managing adverse events associated with T-DM1 therapy.

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Breast cancer is the most common cancer among women in the United States, with an estimated 234,580 new cases diagnosed and 40,030 breast cancer-related deaths occurring in 2013 (Siegel, Naishadham, & Jemal, 2013). Breast cancer comprises multiple distinct subtypes, including estrogen receptor (ER) and progesterone receptor (PR) positive; human epidermal growth factor receptor 2 (HER2) positive; or ER, PR, and HER2 negative (i.e., triple negative). Treatment is individualized based on the biologic-driven mechanism: hormonal (ER and/or PR positive) responding best to antihormonal therapy, HER2 positive responding best to combination therapy that includes anti-HER2 therapy, and triple negative responding best to chemotherapy. HER2 is overexpressed in 25%–30% of breast cancer cases (Carey et al., 2006). Women with breast cancers that overexpress HER2 have a worse prognosis with significantly lower disease-free and overall survival (Carey et al., 2006; Ravdin & Chamness, 1995). To date, the treatment for patients who have breast cancer with overexpressed HER2 involves the use of anti-HER therapy: trastuzumab, lapatinib, and pertuzumab. Trastuzumab was approved in 2006 by the

U.S. Food and Drug Administration (FDA) as the first targeted anti-HER2 agent. Trastuzumab showed improvement in overall survival in metastatic breast cancer in about one-third of patients with HER2-positive breast cancer (Vogel et al., 2002). However, primary or acquired trastuzumab resistance usually occurs and leads to tumor progression in the majority of the patients within a year of treatment initiation (Esteve et al., 2002). The second FDA-approved (in 2007) targeted anti-HER2 *new* agent, lapatinib, in combination with capecitabine, has been associated with improvement in progression-free survival in the metastatic setting and appears to lengthen overall survival in patients with metastatic HER2-positive breast cancer resistant to trastuzumab (Cameron et al., 2008). When combined with letrozole, lapatinib provides an improvement in progression-free survival for women with hormone receptor-positive, HER2-positive metastatic breast cancer (Johnston et al., 2009). The data also suggest that the combination of lapatinib and trastuzumab in patients with heavily pretreated HER2-positive metastatic breast cancer improves median overall survival by 4.5 months (Blackwell, Burstein, et al., 2012). Pertuzumab, approved by the FDA in 2012, targets the HER2 receptor, in combination