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Commentary

on *Trastuzumab deruxtecan in the treatment of adult patients with HER-positive breast cancer*

Breast cancer is a diverse malignancy in terms of molecular characteristics. Approximately 15% of breast cancers are characterized by expression of human epidermal receptor type 2 (HER2) or amplification of the *HER2* gene [1]. HER2-positive cancers have a more aggressive course than HER2-negative cancers; however, the introduction of anti-HER2 drugs (trastuzumab, pertuzumab, lapatinib, tucatinib, and neratinib) significantly improved prognosis in this population. Further progress in the treatment of patients with HER2-positive breast cancer is associated with the introduction of conjugates composed of trastuzumab and cytotoxic drugs, for example, the combination of trastuzumab and emtansine (T-DM1) and trastuzumab and deruxtecan (T-DXd).

The current classification of HER2-positive or HER2-negative breast cancers has changed due to identification of cancers with low HER2 expression (HER2-low category), e.g. with immunohistochemical (IHC) score of 1+ or 2+ without in situ hybridization (ISH) amplification. HER2-low breast cancers may include some triple-negative and luminal cancers [2].

In 2022, the results of the phase III DESTINY-Breast04 study were published, which assessed the value of T-DXd compared to chemotherapy of the investigator's choice (paclitaxel, nab-paclitaxel, gemcitabine, capecitabine or eribulin) in breast cancer patients with low HER2 expression and with or without expression of hormone receptors (HRs). Qualified patients had previously failed chemotherapy and hormone therapy. A significant prolongation of progression-free survival and overall survival was observed, mainly driven by patients with hormone-dependent cancer (10 *vs*. 5 months and 24 *vs*. 17.5 months, respectively). Clinical benefits in patients with HR-negative breast cancer were also significant, but numerically slightly smaller than in patients with hormone-dependent cancer (progression-free survival and overall survival were 8.5 and 3 months and 18 *vs*. 8 months, respectively). Treatment with T-DXd was generally slightly better tolerated, but interstitial lung disease and reduced left ventricular ejection fraction were more common in patients receiving conjugate [3]. Patients receiving T-DXd in the future should be carefully monitored for the risk of both of these complications.

The results of the DESTINY-Breast04 study justified the registration of T-DXd in the treatment of patients with advanced breast cancer with low HER2 expression after previous chemotherapy. The drug is not currently reimbursed in Poland for this indication although the results of this pivotal study provide a convincing justification for the use of T-DXd in another indication in BC patients, apart from those discussed in this publication.

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Conflict of interest

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Supplementary material

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