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Current Challenges in Treating Patients with HER2 Positive Breast Cancer: Leave No Options Behind

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Human epidermal growth factor receptor-2(HER2)-positive breast cancer accounts for 15%-20% of all breast cancers and this cancer subtype was historically associated with poor outcomes. Treatment of HER2-positive early breast cancer has evolved rapidly over the past several years. The addition of HER2-targeting therapies to standard treatment has dramatically improved the prognosis for patients with HER2-positive breast cancer in both the early and metastatic settings.

The introduction of trastuzumab in early-stage, HER2-positive breast cancer was a landmark in the treatment of this disease, improving not only disease-free survival (DFS) but also overall survival (OS) and changing its natural history. A better understanding of tumor biology has led to the development of optimized anti-HER2 drugs and add-on strategies to further improve survival outcomes. In the neoadjuvant setting, dual HER2 blockade with trastuzumab and pertuzumab plus chemotherapy has increased the rate of pathologic complete response, a surrogate marker of improved long-term outcome. Additionally, the use of the antibody-drug conjugate trastuzumab-emtansine has led to a significant improvement in invasive disease-free survival for patients with residual disease following neoadjuvant therapy and delivered the importance of using preoperative therapy to adapt adjuvant treatment.

The combination of trastuzumab, pertuzumab and a taxane (THP) remains the preferred first-line therapy in most scenarios. Results of trials recently presented at the European Society for Medical Oncology (ESMO) Congress 2021 might have direct clinical impact in the second- and later-line settings. The randomized DESTINY-BREAST03 study compared trastuzumab deruxtecan (T-DXd) with trastuzumab emtansine (T-DM1) in patients previously treated with trastuzumab and a taxane. T-DXd significantly improved progression-free survival and showed a trend towards improved overall survival, establishing this agent as preferred second-line therapy. Treatment with T-DM1, or the combination of tucatinib, trastuzumab and capecitabine, are considered reasonable options after second-line therapy. However, TDM-1 is still a good choice if some areas have poor accessibility for T-DXd.

Nevertheless more and more effective treatment options have been developed for HER2+ breast cancer. To stratify patient risks and optimize treatment selection, other biomarkers including intrinsic subtype, level of HER2, and tumor-infiltrating lymphocytes should be further evaluated.