Amplification and/or overexpression of HER2 is an aggressive subtype of invasive breast cancer that is associated with poor clinical outcomes. HER2+ can be found in 15-20% of patients. Advances in molecular biology and drug development have revolutionized the treatment landscape of HER2+ breast cancer. In early-stage disease, combinatorial and sequential use of different HER2-targeted treatments increased cure rates. Neoadjuvant Pertuzumab + Trastuzumab + Chemotherapy increased the pCR rate, especially in HER2+/HR- subtype. Adjuvant Pertuzumab + Trastuzumab + Chemotherapy also achieved a significant improvement on iDFS, particularly in node+ cohort. For those did not achieve pCR after neoadjuvant therapy, adjuvant T-DM1 is the recommended option with significant improvement on iDFS. However, patients with large tumor burden and/or lymph node involvement at baseline, and with non-pCR after neoadjuvant therapy, may possess a higher risk of recurrence. In addition, neither Trastuzumab, Pertuzumab, and T-DM1 have been founded to be effective in preventing CNS metastasis. Neratinib is an irreversible pan-HER (EGFR, HER2, and HER4) TKI that demonstrated promising efficacy in the extended adjuvant treatment of early-stage breast cancer. In the phase III ExteNET study, Neratinib significantly improved the iDFS rate, especially in the HER2+/HR+ population who was treated within 1 year after completion of previous adjuvant therapy. In the subgroup analysis of ExteNET study, patients with nodal status positive and non-pCR diseases may have a greater improvement on iDFS. In addition, Neratinib seems to reduce the incidence of CNS event. Several real-world studies are ongoing, which are exploring the effectiveness of Neratinib extended adjuvant therapy in the real-world treatment landscape of HER2+ early-stage breast cancer.