

Current Treatment Strategies for High-Risk Patients with HER2+ Early-Stage Breast Cancer: Can We Improve Clinical Outcomes?

Diana Lüftner

Director, Prof. Dr. med.

Immanuel Hospital Märkische Schweiz

Buckow, German

The addition of trastuzumab to adjuvant/neoadjuvant chemotherapy has significantly reduced the relapse rate of early HER2-positive breast cancer. However, a significant proportion of patients, in the range of 15 to 20% still relapse in spite of these therapies. The escalation approach is aimed at reducing the relapse rate of these patients by adding new drugs to the combination of chemotherapy and trastuzumab.

ESCALATION THERAPY

There are two different ways of escalating therapy in early HER2-positive breast cancer: the concurrent addition of new drugs and the extended, sequential adjuvant approach. An example of the first approach is the APHINITY trial, in which the addition of pertuzumab to trastuzumab and chemotherapy improved iDFS (invasive disease -free survival), mainly in the node-positive population.

Two examples of extended adjuvant therapy are the KATHERINE and EXTENET trials.

The KATHERINE trial was carried out in patients with her2-positive tumors with residual disease at surgery after neoadjuvant chemotherapy plus trastuzumab plus minus pertuzumab. Patients randomized postsurgically to T-DM1 has a significantly better iDFS than those randomized to standard trastuzumab.

The EXTENET trial enrolled patients with early HER2-positive tumors that had ended therapy with surgery, chemotherapy and one year of trastuzumab. Patients were randomized to one year of neratinib or placebo (in addition to endocrine therapy for those with hormone receptor (HR)-positive tumors). Neratinib significantly reduced iDFS, particularly in the population of patients with HR positive tumors who initiated neratinib up to one year after the end of trastuzumab. The main side effect of neratinib is diarrhea, that can be ameliorated with loperamide and a strategy of neratinib dose-escalation during the first weeks of therapy.

Neratinib, then constitutes a new, attractive option of therapy for patients with early HER2-positive tumors at risk of relapse with conventional therapy.