Antibody treatment in breast cancer patients based on HER2/neu and EGFR

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Breast cancer was the first solid tumour for which targeted treatments were available. Endocrine therapy—targeting the oestrogen receptor—was described more than 100 years ago and major advances in treatment of breast cancer have been made. Classification of molecular subtypes demonstrated the role of the estrogen receptor, the EGFR and HER2 oncogenic pathway. This lead to the development of the anti-HER2/neu antibody trastuzumab.

Several phase III, clinical trials have proven the efficacy of trastuzumab in patients with HER2-overexpressing cancers. In the HERA trial trastuzumab was given as part of primary therapy that included a chemotherapy regimen. Although the results of the comparison of 1 year versus 2 years of trastuzumab have not been released yet, there are available data for 3,387 patients (1,694 in the 1-year trastuzumab arm and 1,693 in the observation arm). Patients who were treated with 1 year of trastuzumab had a 46% lower risk of a first event (hazard ratio [HR], 0.54, corresponding to an absolute DFS benefit of 8.4% at 2 years. The updated results at 23.5 months’ follow-up showed an HR for the risk of death with trastuzumab compared with observation of 0.66 (absolute OS benefit 2.7%). The HR for the risk of an event with trastuzumab was 0.64 (DFS benefit 6.3%). The benefit of trastuzumab was confirmed in several studies, such as NSABP-B-31 and Intergroup NCCTG-N9831 trials. Lapatinib is a small molecule tyrosine kinase inhibitor that is capable of dual-receptor inhibition of EGFR and HER2. In the ALTTO trial lapatinib is being investigated in the adjuvant setting. In a phase III trial, lapatinib plus capecitabine was superior to capecitabine alone. Pertuzumab, the latest development in this field, was effective in combination with trastuzumab/docetaxel for HER2-positive metastatic breast cancer in a randomised, double-blind, placebo-controlled, phase 3 study (CLEOPATRA).