Dokumenttyp: journal article

Autor(en) des Beitrags: Kantelhardt, EJ; Vetter, M; Schmidt, M; Veyret, C; Augustin, D; Hanf, V; Meisner, C; Paepke, D; Schmitt, M; Sweep, F; von Minckwitz, G; Martin, PM; Jaenicke, F; Thomssen, C; Harbeck, N

Titel des Beitrags: Prospective evaluation of prognostic factors uPA/PAI-1 in node-negative breast cancer: phase III NNBC3-Europe trial (AGO, GBG, EORTC-PBG) comparing 6×FEC versus 3×FEC/3×Docetaxel.

Abstract: Today, more than 70% of patients with primary node-negative breast cancer are cured by local therapy alone. Many patients receive overtreatment by adjuvant chemotherapy due to inadequate risk assessment. So far, few clinical trials have prospectively evaluated tumor biology based prognostic factors. Risk assessment by a biological algorithm including invasion factors urokinase-type plasminogen activator (uPA) and its inhibitor plasminogen activator inhibitor type 1 (PAI-1) will assess up to 35-55% of node-negative patients as low-risk and thus avoid chemotherapy. In contrast, a clinical-pathological algorithm will only classify 20-40% of patients as low-risk. High-risk node-negative patients should receive chemotherapy. Anthracycline-based regimens are accepted as a standard, the additional benefit of taxanes remains an open question. The international NNBC3 ("Node Negative Breast Cancer 3-Europe") trial compares biological risk assessment (UP) using invasion factors uPA/PAI-1 with a clinical-pathological algorithm (CP). In this trial, the type of risk assessment (CP or UP) was chosen upfront by each center for its patients. Fresh frozen tissue was obtained to
determine uPA/PAI-1 using an enzyme-linked immunosorbent assay (ELISA). Patients assessed as high-risk were stratified by human epidermal growth factor receptor 2 (HER2) status and then randomised to receive anthracycline-containing chemotherapy 5-Fluorouracil (F)/Epirubicin (E)/Cyclophosphamide (C) or an anthracycline-taxane sequence (FE(100)C*6 versus FE(100)C*3 followed by Docetaxel(100)*3). In this trial, 4,149 node-negative patients with operable breast cancer from 153 centers in Germany and France were included since 2002. Measurement of uPA/PAI-1 by ELISA was performed with standardised central quality assurance for 2,497 patients (60%) from 56 "UP"-centers. The NNBC 3-Europe trial showed that inclusion of patients into a clinical phase III trial is feasible based on biological testing of fresh frozen tumor material. In addition, 2,661 patients were classified as high-risk and thus received chemotherapy. As adjuvant chemotherapy, 1,334 high-risk patients received FE(100)C-Docetaxel(100), and 1,327 received French FE(100)C. No unexpected toxicities were observed. Chemotherapy efficacy and comparison of UP with CP will be evaluated after longer follow-up. clinical Trials.gov NCT01222052.