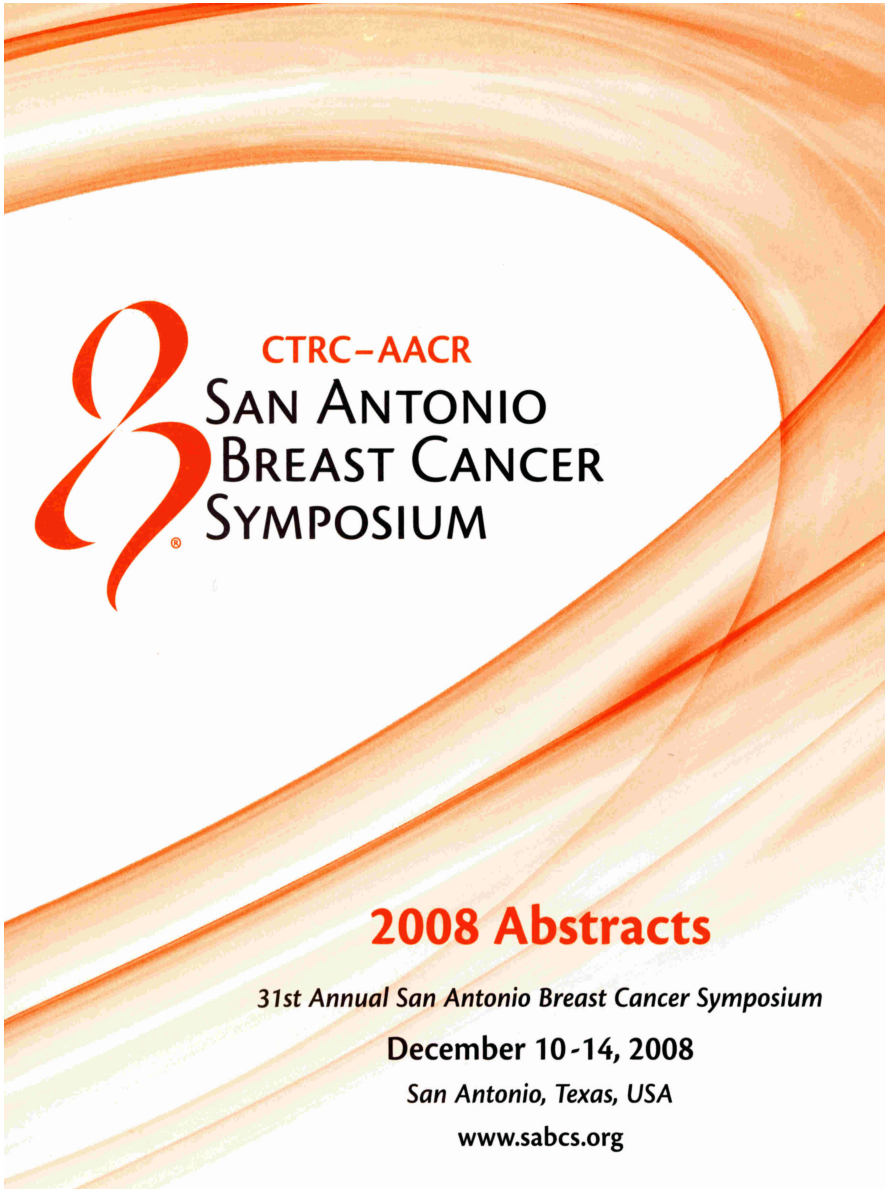

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Metastatic potential of Her2/neu positive and Her2/neu negative circulating epithelial tumor cells (CETC) released during primary systemic chemotherapy.

Pachmann K, Camara O, Gajda M, Rabenstein C, Pachmann U, Runnebaum IB. Friedrich Schiller University Jena, Jena, Germany; Transfusion Center, Bayreuth, Germany

Background: Most tumor patients do not die from the primary tumor but from metastases in vital organs. To form metastases, cells must exit from the original tumor and reach these organs mainly via blood before they can settle and grow. Peripheral blood can be regarded as a transport system for CETC. Here we report on the influence of trastuzumab on the number of CETC and the impact on metastasis formation.

Material and Methods: Tumor cells were quantified with an automated microscope (Laser Scanning Cytometer®, Icis or ScanR) from anticoagulated blood drawn before each new therapy cycle from patients treated with primary systemic chemotherapy and before and after surgery and subsequent maintenance therapy. After red blood cell lysis leucocytes were stained with PE-anti-CD45 and tumor cells with FITC-anti-EpCAM and changes registered as % increase or decrease. The response of CETC to therapy was correlated to outcome.

Results: All breast cancer patients scheduled for primary systemic treatment had CETC before therapy. The number correlated with tumor size. The variable initial decrease in cell numbers highly correlated with the final tumor size reduction in her2/neu negative patients predicting for relapse free survival. All patients responded to the subsequent taxane therapy with an increase in CETC. In her2/neu positive patients who received combined taxane/trastuzumab there was only a modest increase in CETCs whereas patients with her2/neu positive disease who received taxane only showed a steep increase in CETC. 4 her2/neu positive patients who did never receive trastuzumab all had increasing CETC numbers during the postoperative observation time and all have suffered relapse. 6/6 patients who received trastuzumab only after surgery all had decreasing CETC numbers and all are in sustained complete remission after up to 4 years. 6/15 patients showed no change or an increase in CETC in spite of trastuzumab treatment and of these 4 have suffered relapse. Most relapses occurred 1-2 years after stopping trastuzumab.

Discussion: Monitoring CETC will not only provide the earliest and most reliable indicator of successful neoadjuvant treatment and spare patients unnecessary treatment. In patients with the highly aggressive her2/neu positive tumors such cells may have an increased potential to settle and re-grow. This warrants further therapy studies to control what patients may benefit from additional or modified therapy already before metastases appear.