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5030

Behaviour and metastatic potential of her2/neu positive and her2/neu negative circulating epithelial tumor cells (CETC) during adjuvant systemic therapy in breast cancer.

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Background: Most tumor patients do not die from the primary tumor but from metastases in vital organs. Here we report on the influence of adjuvant chemotherapy and trastuzumab on the remnant CETC patients with her2/positive tumors after surgery 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 systemic chemotherapy after surgery and subsequent maintenance therapy with trastuzumab. After red blood cell lysis leucocytes were stained with PE-anti-CD45 and tumor cells with FITC-anti-EpCAM. FISH analysis was performed for determination of the proportion of her2/neu positive cells and changes registered as % increase or decrease. The response to therapy was correlated to outcome.

Results: Almost all her2/neu positive breast cancer patients scheduled for systemic treatment had CETC before therapy. A decrease in cell numbers highly correlated with relapse free survival. Her2/neu positive patients responding to therapy with an increase in CETC were at increased risk to develop further increasing cell numbers also during subsequent trastuzumab treatment. Her2/neu positive patients who did never receive trastuzumab all had increasing CETC numbers during the postoperative observation time and all have suffered relapse. Patients who received trastuzumab only after adjuvant treatment all had decreasing CETC numbers and all are in sustained complete remission after up to 4 years. Of the patients who received trastuzumab together with adjuvant treatment those who showed no change or an increase in CETC in spite of trastuzumab had increasing proportions of FISH high amplified cells and a higher risk of relapse than patients with decreasing CETC during trastuzumab.

Discussion: Monitoring CETC will not only provide the earliest and most reliable indicator of successful adjuvant treatment and spare patients unnecessary treatment but also patients with the highly aggressive her2/neu positive tumors can be discerned into such with high and low risk of relapse even during trastuzumab therapy. This warrants further therapy studies to control what patients may benefit from addition of e.g. small molecules already during therapy before development of metastases.