

patients that profit from therapy according to guidelines. The leading guideline violation was noted for radiation therapy.

FV-Onko 03.17

The impact of trastuzumab on the course of disease in HER2/neu positive breast cancer

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Objective: In 20–25% of invasive breast cancers the ErbB2 growth factor receptor is overexpressed mainly due to an amplification of the HER2/neu gene. Trastuzumab has significantly improved the outcome of these patients; however, not all patients with this amplification do benefit from treatment with trastuzumab. The question arises, why the benefit of trastuzumab is limited and obviously only lasts for a restricted time. Here we report on the influence of trastuzumab on the circulating epithelial tumor cells (CETC) in HER2/neu positive breast cancer patients and correlation to outcome.

Materials and methods: Tumor cells were quantified with an automated microscope from anticoagulated blood drawn before each new administration of trastuzumab from 78 patients treated without or with trastuzumab. After red blood cells lysis leucocytes were stained with PE-anti-CD45 and tumor cells with FITC-anti-EpCAM and changes registered as fold increase or decrease. The same cells were also analysed for their amplification of the HER2/neu gene by FISH analysis. The response of CETC to therapy was correlated to outcome.

Results: Almost all breast cancer patients had CETC before therapy. During trastuzumab therapy there was either a decrease (54% without trastuzumab vs. 69% with trastuzumab) or an increase/highly variable behavior in cell numbers. This behavior of the CETC highly correlated with relapse free survival (hazard ratio 5.5). An increase in CETC was highly significantly followed by relapse and accompanied by an increase in the fraction of cells with highly amplified HER2/neu.

Conclusions: Monitoring CETC will not only provide the earliest and most reliable indicator of successful trastuzumab treatment. It also, for the first time, allows insight into the development of resistance to trastuzumab which is highly predictive for relapse. This warrants further therapy studies to control what patients may benefit from additional or modified therapies already before metastases appear.