UKE Paper of the Month February 2014

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Prognostic relevance of circulating tumor cells in blood and disseminated tumor cells in bone marrow of patients with squamous cell carcinoma of the oral cavity

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ABSTRACT: *PURPOSE:* Current staging methods for squamous cell carcinomas of the oral cavity (OSCC) need to be improved to predict the risk of individual patients. Since hematogenous tumor cell dissemination is a key event in tumor progression we assessed the prognostic significance of disseminated tumor cells (DTCs) in bone marrow (BM) and circulating tumor cells (CTCs) in peripheral blood (PB) from OSCC patients. *EXPERIMENTAL DESIGN:* From 110 patients with OSCC, tumors were surgically resected (R0) without neoadjuvant therapy. The CellSearch#-system was used to enumerate CTCs. BM was aspirated from the iliac crest, and mononuclear cells (MNCs) were enriched by Ficoll density gradient centrifugation. To detect DTCs, MNCs were immunostained with the pan-keratin antibody A45-B/B3. Results were correlated with clinicopathological parameters and clinical outcome such as recurrence and death during follow up time (mean 916 days). *RESULTS:* Ten/80 patients (12.5%) harbored CTCs in PB whereas in 18/90 patients (20.0%) DTCs in BM could be detected. Surprisingly, in only two patients (1.8%) CTCs and DTCs were detected simultaneously. Significant correlations could be found regarding CTCs and tumor size (p=0.04), nodal status and DTCs (p=0.02), and distant metastasis with CTCs (p=0.004) and DTCs (p=0.005). Univariate and multivariate analyses revealed that CTCs and DTCs were significant and independent predictors of recurrence-free survival (p<0.001). *CONCLUSIONS:* Both DTCs and CTCs are independent prognostic markers in OSCC patients, predicting relapse with higher sensitivity at various disease stages than routine staging procedures. Bone marrow might be an interesting target organ for future therapeutic interventions.

STATEMENT: *Current staging methods for oral squamous cell carcinomas (OSCC) need to be improved to detect early metastatic spread and clarify the individual need of therapeutic interventions. The current study indicates that CTCs/DTCs detected in OSCC-patients serve as prognostic markers, predicting relapse at various disease stages supplementary to routine staging procedures. Interestingly, there was little overlap between tumor cell detection in the peripheral blood and bone marrow, indicating that both compartments offer complementary diagnostic information on tumor cell spread in OSCC-patients. The current findings point to the potential future utility of drugs targeting disseminated tumor cells in bone marrow and circulating tumor cells in blood of OSCC-patients.*

BACKGROUND: This work was performed at the Department of Oral and Maxillofacial Surgery in strong collaboration with the Institute of Tumor Biology, UKE by Alexander Gröbe, Marco Blessmann, Sabine Riethdorf and Co-workers. This working group has its major interest in the improvement and expansion of diagnostic and therapeutic possibilities on single cell level in patients suffering from squamous cell carcinomas of the oral cavity. The present study was supported by the "Hamburger Stiftung zur Förderung der Krebsbekämpfung" No. 188 to A.G. and S.R.