Detection of circulating tumor cells (CTCs) in patients with metastatic uveal melanoma - a pilot study

Shari Schneider[1]
Isabel Heidrich[2], Julian Kött[3], Stefan W. Schneider[4], Klaus Pantel[5] and Christoffer Gebhardt[6]
[1] University Medical Center Hamburg-Eppendorf (UKE); Department of Dermatology and Venereology, University Skin Cancer Center Hamburg; Fleur Hiege-Centrum for Skin Cancer Research; Institute of Tumor Biology
[2] University Medical Center Hamburg-Eppendorf (UKE); Department of Dermatology und Venereology
[3] University Medical Center Hamburg-Eppendorf (UKE); Department of Dermatology und Venereology; Fleur Hiege-Centrum for Skin Cancer Research
[4] University Medical Center Hamburg-Eppendorf (UKE); Department of Dermatology and Venereology; Fleur Hiege-Centrum for Skin Cancer Research
[5] Department of Tumor Biology, Center of Experimental Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany;
[6] University Medical Center Hamburg-Eppendorf (UKE); Department of Dermatology and Venereology, University Skin Cancer Center Hamburg; Fleur Hiege-Centrum for Skin Cancer Research

Background & objectives

Uveal melanoma (UM) is a rare disease (incidence: 4-5 cases per 1,000,000 inhabitants per year in Germany) but the most common primary intraocular malignant tumor in adults. Although satisfactory local tumor control and ocular preservation in the majority of patients with various radiotherapeutic and surgical techniques could be achieved, up to almost 50% of patients develop metastatic disease (mUM) after 5-15 years with a very poor prognosis. Because the mUM metastasizes primarily via the blood and not lymphatic vessels, the analysis of circulating tumor products such as circulating tumor cells (CTCs) captured from the bloodstream could represent an alternative, minimally invasive method to obtain biologically and clinically relevant information on metastatic progression of UM.

It is well known from many other tumors (breast cancer, prostate cancer) that detection of CTCs is associated with reduced overall survival. There are currently no reliable prognostic and predictive biomarkers for mUM. Liquid biopsy represents a promising and minimally invasive method that can use circulating tumor products to obtain real-time information about tumor evolution in individual patients. Therefore, in this work, a case series of 8 mUM patients under immunotherapy (bispecific fusion protein tebentafusp) should be summarized, in which the detection of CTCs was determined using CellSearch™ technology. This is a first pilot study on an under-investigated patient group with potential for further projects.

Methods

Presentation of a case series of 8 mUM patients in whom an immunomagnetic isolation using melanoma cell adhesion molecule (MCAM) has been utilized in the isolation of CTCs using the CellSearch™ system. The CTC occurrence under immunotherapy was examined and correlated with clinical-pathological parameters.

Results

CTCs were detected in 3/8 patients (range 2-5 CTCs per 7.5 mL blood). CTC-positive patients had non-resectable metastases in 2-5 organs and multiple metastases in at least one organ. We found that the presence of CTCs was not associated with tumor size or metastatic mass. The 5 CTC-negative patients also showed a high metastasis burden (2-4 organs), with all patients showing hepatic metastasis. Nevertheless, CTC-negative patients showed a longer overall survival compared to CTC-positive patients.

Conclusion

Despite the pilot character of this investigation, mUM patients who showed no evidence of CTCs in their blood tended to progress slower under tebentafusp than CTC-positive patients, suggesting a putative predictive value of CTC detection. This promising preliminary finding deserves therefore a future validation on a larger cohort of patients, which might be carried out at the European level by the European Liquid Biopsy Society (ELBS, www.elbs.eu). Further molecular characterization of single CTCs might provide novel insights into the biology of UM wand might reveal potential targets for therapeutic interventions.