**BACKGROUND**

Cancer of unknown primary (CUP), a primary metastatic malignancy, constitutes a major diagnostic and therapeutic challenge. Standard-of-care empirical chemotherapy typically leads to a median overall survival (OS) of only 7-10 months. The need to better understand CUP pathophysiology in order to improve the management options is therefore urgent. Over the past years, the detection and characterization of circulating tumor cells (CTCs) in the blood of cancer patients have emerged as a promising approach to cancer monitoring and prognostication.

**METHODS**

Patients with a confirmed diagnosis of CUP who presented at the CUP clinic of the University of Heidelberg, Heidelberg, Germany; and the Department of Internal Medicine V, University of Heidelberg, Heidelberg, Germany; and the National Center for Tumor Diseases (NCT), University of Heidelberg, Heidelberg, Germany; and the University Medical Center Hamburg-Eppendorf, Hamburg, Germany; and the Division of Biostatistics, German Cancer Research Center (DKFZ), Heidelberg, Germany; and the Institute of Pathology, University of Heidelberg, Heidelberg, Germany; and the Center for Personalized Medicine (ZPM), University of Heidelberg, Heidelberg, Germany; and the University of Niš, Niš, Serbia; and the Medical University of Vienna, Vienna, Austria; and the Institute of Hematology and Oncology, University of Zagreb, Zagreb, Croatia; and the Medical University of Lübeck, Lübeck, Germany; and the University of Wroclaw, Wroclaw, Poland; and the Royal Care oncology center, Wroclaw, Poland; and the University of Ghent, Ghent, Belgium; and the Medical University of Vienna, Vienna, Austria; and the University of Lucerne, Lucerne, Switzerland; and the Dr. von Haunersche childrens hospital, Munich, Germany; and the University of Helsinki, Helsinki, Finland; and the University of Munich, Munich, Germany; and the University of Wroclaw, Wroclaw, Poland; and the University of Niš, Niš, Serbia.

**RESULTS**

110 patients provided 180 blood samples including 110 baseline and 70 follow-up samples (Table 1). Forty-four of 110 baseline samples, defined as the first blood samples taken for CTC analysis of patients included into this study, were collected at first diagnosis of CUP, 23/110 at disease progression, 26/110 during treatment and 17 samples after completion of a therapy line.

**FREQUENCY OF CTC DETECTION ACROSS PROGNOSTIC SUBGROUPS**

Favorable subtypes were associated with a significantly lower rate of CTC positivity (7/148 patients, 14.6%, P=0.007) and lower CTC counts in CTC(-) patients (median 1, range 1-17 CTCs/7.5 ml, P=0.034) compared to unfavorable CUP (22/62 patients, 35.5%, median 6, range 1-585 CTCs/7.5 ml).

**CONCLUSIONS**

The presenting author has no conflicts of interest to declare.

ABBREVIATIONS: OS overall survival; PFS progression-free survival; CUP cancer of unknown primary; CTC circulating tumor cells; CTC(-) CTC negative; CTC(+) CTC positive; CTC(-) CTC low; CTC(+) CTC high; cCTC CTC favored.

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