Evaluation of Circulating Tumoral Microemboli (CTM) as a Prognostic Factor in Metastatic Colorectal Cancer Patients

Corassa M (A.C.Camargo Cancer Center, Brazil), Fanelli MFF (A.C.Camargo Cancer Center, Brazil),, Braun AC (A.C.Camargo Cancer Center, Brazil), Abdalla E (A.C.Camargo Cancer Center, Brazil), Alves V (A.C.Camargo Cancer Center, Brazil), Silva VS (A.C.Camargo Cancer Center, Brazil), Chinen LTD (A.C.Camargo Cancer Center, Brazil).

BACKGROUND: Much is currently known regarding the role of circulating tumor cells (CTC) in diverse types of cancer, including colorectal cancer. CTC in metastatic colorectal patients determines worst prognosis and outcomes, with diminished survival in diverse previously published papers. Little is studied, however, regarding Circulating Tumoral Microemboli (CTM), that are defined as clusters of three or more clustered cancer cells detected in peripheral blood. Due to the lack of evidence related to CTM in metastatic colorectal adenocarcinoma, we attempted to characterize the presence of CTM in metastatic colorectal cancer (mCRC) patients.

OBJECTIVE: To determine the influence of CTM in progression free survival (PFS), overall survival (OS), and characterization regarding markers of invasion in mCRC patients in order to define CTM as a prognostic factor for mCRC. The characterization of demographic variables was also evaluated.

METHODS: Retrospective evaluation of 54 mCRC (all adenocarcinomas) patients with CTC enrolled previously for research in a single institution. CTC and CTM were detected by ISET (Isolation by Size of Epithelial Tumor Cells, Rarecells, France®) technique. The analysis included frequencies and survival variables. The PFS and OS were calculated based on the date of first CTC collection and after first progression (PFS) or death (OS). Molecular characterization was made by immunocytochemistry for Transforming Growth Factor- ß (TGF-ß) and Matrix Metalloproteinase-2 (MMP-2). The primary endpoint was PFS. Secondary endpoints were OS and differences between molecular characterization.

RESULTS: Dates of endpoints and follow-up were updated by december/2015. Of the 54 patients enrolled, 32 were metastatic at diagnosis and all patients were metastatic when CTC/CTM were analyzed. 26 patients were alive at the time of analysis and 11 patients were positive for CTM. For mCRC patients, presence of CTM was not prognostic for PFS (20.12 x 13.87 months; p = 0.551) and OS (64.47 x 49,83 months; p = 0,313). There was numeric non-significant differences between groups, with increased PFS and OS for patients negative for CTM, warranting an hypothesis for worst outcomes for positivity of CTM.

CONCLUSION: There was no significant difference between groups for TGF-ß and MMP-2 expression, probably due to the low rate of expression in CTMs. Extended follow-up is necessary to further investigate the role of CTM in survival for mCRC patients.