The expression of multidrug resistance protein-1 in CTCs is a predictor of failure to irinotecan-based chemotherapy in metastatic colorectal cancer

Authors: Abdallah, EA (A.C. Camargo Cancer Center, Brazil), Fanelli, MF (A.C. Camargo Cancer Center, Brazil), Silva, VS (A.C. Camargo Cancer Center, Brazil), Alves, VS (A.C. Camargo Cancer Center, Brazil), Machado Netto, MC (A.C. Camargo Cancer Center, Brazil), Dettino, ALA (A.C Camargo Cancer Center), Mello, CAL (A.C. Camargo Cancer Center), Chinen, LTD (A.C Camargo Cancer Center, Brazil).

BACKGROUND: Colorectal cancer (CRC) is the third leading cause of cancer worldwide, and the fourth most common cause of death. So, it is important to look for reliable biomarkers in order to detect response to treatment and recurrence. Circulating Tumor Cells (CTCs) have been appointed for many researchers as a manner to follow up patients at current status. MRP1 protein acts as an ATP-dependent efflux pump, naturally protecting cells from both toxic and therapeutic compounds. It works as a drug resistant protein, generally with irinotecan-based chemotherapy. **OBJECTIVE:** to study MRP1 expression in CTCs and its predictable value in treatment resistance, evaluating the time of progression-free survival (PFS). **METHODS:** This present cohort (n= 19) belongs to a larger cohort of patients (n= 54) treated with many chemotherapeutic agents combined with 5-Fluorouracil (5-FU). The blood (8 mL) was collected prospectively from patients with metastatic CRC, before the beginning of chemotherapy. The samples were filtered in ISET® Technology (Isolation by Size of Epithelial Tumor Cells, Rarecells, France) according to manufacture procedure. CTCs fixed on spots from ISET membranes were stained by immunocytochemistry with anti-MRP1 antibody (ABCC1; Sigma; HPA002380; 1/100) and counterstained with haematoxylin. Leucocytes were identified by anti-CD45 antibody. CTCs were analyzed by light microscope and quantified per 1 mL of blood. **RESULTS:** here we analyzed blood samples of 19 mCRC patients who underwent irinotecan-based chemotherapy, with or without 5-FU. The median age was 53 years-old (32-80) and 73.6% were male. All the patients had tumors classified as adenocarcinoma. The median CTC number detected was 1.6 CTC/ml (0 – 13.75) at baseline. Immunocytochemistry of MRP1 in CTCs was performed in all samples and 4 of them (21%) were found positive staining in CTCs. By Kaplan-Meier and Log-Rank tests, we observed that patients with CTC positive for MRP1 had poorer PFS than patients CTC MRP1 negative (2.1 vs. 9.1 months respectively; P= 0.003). **CONCLUSION:** there is indispensable the development of novel tools to follow up and to predict treatment for mCRC patients. Here, we suggested a potential protein found in CTCs, MRP1, which might represent a powerful tool to manage and triage the patients that will be candidates to receive treatment with irinotecan. Furthermore, we are the first group to demonstrate the role of MRP1 in CTCs as a predictive factor for patients with mCRC.