CAN WE PREDICT TIME TO TUMOR PROGRESSION IN EARLY COLORECTAL CANCER PATIENTS USING CTCs COUNT?

Background: Colorectal cancer is the second most common cause of cancer-related death in Europe. Although significant improvements in the primary surgical and chemotherapeutic treatment, it has been estimated that approximately 30% of colorectal cancer patients develop metastases and die. Haematogenous spreading of tumor cells is a pivotal step in the metastatic process. Circulating tumor cells (CTCs) have potential ability to enter the circulation, invade the target organs and subsequently form metastases. Data suggest that the CTCs count before treatment is an independent predictor of progression free survival (PFS) and overall survival (OS) in patients with metastatic colorectal cancer, meanwhile their prognostic role in patients with early disease is uncertain.

Methods: 76 patients with histological diagnosis of colorectal cancer were included in this study. Disease stage was classified according to modified Astler and Coller as follows: 24/76 (31.6%) stages A + B, 30/76 (39.5%) stage C and 22/76 (28.9%) stage D. 7.5 ml of peripheral blood was collected for CTCs evaluation before the start of treatment or follow up. Mononuclear cells were isolated using Ficoll–Paque density centrifugation. CTCs were isolated from mononuclear cells by immunomagnetic enrichment using anti-CD326/EpCAM microbeads (Miltenyi Biotec) according to the manufacturer’s instructions. After, they were labeled for an epithelial marker such as CD326, for a nucleic acid dye such as DAPI, and for the leukocyte cell surface marker CD45 and then identified by immunofluorescence method as CD326+ DAPI+ CD45− cells. A cut-off of ≥2 CTCs/7.5 ml of blood was chosen for the definition of a positive test. Fisher exact test was used to compare frequency distribution of clinicopathologic findings according to CTCs count. A Kaplan-Meier method was applied for time to progression (TTP) curve.

Results: Twenty-one out of 76 (38%) patients were CTCs+: 4/24 (16.7%), 6/30 (20%), 11/22 (50%) stage A + B, C and stage D respectively. 16/57 (28%) colon and 5/19 (26.3%) rectal cancers were CTCs+. The CTCs positivity showed a correlation with the disease stage (p = 0.01; Table1). At a median follow up of 46.5 months 31 (41%) patients experienced a tumor progression. 62% of the patients with CTCs+ showed tumor progression compared to 33% of those CTCs- (p = 0.03). Tumor progression was significantly correlated with several clinicopathologic features including CTCs (Table2). Time to progression got worse in CTCs positive patients (Figure1)

Conclusion: This study confirms previous reports on negative prognostic role of the detection of CTCs in colorectal cancer. This was demonstrated in cases including both early and advanced stages of disease. The analysis of predictive role of CTCs treated patients is underway.