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P-361 High expression levels of circulating miRNA-618 and miRNA-203a-3p are associated with prolonged survival in patients with metastatic colon cancer

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Background: Circulating microRNAs (miRNAs) are promising non-invasive biomarkers for colorectal cancer (CRC). The aim of the present study was to evaluate the role of five circulating miRNAs — miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, miRNA-203a-3p which are involved in key cell signal processes in tumors such as proliferation, migration, and apoptosis. These miRNAs are thoroughly investigated in tumor tissue, but little is known regarding their levels of expression in the blood of patients with CRC.

Methods: 97 patients with colorectal metastatic disease before starting the chemotherapy and 80 healthy controls were investigated. miRNAs were isolated from serum samples by commercial kit. cDNA was generated from each sample. All miRNA data were analyzed by normalization using U6 as a constitutively expressed endogenous control. qRT-PCR was performed and the relative expression of each miRNAs was calculated by using 2 -ΔΔCt method.

Results: Serum miRNA-618, miRNA-26a-1, miRNA-15b-5p, miRNA-200c, and miRNA-203a-3p were significantly overexpressed in CRC patients. Among all investigated miRNAs only two of them were associated with CRC patient survival. Patients with low expression levels of circulating miRNA-618 had significantly shorter median overall survival (OS) of 14 months (95% CI, 8.63-19.37) as compared with those with high expression - 21 months (95% CI, 14.36-27.64) (p=0.003). Also, patients with low levels of miRNA-203a-3p had a significantly shorter median OS of 14 months (95% CI, 8.81-19,19) compared with 20 months in patients with higher expression in the blood (95% CI, 17.05-22.95) (p=0.012). In addition, Cox proportional hazards regression model showed that low levels of miRNA-618 and miRNA-203a-3p expressions were associated with a shorter OS, HR=2.02 (95% CI, 1.24-3.29; p=0.005) and HR=1.77 (95% CI, 1.08-2.91; p=0.025), respectively.

Conclusion: Our data suggest that only expression levels of anti-oncogenic miRNA-618 and miRNA-203a-3p in sera could be useful as non-invasive prognostic biomarkers in CRC patients.

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P-362 SIBO and lactose intolerance in patients receiving chemotherapy treatment for colorectal or gastric cancer

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Background: Worldwide, colorectal cancer (CRC) and gastric cancer (GC) are respectively the third and the fifth most prevalent cancers. Diarrhea (characterized by ≥3 episodes a day) is a common symptom in chemotherapy or radiotherapy treatment of GC or CRC cancer. Treatment-related diarrhea is the most common toxicity, which may reduce treatment tolerance. However, in addition to surgical resections and chemotherapy, changes in intestinal microbiota can lead to lactose intolerance and small intestinal bacterial overgrowth (SIBO), which cause diarrhea. The aim of the study was to evaluate SIBO and lactose intolerance incidence and the relationship with nutritional status and presence of diarrhea.

Methods: This is a descriptive and observational study with patients of both sexes, over 18 years old, in treatment in the Gastro-Oncology outpatient clinic of the Universidade Federal de Sao Paulo. The study was submitted to the Local Ethics Committee and was approved under CAAE no 81597517.0.0000.5505. Patients with a confirmed diagnosis of CRC or GC during chemotherapy treatment were included. To detect bacterial overgrowth and lactose intolerance, the expired hydrogen test was used. The number and aspects of the evacuations and toxicity degree were collected. For the nutritional assessment, weight and height were performed to calculate the BMI and the Patient-Generated Subjective Global Assessment (PG-SGA).

Results: Thirty tree patients were included, 29 with CRC and 3 with GC. The majority were male (57.57%), mean age of 60.03 (±10.1) years old and 60.6% were more than 60 years old. Most of the tumors were adenocarcinoma (84.9%). Most of the patients underwent chemotherapy with a fluoropyrimidine (5FU or capecitabine) and oxaliplatin (54.5%). Diarrhea was present in 57.5% cases and 13 (39.4%) had grade II/III toxicity. According to BMI, 78.9% were eutrophics, obese or overweight, but according to PG-SGA, 84.9% had moderate or severe nutritional risk grade. Between the patients, 45% had lactose intolerance and 9% SIBO. Although the number of patients was very small, we did not find any relationship between SIBO or lactose intolerance and undernutrition or diarrhea.

Conclusion: Diarrhea was a frequent symptom in patients receiving chemotherapy treatment for CRC or gastric cancer independent of the presence of SIBO or lactose intolerance. Surgery and chemotherapy treatment impacted in the intestinal habit of patients. Diagnosis of other causes of diarrhea may contribute to better tolerance of treatment and improved quality of life.

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P-363 Clinical-pathological correlation of the presence of microsatellite instability in patients diagnosed with locally advanced gastric adenocarcinoma from Costa Rica

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Background: In Costa Rica gastric adenocarcinoma is the second leading cause of cancer-related death. The development of this malignancy is a complex multistep process involving numerous genetic alterations. Gastric cancer development proceeds through three different molecular pathways: the chromosomal instability (CIN) pathway, the mutator phenotype (or microsatellite instability pathway, MSI) pathway and the CpG island methylator phenotype (CIMP) pathway. The mutator phenotype pathway is characterized by frequent mutations in regions of the DNA containing microsatellite sequences. Microsatellite stable tumours have low levels of microsatellite instability (MSS/MSI-L), and they are developped through the CIN pathway, whereas tumours with high microsatellite instability (MSI-H) are considered to develop through the mutator phenotype carcinogenic pathway. The objective of the study is to analyze the clinical, demographic and disease-free survival characteristics of patients with stage II and III clinical cancer who have microsatellite instability.

Methods: An observational retrospective cohort study was formalized; it was developed in patients with confirmed diagnosis of stage II & III gastric adenocarcinoma at the San Juan de Dios Hospital in the period from 2010 to 2015. Data were retrieved from clinical records and MSI was determined by immunohistochemistry.

Results: A total of 255 cases diagnosed with stage II and III gastric adenocarcinoma were analyzed. 60.4% of which were male and 39.6% female, with a mean age of 67.5 years. Moderately differentiated adenocarcinoma was the most frequent reported histology for 37.2%, located in the antrum 45.9%, intestinal type 49%. Clinical stage II was the most frequent stage (91,3%%). A total of 9.2% patients presented MSI, with MLH1 absent in 100%. For patients with MSI, the clinical-pathological characteristics were female sex in 60,8%, with a median age of 67.2 years, predominance of intestinal histology 87%, predominantly antrum location 43,5% and less nodal invasion in 52,2%. The determination of median progression-free survival for the group without MSI was 36.7 (range: 0.07-137.6) months and a median of 17.9 months for the group with MSI present was 73.2 (range: 21.4-120.1) months with a median 65.8 months.

Conclusion: MSI status could be a useful biomarker in local or locally advanced gastric cancer to predict its prognosis. The presence of MSI in gastric cancer was associated with higher progression-free survival than the MSS tumours, as reflected in a more favorable clinical and pathological characteristics.

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P-364 Higher amount of KRAS mutations in pre-operative plasma cell-free DNA predicts shorter survival after liver metastasectomy in colorectal cancer patients

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