Mutational frequency of oncogenic RAS family genes in Bulgarian patients with different localization of colorectal cancer

Neshe Nazifova-Tasinova¹, Galya Mihaylova¹, Desislava Ivanova¹, Vyara Draganova^{2,3}, Kalin Kalchev⁴, Oskan Tasinov¹, Deyana Vankova¹, Eleonora Dimitrova^{5,6}, Nikola Kolev^{7,8}, Nikolay Conev^{5,6}, Maria Radanova^{1,4}, Krasimir Ivanov^{7,8}

1 Department of Biochemistry, Molecular Medicine and Nutrigenomics, Medical University of Varna, Varna, Bulgaria 2 Department of Surgery Diseases, Medical University of Varna, Varna, Bulgaria 3 Second Surgery Clinic, UMHAT "St. Marina", Varna, Bulgaria 4 Clinic of General and Clinical Pathology, UMHAT "St. Marina", Varna, Bulgaria 5 Department of Propedeutics of Internal Diseases, Medical University of Varna, Varna, Bulgaria 6 Clinic of Medical Oncology, UMHAT "St. Marina", Varna, Bulgaria 7 First Surgery Clinic, UMHAT "St. Marina", Varna, Bulgaria 8 Department of General and Operative Surgery, Medical University of Varna, Varna, Bulgaria

INTRODUCTION

Somatic mutations in oncogenic RAS gene family (KRAS and NRAS) are associated with resistance to anti-EGFR monoclonal antibodies in patients with colorectal cancer (CRC). However, the outcome depends on the localization of the tumor. RAS-wild-type right-sided colon cancer treated with anti-EGFR monoclonal antibodies is associated with poor prognosis compared to left-sided colon and rectal cancer.

AIM

The aim of the present study is to evaluate the frequency of RAS mutations in Bulgarian patients and their association with tumor localization.

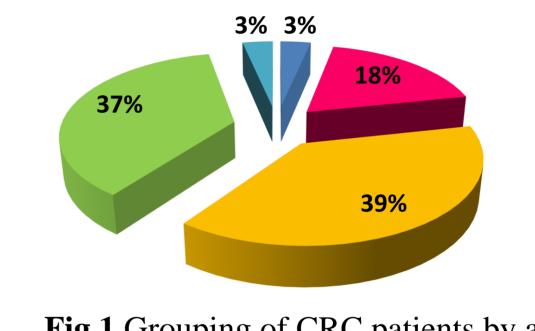
MATERIALS AND METHODS

This study included 61 patients with CRC (28 female and 33 male). DNA was isolated from formalinfixed paraffin-embedded (FFPE) tissue samples. Mutations in RAS were detected by commercial RT PCR kit.

RESULTS

Table 1. Grouping of CRC patients by localization of the cancer localization

TUMOR LOCALIZATION	NUMBER OF PATIENTS	%
LEFT COLON	27	44
RIGHT COLON	14	23
RECTUM	20	33



50-59

Fig.1 Grouping of CRC patients by age

■ 60-69 **■** 70-79 **■** 80-90

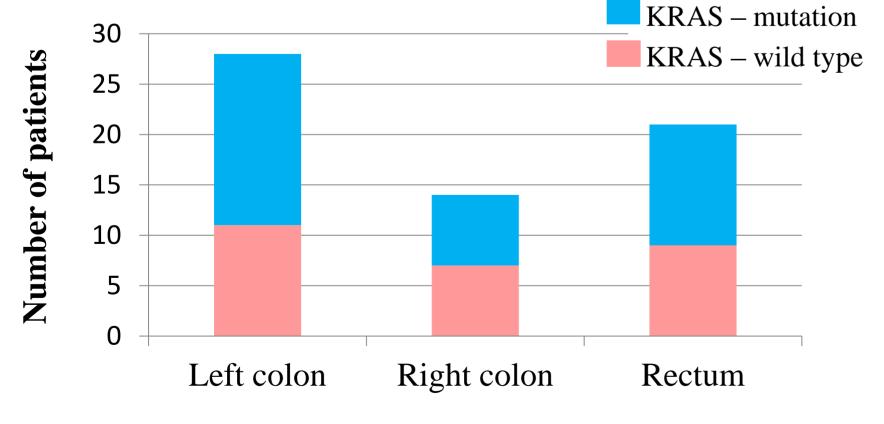


Fig. 2 KRAS mutational status and tumor localization in CRC patients

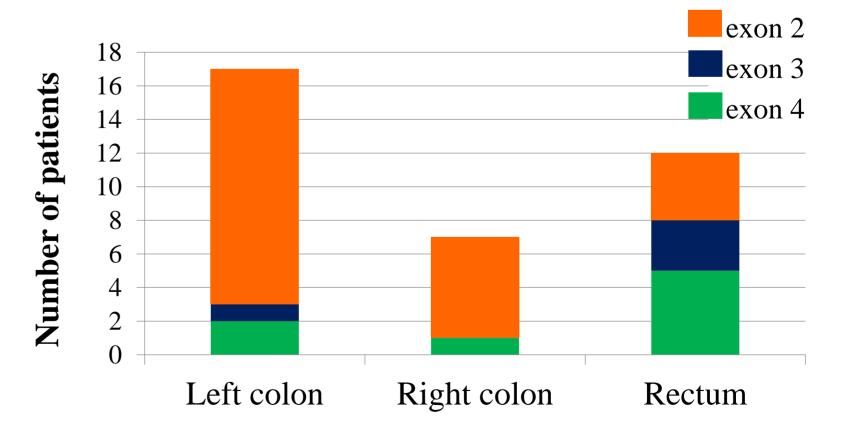


Fig. 3 Mutations in exon 2, exon 3 and exon 4 in KRAS gene in relation to tumor localization in CRC patients

CONCLUSIONS

Exon 4 KRAS mutations are identified in adenomas, but also in primary invasive colorectal tumors suggesting that they occur early in the development of the disease. The clinical importance of the established associations for exon 4 KRAS mutations is the subject of our further work with a larger number of patients.