mutations in the DNA sequence of K-ras gene, especially in codon 12 or 13. Nowadays, EGFR targeted therapies, such as cetuximab and panitumumab were used for CRC and K-ras mutation analysis has gained importance. In this study, possible relationship between ABO-Rh blood groups factor and K-ras status was investigated.
Material and Methods: In 94 patients with CRC, blood group and Rh factor were examined. The relationship of blood groups with wild type K-ras status was evaluated and compared with the healthy volunteer donors control group of 22,821 people which admitted to Ankara University Medical School Blood Center at 2010.
Results: Information on ABO blood type and Rh factor were available for 94 patients. Of patients 34% (32 patients) was female and 66% (62 patients) was male. The most of patients had (40.4%) blood group A. Overall, the ABO blood group distribution of the 94 patients with CRC was similar to that of the general population. There wasn't statistically significant difference ($p = 0.83$) between groups (see Table 1).
Conclusion: This study is the first study done on this issue. In our study, we didn't find any relationship between K-ras status and ABO blood group and Rh factor. However further studies with larger number of patients are needed to establish the role of blood groups in this population.

Table 1: The blood group distribution of patients and control group

Blood groups	K-ras WT patients		Control group	
	n	%	n	%
A Rh (+)	33	35.1	8795	38,54
A Rh (−)	5	5.3	1130	4,95
B Rh (+)	13	13.8	3185	13,96
B Rh (−)	2	2.1	425	1,86
AB Rh (+)	3	3.2	1581	6,93
AB Rh (−)	1	1.1	205	0,90
0 Rh (+)	32	34.0	6550	28,70
0 Rh (−)	5	5.3	950	4,16
Total	94	100	22821	100

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Relatively High Discordant Rate of KRas Mutation Between Primary and Metastatic Sites, and a Different Pattern of KRas Mutational Status According to Metastatic Sites in Korean Patients With Colorectal Cancer

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Background: KRAS mutations predict resistance to cetuximab or panitumumab therapy in patients with metastatic or recurred colorectal cancer (MRCRC). The aim of this study was to determine the concordance rate of KRAS mutational status between primary tumours and related metastases, and to find out the association between KRAS mutational status and clinicopathologic features in Korean patients with MRCRC.
Material and Methods: KRAS mutational status in codon 12, 13, and 61 from formalin-fixed sections of primary tumours and related metastases was analyzed. In addition, the association between KRAS mutational status and clinicopathologic features was evaluated.
Results: Of 128 patients whose primary and matched metastatic tissues were analyzed for the KRAS mutation status, 5 patients were excluded because of a failure in the process of KRAS mutation analysis and 123 patients were finally included in this study. Matched metastatic sites for KRAS analysis were liver (n = 46), lung (n = 27), peritoneum (n = 26), distant lymph node (LN; n = 13), ovary (n = 10) and pancreas (n = 1), respectively. KRAS mutation was observed in 52 (42.3%) of primary tumours, and in 54 (43.9%) of related metastatic sites. Discordance of KRAS status between primary and metastatic sites was observed in 18 patients (14.6%; kappa = 0.702) and KRAS mutation rate considering both primary and metastatic sites was 50.4% (62/123). When the association between KRAS status and initial metastatic sites at the time of diagnosis of stage 4 cancer or recurrence (in the cases of initial stages 1−3) was analyzed, a high percentage of wild type KRAS was observed in patients with initial liver or distant LN metastases compared with patients without liver or LN metastases ($P = 0.001$ in liver; $P = 0.037$ in LN). However, patients with initial lung metastases had a higher rate of KRAS mutation than patients without lung metastasis ($P = 0.002$). Other clinicopathologic features including age, gender, histologic grade, primary tumour site, obstruction or perforation of primary site, and microsatellite instability were not related to the KRAS mutational status.
Conclusions: The discordant rate of KRAS mutation status between primary and metastatic sites was relatively high (14.6%) in Korean MRCRC patients compared with the rate (<10%) previously reported in Western patients. The frequency of KRAS mutation was different according to the initial metastatic or recurred sites.

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Biological Analysis of Phase II Study Evaluating the Activity of Cetuximab Combined to Oxaliplatin and Fluoropirimidine (TEGAFOX-E) as First Line Treatment in Metastatic Colorectal Cancer (mCRC) Pts by the Italian Trials in Medical Oncology (I.T.M.O.) Group

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Background: There is some evidence that *p53* inactivating mutant (mut) confer oxaliplatin resistance, but improve cetuximab benefit in KRAS wt pts *(Oden-Gangloff, 2009)*. On the other hand, KRAS mut predict cetuximab resistance, but increase oxaliplatin sensitivity in a p53-dependent manner (de Bruijn, 2010). We conducted a prospective Phase II evaluating the activity of the cetuximab plus an oxaliplatin-based regimen as first line treatment in mCRC, and the correlation with predictive biomarkers such as *p53* and *KRAS* status.
Methods: Twenty-eight elderly mCRC pts (age $\geqslant$70 yrs) were enrolled in a multicenter, prospective study and treated with TEGAFOX-E regimen (oxaliplatin 120 mg/m^2 d1, UFT 250 mg/m^2 d1−14, cetuximab 400 mg/m^2 initial dose, then 250 mg/m^2 weekly) up to 8 cycles, followed with one-year maintenance cetuximab, or until progressive disease (PD)/unaccectable toxicity. *KRAS, p53*, *BRAF* and *PI3KCA* mut were successfully analyzed by genomic sequencing in 23 samples. A mutant-enriched PCR was performed for codons 12 and 13 of *K-Ras*.
Result: TEGAFOX-E regimen produced a 44% objective response rate. *KRAS* mut were detected in 12/23 (52%) and *p53* mut in 5/21 (24%) samples. Two samples were not evaluable for *p53* status. Except for one case, *PI3KCA* mut (26%) were always coupled with *KRAS* mut. No statistically significant difference could be found between responders and non responders in terms of *KRAS* or *p53* mut. On the basis of their *KRAS* and *p53* status, the samples (21 cases) were molecularly classified in three groups and associated to response and mPFS. Group 1 (*KRAS* mt/*p53* mt): all 2 pts harbouring double mutation showed PD at 9-weeks, i.e., the first reassessment; Groups 2−3 (*KRAS* mt/*p53* wt or *K-ras* wt/*p53* mt): in this cross-interference groups 7/12 pts (58%) showed disease control [5 PR, 2 SD and 5 PD], with mPFS of 11 weeks; Group 4 (*KRAS* wt/*p53* wt group): in this double drug-sensitivity group 86% (5/7) pts benefited from treatment (5 PR, 1 long-lasting SD and 1 PD), with a mPFS of 44 weeks.
Conclusions: TEGAFOX-E combination displayed promising efficacy in pts with both wt *KRAS* and *p53* tumours and these hypothesis-generating results should be verified in larger, prospective and randomised phase III trials.

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Prognostic Role of KRas and BRAF Mutation in Colorectal Cancer

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Background: In numerous studies on the development of cancer induced by K-Ras mutation, raf kinase has been shown to be an important signal transducer in the activation of Ras oncogene. To see whether the mutation of K-Ras gene and BRAF gene is associated with colorectal cancer, in colorectal cancer patients, we compared the presence or absence of the mutation of K-Ras gene and BRAF gene with the clinicopathological characteristics of colorectal cancer patients, and examined the effect of the mutations on survival rate.
Material and Methods: DNA was extracted from 162 cases of colorectal cancer tissues of patients performed surgery for colorectal cancer from 2002 to 2007 and the presence or absence of the mutation of K-Ras and BRAF was assessed by the use of the K-Ras and BRAF detection test kits applying PNA PCR claming method developed recently. The presence or absence of the mutation of K-Ras as well as BRAF was compared with various clinicopathological factors. 5-year survival rate was analyzed by the Kaplan–Meier survival analysis.