bevacizumab. Panitumumab is a fully human monoclonal antibody directed against the epidermal growth factor receptor (EGFR). Study 20050181, a randomized phase 3 trial comparing panitumumab + FOLFIRI with FOLFIRI alone, demonstrated a significant improvement in progression-free survival (PFS) with the addition of panitumumab to second-line treatment of patients with WT *KRAS* mCRC.

Methods: Patients were randomized 1:1 to panitumumab 6.0 mg/kg Q2W + FOLFIRI or FOLFIRI alone. Prior treatments with oxaliplatin or bevacizumab were predefined stratification factors for randomization. Patient eligibility criteria included: $\geqslant$ 18 years old, no prior irinotecan or anti-EGFR therapy, and ECOG $\leqslant$ 2. The co-primary endpoints were PFS and overall survival (OS). This subset analysis reports the efficacy of panitumumab + FOLFIRI versus FOLFIRI alone in WT *KRAS* mCRC patients who had progressed on prior oxaliplatin- or bevacizumab-containing regimens.

Results: In study 20050181, 395 patients with WT *KRAS* mCRC had prior oxaliplatin and 115 patients had prior bevacizumab. 76% (87/115) of patients treated with bevacizumab also received oxaliplatin. Patients with WT *KRAS* mCRC who had received oxaliplatin or bevacizumab in first-line therapy had longer PFS and OS with panitumumab + FOLFIRI versus FOLFIRI alone. Results by prior treatment are shown (table).

Conclusions: Second-line therapy with panitumumab + FOLFIRI may benefit patients with WT *KRAS* mCRC who have progressed on prior oxaliplatin- and/or bevacizumab-containing regimens.

	PFS		Overall Survival	
	Pmab+FOLFIRI (n = 303)	FOLFIRI (n = 294)	Pmab+FOLFIRI (n = 303)	FOLFIRI (n = 294)
Prior ox treatment, n (%)	204 (67)	191 (65)	204 (67)	191 (65)
Median, mos (95% CI)	5.6 (4.6–6.7)	3.7 (3.4–3.9)	14.3 (11.8–15.7)	11.2 (8.9–12.8)
Hazard ratio (95% CI)	0.68 (0.53–0.86)		0.79 (0.63–0.99)	
Descriptive p-value	0.001		0.044	
Prior bev treatment, n (%)	55 (18)	60 (20)	55 (18)	60 (20)
Median, mos (95% CI)	5.8 (5.2–6.7)	3.7 (3.5–5.3)	15.7 (12.6–23.8)	12.5 (9.2–16.1)
Hazard ratio (95% CI)	0.71 (0.45–1.13)		0.68 (0.43–1.07)	
Descriptive p-value	0.150		0.093	

pmab = panitumumab; ox = oxaliplatin; bev = bevacizumab; mos = months; CI = confidence interval

6133   POSTER
High Levels of Immature Blood Vessels in Colorectal Tumours and Metastases Correlate With Survival and Are Independent of Oxidative Damage in the Tumour

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Background: Angiogenesis drives cancer growth, tumour progression and metastases. Hypoxic tumours initiate recruitment of their own blood supply and enhance expression of Vascular Endothelial Growth Factor (VEGF). Bevacizumab is a recombinant humanised monoclonal anti-VEGF antibody which prevents VEGF binding to its receptors. It is the first anti-angiogenic treatment licensed and has been used in Ireland since 2004. Bevacizumab improves overall survival in metastatic colorectal cancer patients when combined with cytotoxic chemotherapy. Currently, bevacizumab is indicated as a first line treatment in all metastatic colorectal cancer patients, however only 38–44% of these patients will have a response to treatment. There is no good marker to predict treatment response. Blood vessels mature by the recruitment of pericytes. We hypothesise those blood vessels that lack pericytes will be more susceptible to regression following treatment with bevacizumab.

Materials and Methods: Gross sections from 80 tumours were stained using dual immunofluorescence staining for factor VIII (an endothelial marker) and α-smooth muscle actin (a pericyte marker). Fluorescent microscopy was used and the mean levels of immature and mature blood vessels were scored and correlated with survival using Spearman correlations and multivariate analyses. TMAs were constructed and stained for the markers of oxidative damage; 8oxodg and 4HNE, and the proliferation marker Ki67.

Results: 37 patients were metastatic at diagnosis and 43 were initially Dukes' A, B or C at diagnosis (early stage) and subsequently developed metastases. 10 patients had matched liver metastases. Patients with higher levels of immature blood vessels had longer survival following treatment with bevacizumab (p value = 0.026). This remained significant following multivariate analyses correcting for gender, stage at diagnosis, whether patients received chemotherapy before or after treatment with bevacizumab and whether or not bevacizumab was first line or not. There was no difference in levels of immature blood vessels between primary and liver metastases. Levels of immature blood vessels did not correlate with levels of oxidative damage in the tumour samples.

Conclusion: We have shown for the first time that the maturity levels of blood vessels in tumours significantly correlates to survival following treatment with bevacizumab. There is no difference in levels between primary tumours and metastases and these levels are independent of oxidative damage in the tumour.

6134   POSTER
The Role of Circulating Levels of Hepatocyte Growth Factor and Vascular Endothelial Growth Factor Receptor 2 in Colon Cancer Patients With Liver Metastases Who Have Responded to Neoadjuvant Chemotherapy Plus Bevacizumab

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Background: Hepatocyte growth factor (HGF) is reported to play important role in angiogenesis and in liver regeneration, while Vascular endothelial growth factor receptor 2 (VEGFR2) is more significant for tumour angiogenesis. In patients (pts) with colon cancer (CC) with liver metastases (LM) an increased circulating levels of HSF have been reported. The study aimed to evaluate the interplay between HGF and VEGFR2 levels in pts with LM from CC who have responded to neoadjuvant Bevacizumab and chemotherapy.

Materials and Methods: We examined 40 plasma and serum samples in duplicate from 4 patients with sigmoid CC and synchronous primary unresectable LM using quantitative sandwich enzyme immunoassay technique (R&D System). Blood samples were drawn at baseline, at 2nd and at 4th cycle of neoadjuvant therapy (XELIRI plus Bevacizumab), on day 7th and one month after operation (radical liver resection), and every two cycles thereafter during postoperative treatment. Control group consisted of 4 healthy women. Immunochistochemical (ICH) staining of LM was performed with polyclonal rabbit antibodies to Flk-1/VEGFR2 (Diagnostic BioSystems) and to HGF (Santa Cruz Biotechnology, Inc). Clinical and biochemical parameters of pts were also collected. The scoring system consisted of intensity of staining and % of tumour cells involved.

Results: The difference between mean values of serum and plasma HGF and VEGFR2 levels in colon cancer pts and healthy women was statistically significant. The Pearson's strong correlation was found between plasma and serum HGF (r = 0.82, p < 0.0001),while plasma and serum VEGFR2 levels correlation was week and did nod reached statistical significance. Positive correlations between plasma and serum HGF and tumour markers CA19-9 and CEA were noticed (p < 0.05), while negative moderate correlation between serum VEGFR2 and CEA (r = 0.43, p < 0.017) was found. Negative correlation between VEGFR2 and HGF levels was also established (r = 0.50, p < 0.001). ICH evaluation of LM revealed that strong intensive staining of HGF (score 3) corresponded with weak or missing VEGFR2 staining (score 1 or 0).

Conclusion: In responders to neoadjuvant chemotherapy and Bevacizumab, VEGFR2 circulating and tissue levels correlate with angiogenesis suppression and chemotherapy response. HGF levels correlate with clinical course of disease, at the diagnosis the HGF levels corresponded to angiogenesis activation, while thereafter they reflect liver regeneration.

6135   POSTER
Relationship Between ABO and RH Blood Groups and K-Ras Phenotype in Patients With Colorectal Adenocarcinoma

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Background: Colorectal cancers (CRC) are the most third cancer in both women and men and responsible for approximately 10% of all cancers. Also CRC are third most common cause of cancer-related mortality for both sexes. For the year 2008 about 1.2 million cases and 600 thousand deaths to be estimated worldwide. Age, adenomatous polyps, smoking, inflammatory bowel disease and dietary factors are some of the risk factors. Some familial cases of colon cancer identified in the etiology of various genetic factors. Familial adenomatous polyposes (FAP), hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome are hereditary factors. ABO blood group genes are mapped at the chromosome 9, in which the genetic alteration is common in many cancers. Aird and his colleagues reported that the relationship between stomach cancer and the A blood group in 1953. Association between ABO blood groups and cancer of the pancreas was recently described. Such a relationship isn't identified for CRC. K-ras (Kirsten rat sarcoma) is a proto-oncogene which located on chromosome 12 and encoded protein that involved in normal cell proliferation and signal transduction. The K-ras becoming oncogene by