favored p.G13D mutation (PFS; HR = 0.29; 95% CI, 0.08–1.10; p = 0.07, OS; HR = 0.23; 95% CI, 0.04–1.54; p = 0.13) (Table).
Conclusions: These results suggest that the use of cetuximab may be associated with improvement of PFS among patients with mCRC who have KRAS p.G13D mutated tumours compared with the other mutated tumours. Further study is needed to clarify the benefit of cetuximab treatment for KRAS p.G13D mutated tumours in mCRC.

Table: Multivariate analysis for PFS and OS in the patients treated with cetuximab

	Total		PFS				OS			
KRAS type	No	%	Median	HR	95% CI	*p*	Median	HR	95% CI	*p*
p.G13D mutation	9	29.0	4.5 m	0.29	0.08–1.10	*0.07*	15.3 m	0.23	0.04–1.54	0.13
Other mutations	22	71.0	2.8 m	1	referent		8.9 m	1	referent	

6015 POSTER DISCUSSION

An International Consortium in Chemo-refractory Metastatic Colorectal Cancer Patients Shows Cetuximab Efficacy in Patients Harboring HER2 Gene Copy Number Gain

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Background: KRAS mutation represents the only validated biomarker used in clinical practice for selection of metastatic colorectal cancer (mCRC) candidate for a therapy with the anti-Epidermal Growth Factor Receptor (EGFR) monoclonal antibody cetuximab. Previous studies, conducted in small cohorts of patients suggested that HER2, the major EGFR partner, could modify the sensitivity to anti-EGFR agents. Aim of the present study was to investigated the role of HER2 gene copy number in a cohort of mCRC patients treated with cetuximab.
Materials and Methods: Chemorefractory mCRC patients treated with cetuximab alone or in combination with irinotecan were collected in an international consortium effort. Her2 gene status was analyzed using the dual color FISH assay LSI HER2/neu-CEP17 (PATHVYSION, Abbott) in one central lab, whereas K-Ras and BRAF mutations were investigated locally. Logrank and Chi-square tests were applied at statistical level.
Results: Four hundred and seven patients were collected. Objective response rate (ORR) was observed in 25.3% of patients. HER2 gene status was evaluable in 288 (70.8%) cases. Two different scores were applied for HER2 gene status evaluation: the Colorado (positive vs negative cases, where positive are $\geqslant$ 4 copies of the gene in $\geqslant$ 40% of cells or gene amplification) and the Locarno score (based on the classical cytogenetic criteria, positive case are those with at least low polysomy). With the Colorado score, positive cases (81 cases, 28.8%) experienced response in 34.6% of patients (vs 15.7% in negative cases, P < 0.001), with an overall median progression free survival (PFS) of 5.14 months (vs 3.0 months in negative cases, P = 0.004) and a median overall survival (OS) of 10.9 months (vs 9.8 months in negative cases, P = 0.44). With the Locarno score, positive cases (81 patients) showed an ORR in 30.3% of patients (vs 11.4% in negative cases, P = 0.027), with a median PFS of 4.1 months (vs 1.8 months in negative cases, P = 0.002) and a median OS of 11.3 months (vs 7.8 months in negative cases, P = 0.2). By stratifying cases with KRAS and BRAF mutations, no significant differences in terms of ORR, PFS and OS were observed between HER2-positive and negative cases using both scores, although similar trends were found.
Conclusions: Data from this large retrospective study suggested that HER2 gene status by FISH may represents an additional marker useful for the identification of mCRC patients who might benefit from EGFR-targeted therapies. The interplay between EGFR and HER2 needs to be more deeply investigated for future best tailored treatments.

6016 POSTER DISCUSSION

Prognostic and Predictive Value of Mucinous Adenocarcinomas in Colorectal Cancer Patients Treated With Chemotherapy and Targeted Therapy

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Background: Mucinous adenocarcinomas (MC) have a different clinical behaviour compared to the more common histological subtypes of colorectal cancer (CRC). The aim of this study was to investigate the prognostic and predictive value of mucinous histology in advanced CRC patients treated with first-line systemic treatment.
Material and Methods: The study population included 552 and 547 advanced CRC patients who participated in the CAIRO and CAIRO2 study, respectively. Patients were classified according to the histology of the primary tumour, and only patients with a MC (n = 99) or adenocarcinoma (AC)(n = 911) were included in our analysis.
Results: In the CAIRO and CAIRO2 study, MC were present in 50 and 49 patients, and AC in 435 and 476 patients, respectively. In both studies, patients with MC had more often a lower serum LDH at baseline (p < 0.01), extrahepatic localization of metastases (p < 0.01), a larger diameter (p < 0.02) and microsatellite instability (MSI) of the primary tumour (p < 0.01) compared to patients with AC. In the CAIRO study, T stage (p = 0.02) of the primary tumour and the number of involved metastatic sites (p = 0.05) were higher in patients with MC. In the CAIRO2 study, the median age at randomisation (p = 0.01) was higher and *BRAF* mutations (p = 0.002) were more frequently observed in patients with mucinous histology compared to patients with AC.
In the CAIRO and CAIRO2 study, the median overall survival (OS) was significantly reduced for patients with MC compared to patients with AC (13.2 vs. 19.2 months; p = 0.03; 13.1 vs. 21.5 months; p = 0.009). In multivariate analysis, mucinous histology remained a strong predictor for OS in both studies. Additionally, the CAIRO2 study showed also a decreased progression free survival (PFS) in patients with MC compared to AC (7.2 vs. 10.6 months; p < 0.0001). In both studies, the overall response rates for patients with MC were significantly worse and they received less cycles of systemic treatment compared to AC patients. The reasons for discontinuation of study treatment were not significantly different between patients with MC and AC. There was no difference in the incidence of grade 3 or 4 adverse events between both patient groups.
Conclusions: This large retrospective analysis showed that patients with advanced mucinous CRC have an unfavourable OS and worse response to first-line fluoropyrimidine based chemotherapy in combination with targeted agents. The mechanisms for treatment resistance should be further investigated.

6017 POSTER DISCUSSION

Quality of Life and Reintegration of Long-Term Survivors of Colorectal Cancer: a Population-Based Study

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Background: The number of long term colorectal cancers is increasing. Cancer and its treatment can cause physical and psychological complications, but little is known about how it impacts on quality of life (QOL) and on reintegration in the long-term 5, 10 and 15 years after diagnosis.
Material and Methods: Cancer survivors were randomly selected from three tumour registries in France in 1990, 1995, and 2000. Controls were randomly selected from electoral rolls, stratifying on gender, age group, and residence area. Participants completed four standardized questionnaires: MOS SF36, EORTC QLQC30, MFI, STAI, and a life conditions questionnaire. Differences in QOL scores between survivors and controls were evaluated using an analysis of variance. Differences of changes in family, social, and professional life were evaluated as relative risks, using a logistic regression.

Results: We included 344 colon cancer and 198 rectal cancer survivors and 1181 controls. In a global analysis, survivors reported a significant QOL decline in social functioning (QLQC30) at 5 years (−5.2 points; p = 0.005), and in diarrhea symptom (QLQC30) at 5, 10, and 15 years after diagnosis (+8.2, p < 0.0001; +10.2, p < 0.0001; +6.4, p = 0.006). In subgroup analyses, QOL of rectal cancer survivors were more affected than controls in the physical functioning (SF36) at 5 years (−9.4; p = 0.002), in the physical fatigue (MFI) at 10 years (+8.6; p = 0.01), and in mental fatigue at 5 years after diagnosis (+8.5; p = 0.006). On the assessment of reintegration, cancer survivors saw their marital relationship has strengthened (RR = 1.82 (1.21–2.75); p = 0.0002), attributing change in quality of this relationship (positive or negative) to their health (RR = 4.89 (2.09–11.44); p < 0.0001). As well, their health closely influenced professional activity more often than controls (RR = 4.50 (1.85–10.95); p < 0.0001). They met more difficulties in loan or insurance requests (RR = 3.83 (1.99–7.37); p < 0.0001) whatever tumour location and gender.
Conclusion: Colorectal cancer survivors may experience the effects of cancer and its treatment on QOL up to 10 years after diagnosis. They noted positive changes or less negative changes in life than controls. However, they still have to face to barriers that are keeping in job by avoiding early retirement and accessing to insurance or a bank loan. Clinicians, psychologist, and social workers must pay special attention for colorectal cancer survivors to improve overall management.

6018 POSTER DISCUSSION

EORTC 22921 Rectal Cancer Trial: Quality of Life (QoL) and Functional Outcome 5 Years After Treatment

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Purpose: Long-term impact of preoperative (chemo)radiation (P(C)RT) on QoL bowel and sphincter function in patients with rectal cancer is unknown. Patient-reported health-outcomes in a cross sectional study attached to EORTC 22921 study are presented.
Patients and Methods: 167 French patients, free of disease and had a sphincter preservation had to complete, on time, two questionnaires (Q). The EORTC QLQC30 Q and the Anal Sphincter Conservative Treatment (ASCT), a validated patient-Q.
Results: 5 years after treatments (1−11 y), the QLQC30 Global Health (GH QoL) score was 73.1, similar with observed in a same age group of general population. CT (concurrent, postop or both) negatively affected QLQC30 social functioning (p = 0.06), GHQoL (p = 0.03) and diarrhoea complaints (p = 0.0003). On ASCT, nearly 60% of patients suffered faecal incontinence (any severity), urgency, soiling, modifications of social life. Faecal incontinence was associated with impaired social life measured by both Q.
Conclusion: Adding CT to PRT negatively affect social life. Patients reported high rate of sphincter dysfunction. These results are similar with those previously reported after short course PRT (5 × 5 Gy).

Poster Presentations (Sun, 25 Sep, 09:30−12:00) **Gastrointestinal Malignancies − Colorectal Cancer**

6019 POSTER

No Association Between Dukes' Stage and Genetic − Epigenetic Markers in Colorectal Cancer

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Background: The colorectal adenoma-carcinoma sequence goes with epigenetic and genetic modifications, which arise during oncogenesis. These modifications have an effect on the methylation status of different gene promoters and mutations in the K-ras and B-raf genes among others. Included are, as we have previously shown (ASCO 2011, abstract accepted): methylation of the gene promoters of H-cadherin, of MGMT deregulating removal of toxic methyl adducts on guanine bases and inducing the activation of K-ras through G to A point mutations, activation of B-raf gene by a V600E mutation, methylation of E-cadherin and PTEN inactivation by promoter hypermethylation in more than 200 patients.
Methods: DNA extraction was obtained by standard methods from resected tumour samples. PTEN methylation was analyzed by methylation-specific PCR, gel electrophoresis after Sybr green staining and UV-photography. From each individual patient we examined germline DNA from white blood cells as described above.
Results: Of the 95 out of 222 tumours (43%) with a PTEN hypermethylation, 77 (81%) were also methylated in CDH13, 52 (55%) were MGMT methylated, 35 (37%) had a K-ras gene mutation and were B-raf wild type as expected, their mutations being mutually exclusive. All results were tumour specific as all the sequenced blood controls were unmethylated respectively wild type. In 86 of these patients the Dukes' stage was determined and classified as early (Dukes' A & B) and late (Dukes' C & D).
Conclusions: The extremes of the correlations between Dukes' and the other markers ranged from −0.063 for Dukes' and MGMT (p = 0.40) to +0.078 for Dukes' and KRAS (p = 0.81). Thus no significant correlation was found between Dukes' and the other variables. The work is proceeding to include the additional 150 patient data available, but the p values are such that a modification of the conclusion cannot be expected.

6020 POSTER

KRas and Braf: Is a Predictor in Metastatic Colorectal Cancer Patients for Bevacizumab?

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Aim: Unlike cetuximab, there is a paucity of biomarkers for bevacizumab to predict outcome of metastatic colorectal cancer (mCRC) patients. Therefore a research for potential biomarker is urgently needed. We aimed to search K-RAS and B-RAF status of our patients whether mutation would effect the outcome of metastatic colorectal cancer treated with first or second line bevacizumab combined with folfiri.
Methods: We retrospectively reviewed the clinical and pathological features of 166 mCRC patients treated in our outpatient clinic between the years 2000 and 2010. KRAS and BRAF mutations were analysed quantitatively by PCR after having extracted the DNA from tumour tissues.
Results: The median age of the patients was 60.5 (27−83). 62% of the patients were male and 37.2% female. Tumour locations were as follows: 36.6% rectum, 25% sigmoid, 16.3% left colon, 1.2% transverse colon, 9.9% right colon, 7.6% cecum. Forty four percent of the patients were KRAS mutant. Eighty patients had BRAF mutation analysis and 6 were found to be BRAF mutant (7.5%). Initial CEA and CA19-9 levels were not correlated with KRAS and BRAF mutations. All 6 patients who were found to have BRAF mutations had rectosigmoid tumours. On the other hand, 41.7% of rectosigmoid, 57% of left colon, 56% of transverse and right colon and cecum were KRAS mutant. Overall, 108 patients had liver metastasis (62.7%). Liver-only disese was 39%. Whereas 43 patients had lung metastasis (25%), 17 had lung-only disease (9.9%). Fourty-six percent of patients who had liver metastasis and 50% of patients who had lung metastasis were found to have KRAS mutation. When both liver and lung metastases were combined KRAS mutation rate rised to 61%. First or second line FOLFIRI and bevacizumab use was not affected by KRAS mutation or wild type status with respect to progression free survival.
Conclusion: KRAS or BRAF mutation was not observed as a potential biomarker in predicting progression free survival in patients with metastatic colorectal cancer who had been treated with first or second line FOLFIRI and bevacizumab. As KRAS mutation was found more frequently in combined lung and liver metastasis, it may represent a more virulant disease.

6021 POSTER

The Role of ABC Transporter Genes in Colorectal Cancer Resistance

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Background: Worldwide, colorectal cancer (CRC) is the third most common malignancy. In terms of CRC incidence, the Czech Republic ranks