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.