Results: At a median follow-up of 7 months (range 1 to 19), 13/16 pts (81%) were alive. Therapy was completed without interruptions in 14/16 patients, with a mean treatment time of 37 days (range 32 to 43 days). RTOG grade III or greater toxicity was experienced by 1/15 patients (enteritis). Five patients had grade II maximum toxicity, including 2/16 pts (12.5%) with hand–foot syndrome and 3/16 pts (18.8%) with GI symptoms. The remaining pts had grade 0/1 toxicity. Following chemoradiation 7 patients underwent surgery: 3 Whipple procedures, 1 total gastrectomy, 1 sigmoidectomy, and 2 operations which were aborted, one secondary to carcinomatosis and one to due to extensive regional nodal involvement. Average time between chemoradiation and surgery was 52 days (range 43–63). Of the surgical patients, 2/7 (29%) demonstrated a pathological complete response. To date, 3/16 pts had experienced distant relapse.
Conclusion: Given the suboptimal median survival, capecitabine with radiotherapy in the treatment of advanced upper gastrointestinal malignancy appears to have a positive impact on survival with favorable toxicity. Vitamin B6 used in conjunction with capecitabine appears to effectively decrease the incidence of hand–foot syndrome. The present RTOG phase 2 combined-modality trial and further phase III trials, which include a capecitabine/radiotherapy platform, will serve to further clarify the impact of such a regimen on loco-regional control and overall survival for this challenging patient population.

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First line therapy of Panitumumab, a fully human antibody, in combination with FOLFIRI for the treatment (txt) of metastatic colorectal cancer (mCRC)

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Background: Panitumumab, a fully human monoclonal IgG2 antibody directed against the epidermal growth factor receptor (EGFr), is being investigated for the txt of solid tumors. Recently, panitumumab in combination with IFL was found to be effective in pts with mCRC (n = 19; RR 47%, OS 16.4 months) (Berlin, ESMO 2004); however, because of unacceptable IFL-related toxicity, the protocol was amended to use FOLFIRI in combination with panitumumab (Part 2). Here, we present results for Part 2.
Methods: Part 2 is a multicenter, open-label phase 2 trial of first line panitumumab and FOLFIRI in pts with mCRC. Key eligibility criteria were ⩾18 years old, mCRC, EGFr expression in ⩾10% of tumor cells, ECOG=0–1, no prior txt for mCRC, and no prior EGFr-targeting agents. Pts received QW panitumumab 2.5 mg/kg IV over 1 hr, immediately followed by FOLFIRI (irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, 5-FU bolus 400 mg/m^2 and 5-FU infusion 2.4–3.0 g/m^2 over 46 hrs) Q2W during a 6-week course (total of 8 courses until disease progression [PD]). The primary endpoint was the incidence of gr 3/4 diarrhea and secondary endpoints included tumor response, PFS, and OS. Tumor response (RECIST) was evaluated every 6 weeks and confirmed no less than 4 weeks after response criteria were first met. Safety and long term follow-up survival data were collected.
Results: Part 2 enrolled 24 pts: 14 (58%) pts were men; mean (SD) age was 60.7 (15.0) years; 22 (92%) had colon cancer and 2 (8%) had rectal cancer. Four (17%) pts had prior adjuvant therapy. Of 19 (79%) pts with diarrhea (all cases), 6 (25%) were gr 3 and none were gr 4. All 19 pts received antidiarrheal medication (1 pt with gr 3 diarrhea discontinued txt). Of 24 (100%) pts with any txt-related skin toxicity, 3 (13%) events were gr 3 (none gr 4). Other txt-related adverse events were fatigue 10 (42%), nausea 8 (33%), anorexia 4 (17%), constipation 4 (17%), and hypomagnesemia 4 (17%). Eight (33%) pts had a partial response, 11 (46%) had stable disease, and 3 (13%) had PD; 2 (8%) pts did not have an evaluable response. PFS (K-M median [95% CI]) was 10.9 (6.0, not estimable) months. There were no cases of anaphylaxis and no cases of panitumumab-induced human anti-human antibodies (n = 11 with both baseline and follow-up samples).
Conclusion: From this small study, panitumumab in combination with FOLFIRI as first line therapy appears to be well tolerated. These findings warrant further investigation in a larger trial.

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Correlations of telomere length, telomerase activity and TRF1 expression in colorectal cancer: prognostic indications

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Background: Telomere maintenance has been proposed as an essential step for cancer cell immortalization. Our aim, in this work, was to investigate mechanisms implicated in telomere length in colorectal cancer (CRC), and evaluate the prognostic impact of telomere status.
Patients and Methods: Ninety-one colorectal adenocarcinomas obtained from patients who underwent surgery were analyzed in order to investigate factors related to telomere function. Thus, we studied telomerase activity, terminal restriction fragment (TRF) length, and telomeric-repeat binding factor (TRF1) expression. Moreover, we analyzed prognostic implications for these factors.
Results: Most of tumors (81.3%) displayed telomerase activity. Overall, telomeres in CRCs were significantly shorter compared to normal adjacent specimens (P = 0.02). Moreover, tumors showing shortened telomeres displayed higher TRF1 levels than those without telomere shortening. In relation to prognosis, we observed a significant poor clinical evolution in the group of patients with tumors showing longer telomeres (P = 0.02), this fact emerging as an independent prognostic factor by the Cox proportional hazards model (P = 0.04, RR = 6.48). In the group of cancers classified as telomerase positive, telomere length ratios T/N ⩽0.66 or TRF1 overexpression conferred a favourable outcome (P = 0.03 and P = 0.05, respectively).
Conclusions: Most of CRCs display telomerase reactivation. However, only the group of cancers displaying telomere elongation confers poor prognosis. Conversely, colorectal tumors overexpressing TRF1 showed telomere shortening, with the final outcome of better clinical evolution.

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Laparoscopic surgical treatment of colorectal cancer: monoinstitutional experience on 599 patients

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Backgrund: To analyze the results of laparoscopic colorectal surgery for cancer on perioperative and medium-term outcome.
Methods: 599 consecutive unselected patients who underwent laparoscopic colon or rectal resection between January 1998 and December 2004 in a single Institution were prospectively evaluated. Tumor classification was by TNM stage. Patients were monitored for postoperative complications for 30 days after surgery. Follow-up was done by direct patient contact. Kaplan-Meier curves were used to estimate overall survival.
Results: Mean (SD) age was 65.8 (11.7) years. Mean (SD) ASA score was 2.0 (0.5). The following operations were performed: 248 left colectomies, 131 right colectomies, 26 sigmoid resections, 164 rectal resections, 21 abdominoperineal resections and 9 total colectomies. Conversion rate was 7.2% (43/599 pts). The overall morbidity rate was 24% (143/599 pts). The mortality rate was 0.3% (2/599 pts). Clinically evident anastomotic leak occurred in 45/599 (7.5%) patients. Re-operation rate was 4.5% (27/599 pts). Mean (SD) length of stay was 9.9 (5.8) days. The mean number (SD) of lymph-nodes intraoperatively collected was 16.7 (9.8). Tumor distribution was as follow: Stage 0: 25/599 (4.1%) patients; Stage I: 137/599 (22.9%) patients, Stage II: 190/599 (31.7%) patients, Stage III: 194/599 (32.4%) patients, Stage IV: 53/599 (8.8%) patients. Median (range) time of follow up was 20.2 (6–68) months. A port-site metastasis occurred in 1 patient at 18 months after surgery. The overall 5-years survival rate was 81%. Local recurrence rate in patients who underwent TME of the rectum was 4.4%
Conclusion: Laparoscopic colectomies are safe and oncological effective in the treatment of colon and rectal cancer.