presented with colorectal cancer. Both presented at 26 and 48 months respectively post-appendicitis following an initially normal colonoscopy.
Conclusions: Despite anecdotal evidence, the results of this study fail to show that appendicitis in older patients is a useful predictor of colorectal cancer. This study shows no evidence to support the need for large bowel investigation in patients aged over 50 with acute appendicitis.

649 POSTER

Erlotinib as single agent in 2nd and 3rd line treatment in patients with metastatic colorectal cancer. Results of a two-cohort multicenter phase II trial

N. Niederle[1], P. Freier[2], R. Porschen[3], D. Arnold[4], F. Lordick[5], T. Hoehler[6], S. Kubicka[7], E. Kettner[8], U. Keilholz[9], H.-J. Schmoll[4]. [1]*Klinikum Leverkusen, Medizinische Klinik 3, Leverkusen, Germany;* [2]*Private Practice, Hildesheim, Germany;* [3]*Klinikum Ost, Bremen, Germany;* [4]*Universitaetsklinikum, Martin Luther Universitaet, Halle/Saale, Germany;* [5]*Universitaetsklinikum, Technische Universitaet, Munich, Germany;* [6]*Prosper-Hospital, Recklinghausen, Germany;* [7]*Medizinische Hochschule, Hannover, Germany;* [8]*Klinikum, Magdeburg, Germany;* [9]*Charité, Campus Benjamin Franklin, Berlin, Germany*

Background: Erlotinib (E, TarcevaTM) is a small molecule tyrosine kinase inhibitor (TKI) targeted against the ErbB1 (EGFR) TK receptor. EGFR-directed antibody treatment has shown efficacy in colorectal cancer, and E and other TKIs have demonstrated clinical activity as single agent in pretreated patients with NSCLC. This trial was conducted to evaluate the efficacy of E as single agent in patients with metastatic colorectal cancer (mCRC).
Methods: Patients (pts.) with mCRC must have previously received either one (cohort 1) or two (cohort 2) 5FU-based chemotherapy regimens, including either irinotecan and/or oxaliplatin. Pts. were treated with E (150 mg/day orally) until disease progression with biweekly toxicity evaluations and 8-weekly tumour assessment.
Results: From Oct 03 to Dec 04, a total of 51 pts. were included, 23 in cohort 1, and 28 in cohort 2, respectively. Median age was 67 years [46–83], median ECOG PS was 1 [0–2]. The treatment was generally very well tolerated without appearance of treatment-related grade 4 toxicity and low rates of treatment-related grade 3 toxicities (detailed information for 39 pts available): diarrhoea 18%, nausea 8%, mucositis 5%, hepatobiliary, muscular and fatigue 1 pt. each. Skin rash was observed in 62% of pts. with grade 3 in 13%.
46 of 51 pts. (5 pending) are available for efficacy analysis so far: PR 4% (2 pts. in cohort 1), SD 28%, resulting in a clinical benefit rate (PR and SD for min. 8 weeks) of 32% with no differences between cohort 1 and 2 respectively. Median duration for disease control (7 pts. ongoing) was 30+ and 32+ [range 7–38+] weeks for both cohorts.
Conclusion: As reported in NSCLC, disease stabilisation can be achieved with E monotherapy in a relevant proportion of pts. No difference between 2nd and 3rd line cohort was observed. Importantly, for the first time in mCRC, partial responses were achieved with a small molecule TKI. Final data including progression free and overall survival will be presented.

650 POSTER

Patterns of failure after TME and neoadjuvant/adjuvant therapy including IORT to the presacral space in patients with locally advanced rectal cancer

J. Dinkel[1], F. Roeder[1], R. Krempien[1], S. Oertel[1], H. Garcia-Schueler[1], M. Eble[2], M. Buechler[3], J. Debus[1], M. Treiber[1]. [1]*University of Heidelberg, Radiooncology, Heidelberg, Germany;* [2]*University of Aachen, Radiooncology, Aachen, Germany;* [3]*University of Heidelberg, Surgery, Heidelberg, Germany*

Purpose: Changes in surgical technique (total mesorectal excision, TME) have effectively decreased local recurrence rates in locally advanced rectal carcinoma, however a benefit from pre- or postoperative radio- or radiochemotherapy (RCHT) further exists. The effectiveness of additional IORT has been shown in locally advanced rectal cancer after conservative resection but not yet after TME. We therefore reevaluated our patients treated with radiochemotherapy including intraoperative electron boost (IORT) with special regard to the site of recurrence in order to appraise the effectiveness of intraoperative target definition after TME.
Patients and methods: We analyzed the outcome of 176 patients with rectal cancer (stage I: 10%, stage II: 31%, stage III: 50%, stage IV: 9%) treated with IORT after TME (R0: 161, R+: 15) and pre- or postoperative radiochemotherapy. 151 patients received pre- or postoperative radiotherapy (EBRT) with a median dose of 41.4 Gy. In 135 patients concurrent 5-FU based chemotherapy was administered.
Results: Local failure was observed in 16 patients (9.1%) who did not differ in age or gender from the overall treated group. Incidence of local recurrence positively correlated with tumor stage (stage I: 6%, stage II: 4%, stage III: 10%, stage IV: 24%) and surgical margin involvement (R0: 7%, R+: 27%). Preoperative treatment decreased local failure rate to 5% compared to 10% after postoperative treatment. Local recurrence rate was increased in patients with T4 stage, positive lymph nodes, tumor localisation in the lower third or high grading. Seven patients developed local failure within the presacral space, resulting in a local control rate of 96% inside the IORT fields. Considering EBRT fields, another 6 in-field recurrences were seen: retrovesical (3), in front of the promontorium (2), and anastomosis (1), resulting in a local control of 92.7% inside the EBRT fields.
Conclusion: IORT as part of additional therapy after TME is a highly effective regimen to prevent local failure especially in combination with preoperative RCHT, but despite this the presacral space remains the site of highest risk for local recurrence. Stage III/IV disease, T4-situation, positive lymph nodes, localisation in the lower third, high grading, and incomplete resection seem to predict an increased risk for local failure.

651 POSTER

Continent colostomy, a new technique

T. Fady Youssef[1], N. Nazem Shams[1], N. Nabil Gad el-Hak[2]. [1]*Mansoura University Oncology Center, Surgical Oncology, Mansoura, Egypt;* [2]*Mansoura Univ Gastroenterology Center, Surgery, Mansoura, Egypt*

Introduction: Abdomino-perineal resection still remains the best oncologically safe operation for carcinoma of the lower third of the rectum. Use of dynamic myoplasty to create a continent stoma has produced promising results. The aim of the study was to establish and test a new model. This new technique was studied on animals and produced promising results.
Patients and methods: Twenty patients with carcinoma of the lower third of the rectum who underwent abdomino-perineal resection were randomized into a control group 10 patients who underwent colostomy by the classical transrectal technique and 10 patients underwent this new technique in which the rectus abdominis muscle was used for wrapping the distal end of the colon in a 270 degrees and fixing the muscle to the anterior rectus sheath, the resulting defect was closed by using a prosthetic mesh.
The two groups were compared in terms of continence degree and the need to wear colostomy appliance during the day time also they were compared using manometric studied. MRI and defecography.
Results: Use of a distal rectus muscle sling surrounding the stoma by 270 degrees achieved a continent colostomy for solid stool in 13 patients. 1 case had post operative mesh infection necessitating removal of the mesh the mean squeeze pressure was double its value for the rectus abdominis sling group compared to the transrectal group.
Discussion: Use of dynamic myoplasty to create a continent stoma has produced early promising results, but long-term stoma continence still waiting for more evaluation and long term follow up of those patients. In contrast to continent perineal colostomy cont abdominal colostomy is associated with minimal complications.

652 POSTER

Treatment of advanced upper gastrointestinal adenocarcinoma with Capecitabine and concurrent radiation therapy: preliminary experience of the San Antonio Cancer Institute

M. Joyner[1], C. Fuller[1], A. Wong[1], A. Siddiqi[1], C.R.J. Thomas[1], J. Dorman[2], M. Fuss[1]. [1]*University of Texas Health Science Center at San A, Radiation Oncology, San Antonio, Texas, USA;* [2]*Audie Murphy South Texas VA Medical Center, GI Cancer Program, San Antonio, Texas, USA*

Purpose: Assessment of the pathologic response rate and toxicity associated with neoadjuvant chemoradiotherapy Capecitabine (Xeloda) and IMRT in patients with upper gastrointestinal malignancies.
Methods: 16 patients (age 47–86 yrs, median 62; 13 male, 3 female) were treated between 12/03 and 10/04. All patients underwent biopsy with 15/16 (94%) histology confirmed adenocarcinoma and 1 neuroendocrine pancreatic tumor. Disease sites in the study were: pancreas (10), cholangiocarcinoma (3), esophageal (1), colon (1), and gastric (1). Tumor stages were T3 (12/16) or T4 (4/16). Radiotherapy was delivered using serial tomotherapeutic IMRT in 12 pts and conformal RT in 4/16. Mean PTV dose was 54 Gy (range 45–58) delivered at 1.8 to 2.0 Gy per fraction. All patients received concurrent chemotherapy Xeloda 825 mg/m^2 on a bid schedule, including 14/15 pts at 1500 mg BID and 1/15 at 2000 mg BID. Two patients required a decrease from 1500 mg to 1000 mg BID secondary to hand–foot syndrome and GI complications. To reduce hand–foot syndromes 13/16 pts were also treated with vitamin B6 at either 50 mg (6/13 – 46%) or 100 mg (7/13 – 54%) TID scheduled dosing.

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.

653 POSTER

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

J. Berlin[1], J. Posey[2], S. Tchekmedyian[3], E. Hu[4], D. Chan[5], I. Malik[6], L. Yang[7], M. MacDonald[7], S. Jerian[7], R. Hecht[8]. *[1]Vanderbilt University Medical Center, Nashville, Tennesse, USA; [2]University of Alabama Comprehensive Cancer Center, Birmingham, Alabama, USA; [3]Pacific Shores Medical Center, Long Beach, California, USA; [4]Central Hematology/Oncology Medical Group, Monterey Park, California, USA; [5]Cancer Care Associates Medical Group, Inc., Redondo Beach, California, USA; [6]Loma Linda University Cancer Institute, Loma Linda, California, USA; [7]Amgen Inc., Thousand Oaks, California, USA; [8]UCLA School of Medicine, Los Angeles, CA, USA*

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.

654 POSTER

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

C. García-Aranda[1], C. Frías[1], C. de Juan[1], A. Díaz-López[1], F.J. Rodriguez-Jiménez[1], A. Sánchez-Pernaute[2], A.J. Torres[2], E. Díaz-Rubio[3], P. Iniesta[1], M. Benito[1]. *[1]Facultad de Farmacia. Universidad Complutense, Dpto. Bioquímica y Biología Molecular II, Madrid, Spain; [2]Hospital Clínico San Carlos, Servicio de Cirugía, Madrid, Spain; [3]Hospital Clínico San Carlos, Servicio de Oncología, Madrid, Spain*

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.

655 POSTER

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

S. Di Palo, A. Tamburini, A. Vignali, E. Orsenigo, C. Staudacher. *Vita-Salute San Raffaele University, Department of Surgery, Milan, Italy*

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.