good side-effect profile, has been used to take further the ongoing phase II trial.
Support to partially fund the trial was provided by BMS.

669 PUBLICATION

Capecitabine and oxaliplatin (XELOX) as first-line treatment for elderly patients (pts) with advanced / metastatic colorectal cancer (MCRC)

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Background: XELOX is a highly active combination in 1st line MCRC, comparable to FOLFOX with less neutropenia and a convenient 3-weekly cycle length. As a well-tolerated, more home-based therapy, XELOX deserves investigation in a more elderly pt population.
Material and methods: Objectives of this phase II study were response rate, safety profile, time to progression and overall survival after XELOX chemotherapy as 1st line treatment in pts aged $\geqslant$70 years with histological confirmation of MCRC. Selection criteria included no prior chemotherapy (except adjuvant therapy), measurable disease according to RECIST, ECOG PS $\leqslant$2 and adequate bone marrow, renal and hepatic function. Patients received oxaliplatin 130 mg/m^2 i.v. D1 followed by oral capecitabine 1000 mg/m^2 twice daily for 14 days (750 mg/m^2 if Cr Cl=30–50 ml/min) every 3 weeks. Toxicity was evaluated according to WHO toxicity criteria.
Results: 50 pts were included: M/F, 36/14, median age 75 years (70–82), ECOG PS 0/1: 54%/46%. 40% of patients presented comorbid disease $\geqslant$1, 74% had mild dependence on help (Barthel Index) and most (M/F 58%/50%) were autonomous (Lawton Index). Median number of metastatic sites was 1 (1 site 78.7%), liver (68.1%), lung (34%) and nodes (12.8%), mainly. Previous treatment included surgery (84%), adjuvant chemotherapy (30%) and radiotherapy (12%). A total of 227 cycles have been administered: median 4.5 (1–8). Median relative dose intensity was 92% for oxaliplatin and 98%/86% (in pts with Cr Cl $\leqslant$50 / Cr Cl >50 ml/min, respectively) for capecitabine. Intent-to-treat efficacy analysis: 5 pts achieved CR, 13 PR, 12 SD, 14 PD and 6 NE (3 toxicity, 1 exitus, 1 lost of follow-up, 1 consent withdrawal), with an ORR of 36% (95% CI: 22.7–49.3). Median follow-up was 10.7 months, median TTP was 5.8 months (95% CI: 3.9–7.8) and median OS was 12.3 months (95% CI: 7.6–16.9). One year survival was 51% (95% CI: 37.0–65.0). There were 1 treatment-related death due to diarrhea and asthenia.
Conclusions: XELOX appears to be effective and well tolerated in 1st line treatment of elderly pts with MCRC.

Grade 3–4 Adverse Events per patient (%)

Diarrhea	22	Febrile neutropenia	2
Asthenia	14	Leukopenia	2
Vomiting	14	Fever	2
Nausea	10	Stomatitis	2
Anorexia	8	Paresthesia	2
Neutropenia	6	Anaemia	2
Thrombocytopenia	6	Abdominal pain	2
Hand–foot syndrome	4	Melaenas	2

670 PUBLICATION

Hepatic arterial infusion (HAI) oxaliplatin and intravenous (i.v.) LV5FU2 after resection of colorectal liver metastases

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Background: There is no consensus regarding adjuvant therapy after resection of colorectal liver metastases (LM). The promising response rate of 64% obtained with HAI oxaliplatin and i.v. 5-fluorouracil (5FU) and leucovorin (LV) in patients with unresectable LM (1) prompted us to assess the tolerance and efficacy of this regimen in the postoperative adjuvant setting.
Methods: An HAI catheter was inserted intra-operatively during resection of colorectal LM in patients (pts) at high risk of recurrence (2). All pts had undergone resection of the primary tumor. Adjuvant treatment consisted of HAI oxaliplatin (100 mg/m^2) plus simplified i.v. LV5FU2 (LV, 200 mg/m^2; 5FU, bolus 400 mg/m^2; 5FU, 2400 mg/m^2 48-hour continuous infusion) and was repeated twice monthly for 4 to 6 months. The endpoints were toxicity and survival.
Results: 24 pts (9 men; median age, 54 years; range, 30–68), of whom 21 (88%) had previously received systemic chemotherapy including oxaliplatin or CPT-11, were included. Intra-operative radiofrequency ablation treatment was performed in 14 pts; LM resection was R0 in 21 and R1 in 3 pts. Adjuvant chemotherapy was possible in 19 pts (79%; median number of chemotherapy cycles, 8; range, 3–12). Five pts (21%) did not receive the treatment due to HAI catheter dysfunction (n = 4) or postoperative sepsis (n = 1). Treatment was discontinued due to HAI catheter obstruction or toxicity in one pt each. Grade 3/4 neutropenia or peripheral neuropathy occurred in 26% and 10% of pts, respectively. There were no treatment-related deaths. The 1- and 3-year overall survival rates were 88% and 44%, respectively. The 1- and 3-year extrahepatic recurrence-free survival rates were 66% and 31%, respectively. The 1- and 3-year intrahepatic recurrence-free survival rates were 83% and 66%, respectively.
Conclusion: HAI oxaliplatin and i.v. LV5FU2 is an effective and safe regimen after resection of colorectal LM. Given the low intrahepatic recurrence rate, HAI oxaliplatin should be evaluated in association with more aggressive i.v. chemotherapy in pts at high risk of recurrence.

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671 PUBLICATION

Radiation therapy (RT) with concomitant capecitabine and celecoxib followed by surgery in patients with locally advanced cancer of the rectum: A phase II study

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Background: Preoperative chemo-RT may increase the rate of complete resections (R0) in the treatment of locally advanced rectal cancer. We evaluated the efficacy and safety of preoperative chemo-RT consisting of continuous per oral capecitabine and celecoxib given concomitantly with RT in patients with fixed/locally advanced rectal cancer.
Methods: Patients with fixed or cT4N0–2M0 rectal cancer were eligible. Pretreatment pelvic MRI and/or CT were performed for staging. RT was given using a 3-field technique up to the total dose of 45 Gy/25 fractions, followed by a boost to 9 Gy/5 fractions. Capecitabine 825 mg/m^2 p.o. bid and celecoxib 400 mg p.o. bid were initiated on d. 1 of RT, and capecitabine was discontinued on the last day of RT. Celecoxib was continued until surgery, scheduled to take place 6 weeks after completion of RT. Toxicity was graded according to the NCI CTCAEv3.0 scale. The primary endpoint was pathologic complete response (pCR).
Results: Between January 2003 and May 2005 17 consecutive patients (14 male, 3 female; mean age 56 years, range 40–72 years; WHO PS 0–2) were enrolled. Fourteen patients are evaluable for pCR and toxicity during chemo-RT (Table 1). Two patients had tumour-related abscess requiring drainage (grade 3), one of these patients had a rectoanal fistula and the other one tumour growth to the seminal vesicles prior to therapy.
All patients responded to therapy and surgery could be attempted in all cases. Three (21%) patients had pCR (95% CI 5–50%), and one further

patient had only microscopic tumour residue (0.3 mm) at surgery. The surgical margins were histologically positive in only 2 (14%) patients.

Table 1.

Grade (%)	Anemia	Leukopenia	Thrombo-cytopenia	Elevated bilirubin	Infection	Hand–foot syndrome	Diarrhoea
1	8 (57)	0	3 (21)	1 (7)	3 (21)	2 (14)	7 (50)
2	2 (14)	4 (28)	0	1 (7)	0	2 (14)	3 (21)
3	0	1 (7)	0	0	2 (14)	2 (14)	0

Conclusions: Capecitabine and celecoxib are generally well tolerated when given during RT. The regimen allows subsequent surgery in the majority of patients with locally advanced rectal cancer. The pCR rate of 21% is encouraging given the large initial size of the tumours. A randomised study comparing capecitabine with 5-FU based regimens is warranted.

672 PUBLICATION

Age demographics from a rectal bleeding clinic support the adenoma-carcinoma sequence

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Background: The adenoma-carcinoma sequence postulates the development of malignancy from polyps, with Morson estimating that this sequence took approximately 10 years. Much of the evidence supporting this theory however, although strong, is circumstantial. The aim of the study is to analyse data from a rectal bleeding clinic for evidence supporting the time interval of the adenoma-carcinoma sequence.
Material & methods: All patients referred to the rectal bleeding clinic over a seven year period were entered into a database. All were assessed by detailed history, clinical examination and flexible sigmoidoscopy. Those with neoplastic lesions (adenoma or carcinoma) diagnosed on flexible sigmoidoscopy underwent subsequent colonoscopy. The final definitive histology of each patient was confirmed by cross-checking with the Histology Department database.
Results: A total of 2175 patients attended the rectal bleeding clinic from November 1997 to Aug 2004, with 230 (10.6%) being found to have significant neoplastic lesions as follows:

Histology	N	Mean Age
Adenoma – Low grade dysplasia	120	62
Adenoma – High grade dysplasia	18	66
Carcinoma	92	69

The subsequent histological staging of the carcinomata is shown below:

Duke's stage	N
A	41 (45%)
B	29 (29%)
C	17 (19%)
D	4 (4%)
X	3 (3%)

Conclusions: Analysis of age-related diagnoses from a rectal bleeding clinic supports the time interval of the so-called adenoma-carcinoma sequence

673 PUBLICATION

Role of neoadjuvant chemotherapy and total mesorectal excision (TME) in local advanced cancer of distal rectum

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Background: Evaluate the impact of neoadjuvant treatment and laparoscopic Total Mesocrectal Excision (TME) in local advanced rectal cancer patients on toxicity, sphincter saving surgery, complications rate and local recurrence
Methods: Between January 1998 and December 2004 110 consecutive unselected patients (69 males and 41 females) mean age 64 (18–83) with locally advanced adenocarcinoma (eT2-eT3 eN+) of distal rectum were treated with preoperative chemoradiation. Mean distance of the anal verge was 6.2 cm (range 2–10). Pretreatment choendoscopic stage (EURS TNM) was T2 in 11 patients, T3 in 84 patients and T4 in 15 patients. Nodal echoendoscopic stage was N0 in 38 and N+ in 72 patients. Oxaliplatin 100 mg/m^2 was administered every 2 weeks for 3 courses plus continous infusion of 5-FU 200 mg/m^2/die for 6 consecutive weeks; concomitant hyperfractioned radiotherapy at a total dose of 45 Gy (1.25 Gy twice a day for 5 days every week with a 4 field box technique, with 6–18 MeV photons). Surgery was performed 4–6 weeks after treatment. Echoendoscopy and pelvic MRI were repeated just before surgery to establish the clinical response.
Results: Neoadjuvant treatment was well tolerated: there was no grade 4 toxicity (NCI-CTC scale), The post treatment EURS TNM was T0 in 18, Tis in 3, T1 in 11, T2 in 29, T3 in 49. All patients underwent radical resection, 107 laparoscopic low anterior resection with TME and 3 abdominal perianal resection. Medial distal margin was 2 cm. No patients died in the postoperative period. Postoperative complications were observed in 25% of patients. Anastomotic leak occurred in 9.4%. Pathological complete response occurred in 20% of patients (22/110), in 37% we had a partial response and in 43% (47/110) no response. The median follow up was 20 months. The local recurrence rate was 3%.
Conclusion: This short preoperative chemoradiation regimen associated with TME in associated with a high rate of downstaging. The sphincter preserving rate was excellent without increase of complications and local recurrence rate.

674 PUBLICATION

Short outcome and quality of life of laparoscopic and open TME

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Background: To compare laparoscopic total mesorectal excision (TME) and open TME or cancer of the rectum on perioperative outcome and quality of life (QOL).
Methods: 138 consecutive unselected patients who underwent laparoscopic or conventional TME in a 6-year (1998–2004) period, in a single institution were prospectively evaluated. Tumor classification was by TNM staging. Patients were monitored for postoperative complications for 30 days after surgery. Quality of life was evaluated using a modified version of SF 36 before surgery and at 1 year following operation.
Results. There were 74 patients in the laparoscopic group (LPS) and 64 in open. The two groups were homogeneous with respect to age, demographics, co-morbidities on admission (ASA), distance of the tumor from anal verge, number of patients who underwent preoperative radio-chemotherapy and QOL baseline values. Laparoscopic TME was successfully completed in 67/74 patients. Conversion rate was 9.4%. Converted patients remained in the LPS group used an intent to treat analysis. In LPS group, operating time was significantly longer ($p = 0.03$). No difference was observed between the two groups with respect to intraoperative blood loss ($p = 0.22$), blood transfusion rate ($p = 0.66$) and amount of perioperative transfused blood ($p = 0.58$). Tumor stage as were the number of lymph-nodes intraoperatively collected were similar in the two groups. The overall morbidity rate was 25.6% (19/74 pts) in LPS and 21.8% (14/64 pts) in open ($p = 0.39$). No patient died in the postoperative period in both groups. Anastomotic leak rate was 9.4% (7/74 pts) in LPS and 10.9% (7/64 pts) in open group ($p = 0.88$). Re-operation rate was 4.1% in open and 3.1% in LPS. Postoperative length of stay was shorter in LPS group ($p = 0.05$). All patients completed at least 1 year of follow-up. No port-site or surgical wound recurrences were found in both groups. The local recurrence rate was 4.4% in LPS and 4.6 in open. Patients in LPS scored an overall QOL of 89, while in open group the overall QOL score was 79.8 ($p = 0.60$).
Conclusions: laparoscopic TME is a safe option in cancer patients which does not jeopardize complication rate and QOL.