(TME) for rectal cancer. The feasibility and efficacy of laparoscopic TME has been proved by several reports but oncologic outcomes remains unclear. The aim of this study was to define the oncologic outcomes of laparoscopic TME.

Patients and Methods: This prospective nonrandomized longitudinal cohort study conducted from January 1998 to August 2006 regards patients with histologically proven adenocarcinoma of the middle and low rectum. Those staged as II and III underwent a long course preoperative radio chemotherapy. Oncologic outcomes measures of the laparoscopic group (LTME) were compared with a computerized, case-matched open resection group (OTME), the matching variables being age, gender and TNM stage. The follow up was conducted prospectively.

We analysed in both groups the radicality of resection (quality of mesorectum, Circumferential Resection Margin [CRM], length of resection margins and lymph node's sampling) the local recurrence rate and overall survival.

Results: The LTME group consisted in 188 patients (mean age 63.9 years) The OTME group 188 (mean age 64.48 years). Mean follow up was 39.4 months (range 3−93). The TNM stage distribution was Stage 0 (7.1%), Stage I (22.1%), Stage II (35.0%), Stage III (27.0%) Stage IV (8.2%) tumours for LTME and 5 Stage 0 (2.3%), 38 Stage I (20.1%), 50 Stage II (26.6%), 71 Stage III (38.1%) 24 Stage IV (12.9%) tumours for OTME. Thirty-day mortality was 0.6% for LTME and 0.9% for OTME ($p = 0.433$). Early and late complication incidences were comparable ($p = 0.952$). Quality of mesorectum ($p = 0.534$), negative CRM ($p = 0.732$) and R1-rate ($p = 0.36$) were the same in both groups. The mean lymph node's sampling was 14.35 ± 5.7 for LTME and 13.33 ± 7.3 for OTME ($p = 0.822$). Local recurrence were observed in 12 patients (6.3%) in LTME and in 14 patients (7.4%) in OTME ($p = 0.31$). The Kaplan-Meier statistical analysis performed confirmed that TNM stage for stage overall survival was similar in the LTME and OTME group (log rank $p = 0.956$).

Conclusion: Notwithstanding the drawbacks of a non randomised study our results are consistent in showing that laparoscopic TME could potentially offer all benefits of a minimally approach and achieve short and long term results that compare favourably with conventional rectal surgery.

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Final data from a large phase II trial of first-line bevacizumab plus classic or modified FOLFIRI in metastatic colorectal cancer (CRC)

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Background: Bevacizumab (Avastin®) significantly improves overall (OS) and progression-free (PFS) survival when combined with first-line irinotecan plus bolus 5-fluorouracil (5 FU) and leucovorin in patients with metastatic CRC. An ongoing, multicentre open-label trial is evaluating the efficacy and safety of first-line bevacizumab in combination with irinotecan and infusional 5-FU (FOLFIRI).

Methods: Eligibility criteria: metastatic CRC; no surgery within 28 days; ECOG PS 0/1, adequate organ function; no CNS metastases. Chemotherapy: a minimum of 6 two-weekly cycles of FOLFIRI; variations (modified FOLFIRI [mFOLFIRI], weekly regimen) were allowed. Bevacizumab 5 mg/kg was given on day 1 with chemotherapy, and then every 2 weeks until disease progression. The primary objective was PFS; secondary objectives included safety, overall response rate (ORR), duration of response (DOR) and OS.

Results: A total of 209 patients were enrolled at 31 centres between April 2005 and November 2005. Median patient age was 61.9 years (range 31–82) and 60% were male. Median followup was 13.3 (0.8−20.1) months. Median duration of treatment with bevacizumab was 9.2 months and approximately 6.5 months with FOLFIRI. 22% of patients discontinued study treatment for toxicity; 18% from chemotherapy discontinuation alone. The most common bevacizumab-associated adverse events were epistaxis (38%; grade $\geqslant$3, <1%), hypertension (26%; grade $\geqslant$3, 3.8%) and venous thromboembolic events (26%; grade $\geqslant$3, 19.6%). 78% of all patients had a dose modification; 63% interruption of bevacizumab (major reasons: neutropenia [30%], diarrhoea [5%], hypertension [5%]), 76% had modification of FOLFIRI (major reasons: neutropenia [41%], diarrhoea [13%], mucositis [7%], febrile neutropenia [5%]). Sixty (29%) deaths have been reported, the majority associated with progressive disease. Efficacy data are comparable with previous first-line bevacizumab studies (Table).

Conclusions: The safety profile of bevacizumab plus FOLFIRI is similar to that of bevacizumab and other chemotherapy combinations. Efficacy data indicate a promising benefit with regard to response rate and PFS. Bevacizumab plus FOLFIRI represents a safe and effective first-line therapy option for patients with metastatic CRC.

	Overall (n = 209)	Bevacizumab + FOLFIRI (n = 156)	Bevacizumab + mFOLFIRI (n = 53)
Median PFS, months	11.07	11.30	9.99
DOR, months	8.54	9.00	8.34
ORR, %			
CR	3.3	3.2	3.8
PR	49.8	50.0	49.1
SD	32.5	31.4	35.8
PD	7.2	7.1	7.5
Missing	7.2	8.3	3.8

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Phase I/II study of novel oral fluoropyrimidine S-1 in combination with oxaliplatin (SOX) as first-line chemotherapy for metastatic colorectal cancer (mCRC)

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Background: An oral fluoropyrimidine, S-1 showed high activity for untreated mCRC with a response rate of 35%. It has shown good tolerability with the convenience of an oral administration schedule, which warranted further investigations particularly in combination with oxaliplatin (L-OHP) as an alternative to 5-FU and L-OHP (FOLFOX). The objectives of this study were to determine the maximum tolerated dose (MTD) and the recommended dose (RD) of SOX, and evaluate the efficacy and safety of SOX as first-line chemotherapy for mCRC.

Material and Methods: The inclusion criteria included histologically proven colorectal cancer with unresectable lesions, ECOG Performance Status (PS) of 0 or 1, patients (pts) aged 20 to 74 years with measurable lesions, adequate organ functions, and no prior history of chemotherapy. The chemotherapy consisted of a 2-hour infusion of L-OHP at escalating doses of 100 mg/m^2 (level 1) and 130 mg/m^2 (level 2) on day 1, and S-1 twice daily on days 1−14 at a dose of 80 mg/m^2/day, repeated every three weeks.

Results: A total of 32 pts were enrolled in the study between March 2005 and June 2006. Twenty three pts were male (72%) and the median age was 57 (range, 34−71) years. Twenty nine pts had an ECOG PS of 0. Median of 6 courses was administered (range, 2−11). Although a total of 9 pts were enrolled in phase I, no dose-limiting toxicities were observed and level 2 was determined as RD. A total of 29 pts received RD of L-OHP. Therefore, the median treatment courses actually administered were 6 (range, 2−11). Grade 3 and 4 major adverse reactions at RD were neutropenia (14%), thrombocytopenia (28%), and diarrhea (3%). Peripheral neuropathy was observed in all of 29 pts treated with RD, but none developed grade 3 peripheral neuropathy. Hand–foot syndrome was not observed. Pharmacokinetic profiles of L-OHP and S-1 were consistent with the data of both monotherapy studies reported previously. Two pts had complete responses and 13 had partial responses, hence the overall response rate was 54% (95% CI, 33.9−72.5) according to the RECIST. Two pts have continued to receive treatment with SOX for more than 11 courses. After a median follow-up time of 213 days, the median progression free survival was 189 days and median survival time has not yet been reached.

Conclusions: The SOX regimen demonstrated a promising activity with acceptable toxicity for the first-line treatment of mCRC, and the current data warrants further investigation.