Methods: From 16 May 2003 to 31 August 2004, 177/304 pts have been randomized to receive either XELOX (91 pts: X 1000 mg/m^2 bid d1–14, oxaliplatin 130 mg/m^2 d1, q3w, maximum 8 cycles) or FOLFOX-6 (86 pts: 5-FU 400 mg/m^2 i.v. bolus then 2400–3000 mg/m^2 46-hour infusion, LV 400 mg/m^2 2-hour infusion, oxaliplatin 100 mg/m^2 d1, q2w, maximum 12 cycles).
Results: Baseline pt demographics were comparable in the XELOX vs. FOLFOX-6 arms: M/F (60%/40% vs. 62%/38%); median age: 65 (range32–83) vs. 63 (45–84). 91% of pts in the XELOX and 93% in the FOLFOX-6 arms had ECOG PS 0–1. Other baseline characteristics were well balanced. To date a median of 6 XELOX cycles (range 1–8) and 11 FOLFOX-6 cycles (range 1–12) have been administered. It is important to note that 1 cycle of XELOX = 3 weeks and 1 cycle of FOLFOX-6 = 2 weeks. Clinical adverse events were acceptable and generally similar in the XELOX and FOLFOX-6 arms (see table). There was a similar rate of diarrhea, nausea, vomiting and fever in both groups. XELOX led to more hand–foot syndrome, but less neuropathy, asthenia, alopecia and stomatitis. There was a similar rate of grade 3/4 diarrhea, nausea, vomiting, fever and asthenia in both groups. XELOX led to less grade 3/4 paresthesia and neuropathy. One toxic death was reported in each arm. Pts receiving XELOX experienced less grade 3/4 neutropenia and more thrombocytopenia than those on FOLFOX-6.
Conclusions: These data show that XELOX and FOLFOX-6 are well tolerated in first-line MCRC. If the final results from this study confirm this preliminary analysis, XELOX offers benefits to the pt in terms of clinical safety. The planned enrollment of 304 pts is now complete and updated safety results will be reported at the meeting.

	% of pts with Adverse events (NCIC-CTC grade)			
	XELOX (n = 91)		FOLFOX-6 (n = 86)	
	1/2	3/4	1/2	3/4
Diarrhoea	47	9	45	7
Hand–foot syndrome	19	0	12	0
Nausea	54	2	62	2
Vomiting	36	3	36	1
Asthenia	31	9	54	7
Neuropathy	11	1	11	11
Paresthesia	63	3	65	14
Anaemia	13	2	19	5
Neutropenia	21	6	16	49
Thrombocytopenia	12	14	50	6

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CAPOX vs CAPIRI in combination with concomitant boost 3D-conformal radiotherapy in neoadjuvant treatment of locally advanced rectal cancer

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Background: Several randomised trials have demonstrated the role of preoperative chemo-radiotherapy in the treatment of local advanced rectal cancer to reduce the rate of local recurrence, but there is no agreement on the chemotherapy and radiotherapy schedule. The aim of this study is to compare the combination of oral Capecitabine with Oxaliplatin or Irinotecan (CPT-11) in association with high dose radiation therapy.
Patients and methods: Thirty-three patients (21 males/12 females, median age 59 years and ECOG-PS 0–1) with a histologically proved uT3–4 N-/+ or uT2 N+ rectal cancer entered the study, from January 2003 to December 2004. No patient showed systemic disease at the time of diagnosis. They were randomly assigned to receive Oxaliplatin 130 mg/m^2 on days 1, 22 and 43 (17 pts, CAPOX GROUP) or Irinotecan 180 mg/m^2 on days 1, 22 and 43 (16 pts, CAPIRI GROUP) in combination to Capecitabine 1250 mg/m^2 bid days 1–14 and then 825 mg/m^2 bid on days 22–55, concomitant with radiotherapy started on day 22. The radiotherapy was administered to the whole pelvis to a dose of 45 Gy (1.8 Gy/fraction), with a concomitant boost to the CTV to a dose of 9 Gy (1.5 Gy/fraction, during the last 6 days of treatment with a 6-hour inter-fraction interval): the total dose to the primary tumor was 54 Gy with a 3D-conformal technique. Surgery was carried out 6–8 weeks after the completion of chemo-radiation by the same surgical team.
Results: Among all treated patients, in one patient in CAPIRI GROUP the chemo-radiation treatment was discontinued for GI toxicity and the patient came out the study; the other 32 pts received 95% and 92% of the planned chemotherapy dose, respectively 17 pts in CAPOX GROUP and 15 CAPIRI GROUP. The dose-limiting toxicity was grade III-IV diarrhoea, occurring in 1 pt (CAPOX GROUP) and 3 pts (CAPIRI GROUP). Neurotoxicity was very limited, as only 5 patients experienced grade I toxicity in CAPOX GROUP. A clinical and pathological downstaging was detected in 12 pts (70%) in CAPOX GROUP and 11 pts (73%) in CAPIRI GROUP. A complete pathological remission was seen in 4 pts (23%) in CAPOX GROUP and 4 pts (26%) in CAPIRI GROUP. Twenty-three patients (72%) underwent sphincter-saving surgery, 12 (70%) in CAPOX GROUP and 11 (73%) in CAPIRI GROUP; nine patients were treated with Miles abdomino-perineal resection. All patients are alive after a median follow-up of 16 months (range 2–24 months), but 4 of them, equally distributed in the two groups, developed distant metastases.
Conclusions: both CAPOX and CAPIRI are feasible and effective, resulting in excellent results, comparable to those of best series of neoadjuvant treatment. CAPOX was better tolerated than CAPIRI, as diarrhoea was more frequently associated with Irinotecan infusion. Moreover, it was reported an increased radio-chemo induced-fibrosis in CAPIRI GROUP. Further studies are needed to assess the superiority of a particular treatment schedule.

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Distal clearance margin less than 9 mm: a safe margin in rectal cancer patients

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Background: Recent reports suggest that a distal clearance of 10 mm at the lower surgical margin may be considered adequate in the surgical treatment of rectal cancer.
Methods: We report the experience of the National Cancer Institute of Milano (Italy) in the treatment of low rectal cancer with the technique of total rectal and mesorectal resection (TRR) with coloendoanal anastomosis (CEAA). Between March 1990 and December 2002 we performed 557 consecutive TRR and CEAA at our Institute. 178 patients of this series with a minimum follow up of 18 months (mean 61 months) were treated for a primary cancer without preoperative chemoradiotherapy.
There were 94 patients with distal clearance margin (DCM) <9 mm and 84 with DCM >10 mm. Each group was stratificated by pathological stage and nodal status. The local recurrence subsets was stated. All B2 and C1–2 Astler Coller stage patients in this series received post operative chemo-radiotherapy.
Results: see table.
Conclusions: Our data suggest that the distal clearance margin of resection less than 9 mm eventually in combination with post operative chemo-radiotherapy do not affect local recurrence rate in N0 and N+ patients.

Table 1. Number of events by DCM group.

	DCM			
	Negative ⩾1 cm		Negative <1 cm	
	No.	%	No.	%
Total subjects	84	41.4	94	46.3
First event:				
Local relapse	6	7.1	7	7.5
Distant metastasis	*15	17.9	*21	22.3
Second malignancy	3	3.6	–	–
NED death	7	8.3	2	2.1
Deaths	28	33.3	16	17.0

DCM: Distal Clearance Margin; * One distant metastasis was concurrent with local relapse

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Phase I/II study of PTK/ZK, a novel, oral angiogenesis inhibitor in combination with FOLFIRI as first-line treatment for patients with metastatic colorectal cancer

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Background: Vascular endothelial growth factors (VEGFs) and VEGF receptors (VEGFRs) are important mediators of tumor growth and metastasis, and their expression is associated with poor prognosis in