grade 3 diarrhea; so this level was determined as MTD. Level 2 was set as RD. A Phase II study is now ongoing and 16 pts were assigned to level 2 up to now. Altogether, 22 patients (including 5 pts with prior CT and 12 pts with adjuvant CT) had received a total of 101 courses and were available for the evaluation of the results. CR was noted in 2 pts and PR in 12 pts, for a response rate of 64% (14/22). Grade 3 leucopenia occurred in 2 pts, G3 anemia in 1 pt, G3 diarrhea in 6 pts, G3 nausea in 5 pts, G3 vomiting in 4 pts. None suffered G4 toxicity.
Conclusion: It was suggested that a combination therapy of 24-hour continuous infusion of CPT-11 and sequential oral UFT/LV appeared to be well tolerated and shows high efficacy for MCRC.

	CPT-11 (mg/m^2/day)	UFT (mg/m^2/day)	LV (mg/body/day)
Level 1	100	233	75
Level 2	100	300	75
Level 3	110	300	75
Level 4	120	300	75

666 PUBLICATION

Anatomical segmentectomy (SGX) is the oncologic equivalent of hemi-hepatectomy (H-HPX) for the treatment of small volume unilobar colorectal liver metastases (CLM)

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Introduction: HPX is the only potentially curative treatment for CLM. As methods of detection of CLM and awareness of the benefits of HPX improve, smaller volume disease is being diagnosed increasingly. Historically, most patients underwent H-HPX, but the recent trend is towards more local resections towards increasing hepatic preservation. Furthermore, many patients with initially inoperable disease are now coming to HPX (often SGX) after successful downstaging with systemic chemotherapy. This trend raises questions of oncological benefit, whether this approach increases the risk of residual disease in the ipsilateral remnant liver. This study examines the site of liver only recurrence (LOR) with particular reference to ipsilateral-LOR after unilateral SGX.
Methods: Prospectively collected single centre 5-yr follow-up of 184 patients post-HPX for CLM. Data stratified for type of surgery, survival, LOR (ipsilateral, contralateral, bilateral).

Results

	No. pts	% Op. Mort.	Ipsilat LOR	Contra/Bilat LOR	5 year survival %
Unilat SGX	98	0	13	13	44
Bilat SGX	29	0	–	23	21
Hemi-HPX	27	3	–	15	34
Extended-H-HPX	31	3	–	19	26

5 patients underwent re-HPX for recurrent LOR after unilateral SGX. There were no re-HPX for LOR in any of the other groups.
Conclusions: 13/98 (13%) of LOR were ipsilateral, 29/98 (28%) were contra or bilateral after unilateral-SGX. Since 57/85 (67%) LOR were either contralateral or bilateral following either bilat-SGX or H-HPX, then these data would support the continuing use of unilateral SGX for small volume unilateral CLM.

667 PUBLICATION

Capecitabine and oxaliplatin (XELOX) in combination with bevacizumab in the treatment of metastatic colorectal cancer: results of a phase II trial

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Background: Bevacizumab (BV) improves survival when added to first-line (5-FU/LV and IFL) and second-line (FOLFOX) chemotherapy for metastatic colorectal cancer (mCRC). The FOLFOX regimen is superior to bolus IFL, but requires the use of an ambulatory infusion pump. Capecitabine, an oral fluoropyrimidine, is a convenient alternative to 5-FU. We designed a phase II trial to investigate the safety and efficacy of capecitabine and oxaliplatin in combination with BV (XeloxA).
Methods: Patients (pts) with untreated mCRC received oxaliplatin 85 mg/m^2 day 1, capecitabine 1000 mg/m^2 bid days 1–5 and 8–12, and BV 10 mg/kg day 1 of a 2-week cycle. The starting capecitabine dose was changed to 850 mg/m^2 bid due to toxicity in the first 27 pts. The primary endpoint was response rate. Safety was analysed for excess 60-day mortality (>15%) or grade 4 adverse events (>50%). Data were analysed using the intent to treat method.
Results: 30 pts have received therapy: 16 men, 14 women; median age 55.2 (range 24–76); all performance status 0. Grade 3 diarrhoea was seen in 30% of pts; no pt experienced grade 4 diarrhoea. Of 3 pts started at the 850 mg/m^2 bid capecitabine dose, none have experienced >grade 1 diarrhoea. Hand–foot syndrome (HFS) was seen in most pts; 6/30 (20%) with grade 1, 12/30 (40%) with grade 2 and 1/30 (3%) with grade 3 HFS. Other toxicities were minimal, including grade 3 neutropenia (7%), grade 3 nausea and vomiting (7%), and grade 3 peripheral neuropathy (10%). 20 pts (66%) required at least one capecitabine dose reduction, and 12/30 (40%) required 2 or more reductions during treatment, typically for diarrhoea and/or HFS. There were 16 partial responses and one complete response (RR 57%; 95% CI: 37–75%); 11 (37%) pts had stable disease. Median TTP was 11.9 months (95% CI: 9.8-∞).
Conclusions: The initial capecitabine dose used in this trial was decreased due to toxicity, primarily HFS and diarrhoea, and appears to be better tolerated. Preliminary evidence suggests that the XeloxA regimen is highly active. This is supported by response data from a randomised phase II trial [Hochster et al. J Clin Oncol 2005;23 (June 1 Suppl): Abstract 3515]. The reported median TTP is among the highest obtained in the first-line treatment of metastatic colorectal cancer. Insights into management of pts on long-term therapy will be reported. Enrollment continues to a planned accrual of 50 pts.

668 PUBLICATION

Concurrent irinotecan, oxaliplatin and uft/lv triple therapy as first-line treatment for advanced colorectal cancer (ACRC)

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An open label dose-finding study of concurrent irinotecan (Ir), oxaliplatin (Ox) and oral UFT/LV was conducted in patients (pts) with ACRC. The aim was to find a recommended dose while providing an efficacious treatment in a first-line setting, which was well tolerated by alternating the Ir with the Ox every 2 weeks. All pts received Ir (d1), Ox (d15) and UFT/LV on days 1 to 21 of a 28-day cycle. Using conventional dose escalation criteria, pts were treated in cohorts of 3 and in the absence of grade 3 toxicity (assessed at 1 month), pts were entered at the next dose level (DL). There was no intra-pt dose escalation.

	UFT (mg/m^2/day)	Ir (mg/m^2)	Ox (mg/m^2)
DL-1 (6 pts)	200	180	85
DL-2 (6 pts)	250	180	85
DL-3 (9 pts)	250	180	100
DL-4 (4 pts)	300	180	100

The intended duration of chemotherapy was 24 wks, with response evaluation every 8 wks. 25 pts, median age 63 (range 24 to 79) with WHO PS 0 to 2, were recruited between Feb 2004 to Apr 2005. All pts had measurable disease with a median of 4 marker lesions at baseline (range 1 to 10). At DL-4, 4/4 pts suffered multiple grade 2 toxicities and 3/4 a grade 3 toxicity. Diarrhoea, lethargy and vomiting were the dose-limiting toxicities (DLT). 3 pts were initially entered at DL-3 and a further 6 pts were then entered once the MTD had been reached. At this dose-level, 3/9 pts endured grade 2 toxicities and 1/9 a grade 3 toxicity. One pt (PS 2) who had extensive disease was admitted 5 days after the first dose of chemotherapy (DL-1), with neutropaenic sepsis which was thought to be highly atypical; a question of DPD deficiency was raised. A further pt, also at DL-1, who had demonstrated a PR by RECIST criteria, died from a cardiac event in the third month of treatment. He had no prior cardiac history and no symptoms of angina during the chemotherapy. At this time, 19 pts are evaluable for response giving an ORR of 68% and tumour control rate of 79% (PR- 13, SD- 2, PD- 4). The median duration of response has not been reached. One pt with residual lymph node disease, is awaiting XRT and another patient is awaiting a partial hepatectomy. 6 out of 25 patients have died and as yet the median OS has not been reached. We have established a MTD of Ir 180 mg/m^2 d1, Ox 100 mg/m^2 d15 and UFT/LV 250 mg/m^2/day d1–21 of a 28-day cycle. This combination, which provides a high response rate and a